REVIEW ARTICLE

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Chronic Dizziness

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ABSTRACT

PURPOSE OF REVIEW: Determining the etiology of disorders that manifest with chronic dizziness can seem a daunting task, but extracting some basic elements of the patient's history can reduce the differential diagnosis significantly. This includes determining initial triggers, timing of symptoms, associated features, and exacerbating factors. This article covers distinct causes of chronic dizziness including persistent postural perceptual dizziness, mal de débarquement syndrome, motion sickness and visually induced motion sickness, bilateral vestibulopathy, and persistent dizziness after mild concussion.

RECENT FINDINGS: To date, none of the disorders above has a cure but are considered chronic syndromes with fluctuations that are both innate and driven by environmental stressors. As such, the mainstay of therapy for chronic disorders of dizziness involves managing factors that exacerbate symptoms and adding vestibular rehabilitation or cognitive-behavioral therapy alone or in combination, as appropriate. These therapies are supplemented by serotonergic antidepressants that modulate sensory gating and reduce anxiety. Besides expectation management, ruling out concurrent disorders and recognizing behavioral and lifestyle factors that affect symptom severity are critical issues in reducing morbidity for each disorder.

SUMMARY: Many syndromes of chronic dizziness can be diagnosed by recognition of key features, although many symptoms overlap between these groups. Symptoms may be manageable and improve with time, but they are often incompletely relieved.

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UNLABELED USE OF PRODUCTS/INVESTIGATIONAL USE DISCLOSURE:
Dr Cha discusses the unlabeled/investigational use of selective serotonin reuptake inhibitors in the treatment of mal de débarquement syndrome and persistent postural perceptual dizziness.

INTRODUCTION

Patients who present with chronic dizziness can be clinically challenging because of the wide range of potential causes, but methodical determination of factors such as timing, triggers, associated symptoms, and the presence of any asymptomatic periods can quickly narrow the differential diagnosis. It is helpful to determine whether the patient has episodic dizziness with asymptomatic periods versus chronic constant symptoms with episodic exacerbations. This article discusses five major syndromes that cause chronic constant dizziness: persistent postural perceptual dizziness (PPPD), mal de débarquement syndrome, motion sickness and visually induced motion sickness, bilateral vestibulopathy, and persistent dizziness after mild concussion.

The terms *dizziness* and *vertigo* are used according to definitions outlined in the International Classification of Vestibular Disorders established by the Bárány

Society Classification Committee.[1] *Dizziness* and *vertigo* are nonhierarchical terms that are used distinctly to relate a person's subjective experience. Dizziness is defined as, "the sensation of disturbed or impaired spatial orientation without a false or distorted sense of motion," whereas vertigo is defined as, "the sensation of self-motion when no self-motion is occurring or the sensation of distorted self-motion during an otherwise normal head movement."[1] Dizziness and vertigo can and frequently do occur together, but being able to distinguish different components of the patient's experience can be helpful, especially because many of the most common disorders of dizziness do not involve any symptoms of vertigo.

KEY POINT

- **Persistent postural perceptual dizziness is a chronic disorder of postural instability that lasts at least 3 months but can have fluctuations that are both innate as well as driven by environmental stimuli such as passive or active motion and visual stimuli.**

PERSISTENT POSTURAL PERCEPTUAL DIZZINESS

This section reviews the clinical features, diagnostic criteria, causes, time course, and treatment for PPPD, a syndrome characterized by persistent postural instability and visually induced dizziness. It has become a major diagnostic entity that encompasses many triggers of chronic dizziness. PPPD and its precursors represented a shift away from thinking about vestibular disorders as involving only measurable damage to pathways along the peripheral or central vestibular system.

Clinical Syndrome

The term *PPPD* represented the culmination of efforts to bring previous designations such as chronic subjective dizziness, space and motion discomfort, and visual vertigo into a common diagnostic framework.[2] All of these disorders were originally described as entailing a combination of dizziness, postural instability, and discomfort in visually complex or motion-rich environments, although with differing degrees of emphasis in each. Of note, *visual vertigo* was a term referenced for historical purposes in the designation of PPPD.[3] After the presentation of the International Classification of Vestibular Disorders in 2009, the *visual vertigo* term was replaced by *visually induced dizziness* because the phenomenon is related to visually induced feelings of disorientation rather than an actual feeling of motion.[1] A closely related disorder, phobic postural vertigo was not included under PPPD because phobic postural vertigo was defined as including primary mood or anxiety diagnoses or obsessive-compulsive personality traits as inherent components.[4] In contrast, in PPPD, any mood or anxiety disorder or personality trait is considered a comorbid condition that may be a risk factor but not the primary driver of symptoms.

Criteria

Criteria for PPPD were established by the Bárány Society for International Classification of Vestibular Disorders in 2017 (TABLE 6-1).[2] Patients are diagnosed with PPPD when they experience a syndrome complex lasting at least 3 months that is characterized by dizziness, unsteadiness, or nonspinning vertigo that is present for most of the time and is worsened by being upright, by being in motion, or during exposure to visual motion or complex visual patterns. Significant distress or functional impairment must be present and caused by the associated symptoms. As is the case for all Bárány Society criteria, a diagnosis of PPPD requires that symptoms are not better accounted for by another disease or disorder. PPPD can, however, coexist with the disorder that initially triggered it. Because the triggering events for PPPD can be quite varied, patients

may initially present to a variety of physicians including primary care physicians, neurologists, psychiatrists, ophthalmologists, or otolaryngologists before ultimately being diagnosed with PPPD.

Causes

PPPD can be precipitated by severe homeostatic derangements such as psychological distress, a medical illness, or a neurologic or vestibular disorder. PPPD can develop after varied causes such as vestibular neuritis, concussion, autonomic dysfunction, and severe panic attacks; it is a diagnosis that is independent of the initial trigger. PPPD can be present with other vestibular disorders such as vestibular migraine, Ménière disease, vestibular neuritis, or benign paroxysmal positional vertigo (BPPV) but is diagnosed separately and in addition to those disorders (CASE 6-1). Even if the precipitating factor has resolved, PPPD can continue without an ongoing trigger. Thus, PPPD can be diagnosed as a sequela to or concurrently with vestibular, cardiac, autonomic, or other neurologic disorders as long as all of the symptom components of the diagnostic criteria are met.

Time Course

The time course for PPPD development can vary depending on the initial trigger, but PPPD generally develops in relation to an acute event rather than

TABLE 6-1 **Diagnostic Criteria for Persistent Postural Perceptual Dizziness[a]**

Persistent postural perceptual dizziness is a chronic vestibular disorder defined by criteria A through E below. All five criteria must be fulfilled to make the diagnosis.

- **A** One or more symptoms of dizziness, unsteadiness, or nonspinning vertigo are present on most days for 3 months or more.
  - **1** Symptoms last for prolonged (hours-long) periods of time but may wax and wane in severity.
  - **2** Symptoms need not be present continuously throughout the entire day.
- **B** Persistent symptoms occur without specific provocation but are exacerbated by three factors:
  - **1** Upright posture,
  - **2** Active or passive motion without regard to direction or position, and
  - **3** Exposure to moving visual stimuli or complex visual patterns.
- **C** The disorder is precipitated by conditions that cause vertigo, unsteadiness, dizziness, or problems with balance including acute, episodic, or chronic vestibular syndromes, other neurologic or medical illnesses, or psychological distress.
  - **1** When the precipitant is an acute or episodic condition, symptoms settle into the pattern of criterion A as the precipitant resolves, but they may occur intermittently at first, and then consolidate into a persistent course.
  - **2** When the precipitant is a chronic syndrome, symptoms may develop slowly at first and worsen gradually.
- **D** Symptoms cause significant distress or functional impairment.
- **E** Symptoms are not better accounted for by another disease or disorder.

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insidiously. The initial acute event can be of varied etiology (eg, after vestibular neuritis), or it can have an initial stuttering course if the trigger is episodic (eg, vestibular migraine). In all cases, PPPD is defined as the chronic state that develops after these initial triggers and typically does not include any asymptomatic periods. PPPD can be diagnosed without a known trigger, however, which is often the case in patients who have had prolonged symptoms and cannot remember the circumstances surrounding the symptom onset. However, a slowly progressive time course that does not have a clear onset should raise suspicion for another process, such as a neurodegenerative disorder.

CASE 6-1

A 36-year-old man experienced a bout of severe spinning vertigo and nausea with no hearing loss that lasted several days. He had recovered from a viral illness several weeks prior. He was seen in the emergency department and had a normal cranial nerve examination except for a positive head impulse test to the right side, signifying a right-sided vestibulopathy. He tended to veer to the right on gait examination. He was diagnosed with a right-sided vestibular neuritis and sent home with instructions to take meclizine as needed. The patient was able to ambulate in about 1 week and was able to return to work in 2 weeks. Despite continued recovery, at 3 months he was still experiencing a persistent sense of imbalance, head motion–induced nausea, unsteadiness, and a reduced ability to tolerate visually busy environments, particularly the grocery store. He developed agoraphobia and anticipatory anxiety going to social events and subsequently severely curtailed outings with his friends.

His neurologic examination was normal, including resolution of an initially abnormal head impulse test to the right side. He walked with a stiffened gait, however.

His neurologist diagnosed him with persistent postural perceptual dizziness (PPPD) and prescribed him vestibular rehabilitation, a selective serotonin reuptake inhibitor (SSRI), and cognitive-behavioral therapy. The vestibular therapist worked with the patient on habituation exercises to increase his tolerance for visual stimulation. The clinical psychologist helped the patient develop reappraisal strategies when he started to feel trapped in crowded environments. Within about 6 months, his symptoms decreased to the point that he was able to socialize with friends again.

COMMENT

PPPD can develop after a variety of homeostatic perturbations, such as an episode of vestibular neuritis. A prolonged recovery can become a setup for maladaptive postural responses and behavioral inhibition, which can lead to multiple layers of functional impairment. Vestibular rehabilitation can promote habituation to greater degrees of head movement and visual stimulation while cognitive-behavioral therapy can help avoid the development of maladaptive emotional responses that can lead to social isolation. The addition of a serotonergic antidepressant may be helpful in raising tolerance for sensory stimuli and the threshold for developing anxiety.

Treatment

The three strategies for treating PPPD are vestibular rehabilitation, cognitive-behavioral therapy (CBT), and serotonergic antidepressants.[5] Providing patients with a positive diagnosis of PPPD and an explanation of the interplay between acute triggers and the persistence of maladaptive responses can itself be therapeutic.

One mechanism for the development of PPPD is overreliance on the visual and somatosensory systems after a vestibular perturbation has occurred, as well as the activation of high-vigilance mechanisms of postural control that are no longer adaptive during the recovery phase.[6] These mechanisms may have been appropriate in the initial triggering event, such as when active vertigo creates a real threat of falls or vestibular input is not reliable (eg, during a Ménière disease attack). However, as the triggering event resolves, these initial postural strategies are not only no longer appropriate, they can lead to worsened balance. Some inappropriate strategies include shortening of stride length, stiffening of posture, and co-contraction of agonist and antagonist muscles. These behaviors may persist after a balance perturbation as a conditioned response to threatened balance. During nonstressed gait, these behaviors can increase the energy expenditure of normal walking while providing no protection against falls.

VESTIBULAR REHABILITATION. The reweighting of sensory inputs through vestibular, visual, and somatosensory systems can be accomplished through focused vestibular rehabilitation. Vestibular therapy must be done gently, however, as overaggressive treatment can lead to greater anxiety and perpetuation of an abnormally strong conditioned fear response to motion. Despite the strong fear of falling, patients with PPPD generally do not fall; this may reflect an impairment of higher cognitive appraisal of actual fall risk. If a patient has frequent falls despite resolution of the initial triggering event, an alternative diagnosis to PPPD should be sought.[7]

In general, patients who do well with vestibular rehabilitation have a resilient mindset, have higher satisfaction with life, and are generally optimistic. Negative prognostic factors include anxious temperament, introversion, hypervigilance about physical symptoms at the time of injury, and catastrophic thinking about the outcome of therapy.[8-11]

COGNITIVE-BEHAVIORAL THERAPY. CBT has been found to be helpful in PPPD, even in the long term. Anticipatory anxiety to potential threats to postural control can reduce the threshold for engaging in high-threat postural strategies that are contextually inappropriate. Developing awareness of this pattern, reappraising environmental threats to balance, overcoming the fear of falling, and being able to actively think through strategies to deal with feelings of disorientation (rather than trying to escape) are all tasks that can be addressed with regular focused CBT. CBT can help address some of the cognitive and emotional barriers to improvement in a vestibular rehabilitation program.

ANTIDEPRESSANTS. Serotonergic antidepressants (selective serotonin reuptake inhibitors [SSRIs]) or those that also include action on the norepinephrine system (SSRIs/serotonin norepinephrine reuptake inhibitor [SNRIs]) can be helpful in PPPD. The mechanism of efficacy is unclear because the serotonergic system in the brainstem projects nearly ubiquitously to the cerebrum. Sensory gating

and reweighting of visual versus vestibular inputs are theoretical mechanisms, however. Patients with balance disorders are generally sensitive to additional homeostatic perturbations, and this includes sensitivity to medication side effects. It is prudent, therefore, to start these agents at one-quarter to one-half of the usual starting doses used to treat depression and to proceed with a gentle titration. Clinical effects can take 2 to 3 months, particularly because the titration phase is usually slower than is typical for these medications when used for other disorders.

MAL DE DÉBARQUEMENT SYNDROME

This section reviews the clinical features, diagnostic criteria, causes, time course, and treatment for mal de débarquement syndrome. *Mal de débarquement* translates to *sickness of disembarkation* and has been recognized as a post–motion exposure phenomenon for centuries. However, it has only been in recent history that this phenomenon has become well known because of increased travel opportunities of humans to boats, planes, and cars.

Clinical Syndrome

Mal de débarquement syndrome refers to the chronic feeling of oscillating vertigo, generally described as, "rocking," "bobbing," or "swaying," that occurs after prolonged exposure to motion. The term *oscillating* denotes the actual feeling of motion rather than a temporal pattern of vertigo coming and going. Most cases occur after water-based travel, such as after disembarking from a cruise. However, a growing number of cases are being seen after air travel and prolonged land travel. Patients with mal de débarquement syndrome frequently report feeling like they are "still on the boat." In many cases, the exact frequency of the oscillation can be measured. A hallmark feature of mal de débarquement syndrome is the reduction in motion perception with reexposure to motion, such as driving a car or getting back on the boat. Because of the modulating effect of motion, some patients find that walking or running is better than standing still. The temporary reprieve from symptoms with motion is often associated with a temporary exacerbation once the motion stops, however. This is particularly apparent when the patient has a reduction in symptoms when driving a car but feels like he or she is still moving when the car stops.

Mal de débarquement syndrome is associated with a variable number of other symptoms including visually induced dizziness, cognitive difficulties (patients use the term "brain fog"), new or exacerbation of headaches, chronic fatigue, anxiety, sleep disturbance, tinnitus, general sensory hypersensitivity, and leg heaviness. The feeling of a gravitational, or "G-force," on the body is a common description. It is not typical for mal de débarquement syndrome to be associated with nystagmus, extraocular movement abnormalities, hearing loss, or spinning vertigo, however. The presence of any of these features should prompt a search for an alternative diagnosis. Typical cases of mal de débarquement syndrome are not associated with any abnormalities in neuroimaging or vestibular or auditory testing (CASE 6-2).[12]

Mal de débarquement syndrome typically occurs in women and has a peak age of onset between 40 and 50 years with a bell-shaped curve around this peak (CASE 6-2). The proportion of men with mal de débarquement syndrome has been reported to be as high as 25% to as low as 0%.[12] In all case series, women significantly outnumber men. Hormonal state may be relevant because the

KEY POINTS

- Persistent postural perceptual dizziness may be triggered by any severe homeostatic perturbation such as a vestibular disorder or medical, neurologic, or psychological process. Symptoms may continue despite resolution of the initial trigger or can coexist with an ongoing trigger.
- A slowly progressive disorder without a clear precipitant is not consistent with persistent postural perceptual dizziness.
- The mainstays of therapy for persistent postural perceptual dizziness include vestibular rehabilitation, cognitive-behavioral therapy, and serotonergic antidepressants.
- Mal de débarquement syndrome is a disorder of post–motion-induced persistent oscillating vertigo lasting more than 48 hours.
- The perception of motion in mal de débarquement syndrome is usually described as rocking, bobbing, or swaying. This perception decreases when the individual is back in motion such as when driving.
- Symptoms associated with mal de débarquement syndrome include chronic fatigue, visually induced dizziness, headaches, tinnitus, and anxiety. It is not typical for mal de débarquement syndrome to be associated with nystagmus, extraocular movement abnormalities, hearing loss, or spinning vertigo.

majority of women who develop mal de débarquement syndrome are perimenopausal, and the majority of premenopausal women with mal de débarquement syndrome note that their symptoms are worse before menses.[13]

New-onset headaches, worsened existing headaches, and hypersensitivity to light and sound can develop along with mal de débarquement syndrome. The prevalence of headaches that meet criteria for migraine is almost 50% in mal de débarquement syndrome.[14] Mal de débarquement syndrome does not meet the current criteria for vestibular migraine.[15] Mal de débarquement syndrome

CASE 6-2

A 50-year-old woman went on a 7-day cruise and felt well on the trip. While waiting at the airport to catch her flight home after disembarking from the cruise, she noticed a feeling of rocking, as if she were still on the cruise ship. She did not notice this so much during the flight itself or the car ride home after the flight. Once she got home, however, she noticed a stronger sense of motion. She nearly fell over while taking a shower that evening. The next morning, she woke up with a strong sense of rocking, as if she were still on the cruise ship. The rocking feeling only subsided when she was driving a car again. In addition, she felt fatigued, had slowed cognitive processing, and had a difficult time tolerating visual stimuli at the grocery store. She noticed heightened light and sound sensitivity and a persistent headache. She was otherwise in excellent health with no chronic illnesses. She did note the recent onset of hot flashes that raised concerns of oncoming menopause. Her neurologic examination was normal.

Her neurologist ordered neuroimaging and vestibular and auditory testing, which all returned within normal limits. Her symptoms were persistent at 3 months, and she had to take a leave of absence from work. She was eventually started on clonazepam 0.25 mg 2 times a day and venlafaxine extended release 75 mg every morning. This medication combination decreased her symptoms enough to allow her to return to her work, but they were not completely relieved.

COMMENT

The persistent oscillating vertigo of mal de débarquement syndrome is generally described as a rocking sensation that decreases with reexposure to passive motion, usually with driving a car. The most common trigger for mal de débarquement syndrome is ocean travel on a cruise, and the most common demographic affected with mal de débarquement syndrome is middle-aged women. Mal de débarquement syndrome is associated with a variety of symptoms such as cognitive slowing, fatigue, headache, and visually induced dizziness that can be as debilitating as the persistent vertigo. Patients with mal de débarquement syndrome can have symptoms exacerbated in closed spaces such as showers or in very wide-open spaces with poor focal points such as grocery stores. Medications such as selective serotonin reuptake inhibitors (SSRIs) and benzodiazepines can be helpful, but they rarely lead to a complete resolution of symptoms.

occurs without a history of migraine in more than 50% of affected individuals and is a persistent syndrome that has fluctuations but no significant periods of reprieve. Vestibular migraine requires time-limited vestibular symptoms that occur in episodes in someone who meets criteria for migraine headaches.

Criteria

Diagnostic criteria for mal de débarquement syndrome have been published by the Classification Committee for the Bárány Society (TABLE 6-2).[16] Mal de débarquement syndrome is diagnosed when oscillating vertigo occurs after disembarkation from a moving vessel such as a boat, plane, or car with symptoms lasting for at least 48 hours. Symptoms temporarily improve with exposure to passive motion. Symptoms that last for more than 48 hours but less than 1 month are designated as *transient mal de débarquement syndrome*. Symptoms that last for more than 1 month are designated as *persistent mal de débarquement syndrome*. If at least 1 month of observation time has not passed, mal de débarquement syndrome is designated as *in evolution*. Postmotion unsteadiness lasting less than 48 hours should be termed *land sickness* and not mal de débarquement syndrome. Land sickness is extremely common, affecting up to three-fourths of healthy adults, and shows an equal sex distribution.[17–20]

Causes

The most common triggers for mal de débarquement syndrome relate to water-based travel, followed by air- and then land-based travel. However, any kind of persistent passive motion exposure can lead to mal de débarquement syndrome. Patients have described triggers such as sleeping on waterbeds, living on houseboats, running on treadmills, and spending the day in a swaying tower as all preceding the onset of very typical mal de débarquement syndrome symptoms.[12] Although the trigger itself is important, individual factors may raise susceptibility. These factors include age, sex, low estrogen state, and stress during motion exposure.[13]

Diagnostic Criteria for Mal de Débarquement Syndrome[a] TABLE 6-2

- **A** Nonspinning vertigo characterized by an oscillatory perception ("rocking," "bobbing," "swaying") present continuously or for most of the day
- **B** Onset occurs within 48 hours after the end of exposure to passive motion
- **C** Symptoms temporarily reduce with exposure to passive motion
- **D** Symptoms continue for >48 hours
  - D0: Mal de débarquement syndrome in evolution: symptoms are ongoing, but the observation period has been less than 1 month
  - D1: Transient mal de débarquement syndrome: symptoms resolve at or before 1 month, and the observation period extends at least to the resolution point
  - D2: Persistent mal de débarquement syndrome: symptoms last longer than 1 month
- **E** Symptoms not better accounted for by another disease or disorder.

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Time Course

The duration of mal de débarquement syndrome in any individual is difficult to predict, but the longer the symptoms persist, the lower the probability of resolution. Symptoms lasting longer than 6 months generally have a low chance of spontaneous remission. Curiously, when symptoms remit, they can do so over a very short period of time. Patients may even say that the symptom went away, "like a light switch." Recurrent episodes of mal de débarquement syndrome tend to be either the same length or get progressively longer with repeated motion exposure.[20] In any given episode, symptoms do tend to get better with time. Symptoms that get worse with time should trigger a search for a concurrent diagnosis such as severe anxiety or another cause for balance dysfunction.

Treatment

No cure for mal de débarquement syndrome exists because symptoms arise from the brain's natural ability to entrain to periodic motion. Some experimental protocols have been able to put mal de débarquement syndrome into remission or reduce symptoms to more manageable levels. These experimental procedures involve neuromodulation methods such as transcranial magnetic stimulation, transcranial electrical current stimulation, or readaptation of the vestibular ocular reflex.[21–24] In the clinical realm, however, treatments consist of lifestyle modifications including precautions taken before travel, as well as serotonergic antidepressants and benzodiazepines.

LIFESTYLE MODIFICATIONS. Mal de débarquement syndrome symptoms are exacerbated by emotional stress and poor sleep; these two factors are the most important for successful symptom management. Patients with mal de débarquement syndrome frequently feel overwhelmed by sensory stimuli in places such as grocery stores, shopping malls, and large open warehouse-type stores; conversely, very small spaces such as bathrooms and shower stalls can make them feel unstable. Thus, finding the right balance of open spaces and a tolerable amount of visual stimulation can be challenging. Generally, noisy environments, low-light conditions, and excessive visual motion stimulation should be avoided. No evidence has been found that severe dietary restrictions or low-salt diets are helpful for mal de débarquement syndrome symptoms.[13] Patients frequently find that their tolerance for alcohol is reduced because it impairs their balance. The effect of caffeine is variable.

SEROTONERGIC ANTIDEPRESSANTS. Antidepressants in the SSRI category are typically much more effective than those that primarily work on the norepinephrine system, for example, tricyclic antidepressants and SNRIs, for mal de débarquement syndrome symptoms.[13] Commonly used SSRIs include citalopram, escitalopram, sertraline, paroxetine, and fluoxetine. The choice of agent depends on tolerance and side effects. Of the antidepressants that have activity on both the serotonin and norepinephrine systems, venlafaxine is the most widely used among neuro-otologists, but no head-to-head trials have been conducted to support its use above others in its class. Patients with mal de débarquement syndrome are typically very sensitive to medication side effects and should be started at lower than the usual starting doses of these medications (generally at one-quarter to one-half of the usual adult dose) with a slow titration. When done slowly, they can usually reach a standard adult therapeutic dose.

BENZODIAZEPINES. Benzodiazepines are the most quickly acting and effective symptomatic treatment for mal de débarquement syndrome.[13,20] Because mal de débarquement syndrome symptoms are typically chronic and are present to some degree all day, most patients who are put on benzodiazepines use clonazepam because of its long half-life (12 to 24 hours). A history of medication sensitivity should be assessed in patients with mal de débarquement syndrome. A typical starting dose of clonazepam is 0.25 mg 1 time a day with a titration up to no higher than 0.5 mg 2 times a day. Dosing higher than this level is typically not additionally effective.

Agents with intermediate half-lives such as lorazepam or diazepam can be used before traveling to reduce post–motion exposure exacerbation of symptoms. Doses as low as 0.5 mg to 1 mg of diazepam can be sufficient for this particular application. Flights that are longer than 6 hours may require a second dose midflight. Benzodiazepines should not be used in combination, however (eg, diazepam on top of clonazepam). Patients should be advised not to drive or consume alcohol when they are taking benzodiazepines.

KEY POINTS

- Clinically available treatments for mal de débarquement syndrome include serotonergic antidepressants and benzodiazepines; vestibular therapy is generally not helpful.
- Motion sickness and visually induced motion sickness are generally self-limited processes that end when the stimulus is over. Symptoms may include nausea/vomiting, stomach awareness, headache, sweating/pallor, dizziness, drowsiness, or eyestrain.

MOTION SICKNESS AND VISUALLY INDUCED MOTION SICKNESS

This section reviews the clinical features, diagnostic criteria, causes, time course, and treatment for motion sickness and visually induced motion sickness. These phenomena are normal physiologic responses to motion that become defined as disorders depending on severity. These nuances are discussed in this section.

Clinical Syndrome

Motion sickness is a polysymptomatic disorder that can be experienced by all individuals who have a functioning vestibular system given a strong enough stimulus. The induction of sick feelings in the form of nausea, stomach awareness or discomfort, thermoregulatory dysfunction, headache, dizziness, or drowsiness is a normal physiologic response and may be accompanied by signs such as vomiting, cold sweating, or pallor. However, when the threshold of experiencing these symptoms is very low and habituation to repeated stimuli is lacking, the morbidity from motion sickness can be extremely high. This can lead to restrictions in social, personal, and professional activities (CASE 6-3).

Motion sickness can be divided into sickness induced by physical motion of the person or by visual motion. Susceptibility to one kind of motion sickness does not necessarily predict susceptibility to the other. For practical purposes in this article, the term *motion sickness* is used for physical motion of the self, whereas *visually induced motion sickness* refers to sickness caused by visual motion.[25,26]

MOTION SICKNESS. Motion sickness is generally a benign self-limited condition that starts during exposure to motion, whether active or passive. Most causes of motion sickness are due to passive motion exposure such as occurs on boats, airplanes, or cars. The sickness symptoms gradually arise during the motion exposure and abate after the motion stops. Most cases of motion sickness resolve within hours if not within minutes of the end of stimulation. The exception is headache. When a headache is triggered by motion, it can last well after the motion has ended and only resolve after it has been specifically treated. Motion sickness symptoms can continue past the cessation of motion to some degree, but symptoms that arise only after the motion has ended should not be considered

motion sickness; these individuals may have land sickness or may progress to developing mal de débarquement syndrome.

Nausea is the most ubiquitous symptom of motion sickness. If retching or vomiting is to occur during a motion sickness episode it is generally preceded by stomach awareness and worsening nausea. People who are very susceptible to motion sickness can experience the "avalanche phenomenon," which is characterized by a rapid onset of vomiting after motion exposure. In very rare cases, typically in situations in which an individual has learned to ignore the premonitory symptoms of motion sickness, he or she can go straight to vomiting.[26] Motion exposure can lead to drowsiness in some individuals; they may fall asleep before developing any other symptom. This has been called the *sopite syndrome* and can also take the form of motion-triggered tiredness, lethargy, fatigue, or yawning.[27]

VISUALLY INDUCED MOTION SICKNESS. Visually induced motion sickness is caused by visual stimuli such as occurs with simulation equipment, IMAX screens, virtual reality displays, computers, televisions, and even smartphone screens.[26] In addition to the usual symptoms of motion sickness, visually induced motion sickness is associated with eyestrain and blurred vision. Nausea to the point of

CASE 6-3

A 24-year-old woman took the shuttle from the park-and-ride to her office every day. The ride took a lot of turns and made several stops along the route. She noticed that, around 10 minutes into the ride, she always started to feel nauseated and developed a slight headache. It was worsened by the smell of the exhaust from the vehicle when the shuttle briefly stopped along the route. She never vomited from the nausea, but she could feel a discomfort in her stomach before frank nausea began. The ride was over before her symptoms got too severe. She found that if she looked at her smartphone during the ride, the nausea was worse.

The nausea got better as soon as the bus ride was over, and she generally recovered within 15 minutes of getting off the bus. Because this happened so frequently, the woman eventually decided to ride her bike to work and avoid taking the shuttle. She was otherwise in good health and had no neurologic deficits.

COMMENT

The presence of a normally functioning vestibular system creates a risk for the development of motion sickness. A normal response to predictable vestibular stimulation that induces nausea is to eventually habituate to the motion. However, when the features of the motion stimulus are beyond the person's adaptive capability, motion sickness symptoms can arise. These include nausea, stomach awareness, sweating, pallor, headache, dizziness, and drowsiness. Nausea can increase to the point of vomiting. Motion sickness symptoms usually decrease after the stimulus is over, although headache can persist until it is specifically treated. In many cases, such as in this example, people modify their behavior to avoid sickness-inducing situations.

vomiting is unusual in visually induced motion sickness, namely because the individual can close his or her eyes to avoid continued stimulation. Headache and eyestrain are generally more common with visually induced motion sickness than physical motion–induced motion sickness. Visually induced motion sickness is different from visually induced dizziness and from the phenomenon of vection.[28] Although these symptoms can all coexist, they refer to different aspects of the experience. Visually induced dizziness specifically refers to a sense of spatial disorientation during exposure to visually complex or moving visual stimuli (see the Persistent Postural Perceptual Dizziness section), whereas vection refers to the illusion of self-motion that is induced by motion of the visual field.

In healthy individuals, repeated exposures to the same kind of motion, whether physical motion or visual motion, lead to habituation and a higher threshold for inducing sickness symptoms with subsequent exposures. Individuals very susceptible to motion sickness and visually induced motion sickness do not habituate to the motion and frequently develop aversive emotions before motion exposures and may change behaviors to avoid further motion exposures.

The prevalence of motion sickness in the general population is difficult to assess because susceptibility varies by age and sex and can be very specific to each kind of motion. Infants and toddlers younger than 2 years old seem relatively protected against motion sickness. Thereafter, susceptibility rises until it peaks between the ages of 7 and 12 years and then gradually declines. In primary school–aged children before puberty, the rate of carsickness is about 30% to 40%.[29] Susceptibility in adults hovers between 14% and 25% and is stable until around the age of 60 years, at which time susceptibility goes down significantly to about 7%.[30,31] One difference between motion sickness and visually induced motion sickness is that visually induced motion sickness susceptibility tends to increase with age, with the highest prevalence in those older than 60 years.[32] These statistics represent general population trends, whereas individuals can follow a specific course.

Susceptibility is generally higher in women than men, particularly around the menstrual cycle.[33] Even at the same level of motion sickness severity, women are more likely to experience vomiting.[34] The age effect is much stronger than the sex effect in motion sickness susceptibility, however.[35]

KEY POINT

- **Motion sickness susceptibility peaks at the ages of 7 to 12 years, is stable through adult years, and declines after age 60 years. Visually induced motion sickness generally worsens with age.**

Criteria

Criteria for motion sickness and visually induced motion sickness have been drafted by the Bárány Society for both an episode of motion sickness/visually induced motion sickness and for motion sickness and visually induced motion sickness as disorders.[36] Because motion sickness induction can be very specific to a specific trigger (eg, sickness in boats but not in cars), the criteria require that the sickness is induced by the same or similar kind of trigger.

Many scales for motion sickness severity have been developed over the past 60 years, generally motivated by the armed forces and space exploration. Some severity scales include the Simulator Sickness Questionnaire (SSQ),[37] the Motion Sickness Assessment Questionnaire (MSAQ),[38] the Nausea Profile,[39] the Misery Scale,[40] and Fast Motion Sickness Scale,[41] among several others. Several motion sickness susceptibility scales have also been developed, although far fewer of these exist. The Motion Sickness Susceptibility Questionnaire (MSSQ)

Short-form is the most widely used susceptibility scale because it has been validated through time and translated into multiple languages.[42] Because susceptibility changes dramatically with age (reducing with older age), the Motion Sickness Susceptibility Questionnaire divides susceptibility into subscales for individuals 12 years old or younger and for those older than 12 years.

A specific scale can be used for its individual strengths. However, from a practical standpoint, a short Likert-style scale that queries whether the patient is "always," "often," "sometimes," or "never" affected by motion sickness can be used in the office setting. Because individuals can also modify activities to avoid becoming motion sick, this simple scale can also be used in the context of how often the patient avoids motion exposure to prevent becoming sick.

Causes

Many theories exist for why motion sickness persists in the modern day. The most common theory is the sensory conflict and mismatch theory. This refers to the discrepancy between expected versus experienced sensory inputs through the visual, vestibular, and somatosensory systems.[43] These systems may be in conflict with each other (eg, vision versus vestibular), may be in conflict with itself (eg, canal versus otolith input), or reflect a mismatch in perceived versus expected verticality. It is also possible that the overlap between vestibular and autonomic pathways makes autonomic activation an unfortunate byproduct of vestibular stimulation that serves no purpose.[44]

Certain disorders such as migraine, vestibular migraine, and Ménière disease are associated with much higher rates of motion sickness susceptibility than other vestibular disorders.[45] The rate of motion sickness is no higher in BPPV or compensated vestibular neuritis than in healthy controls without vestibular disorders.[46] A functioning vestibular system may be a critical component of motion sickness because susceptibility is much lower in individuals with bilateral vestibulopathy.[47,48]

Time Course

Because motion sickness susceptibility generally declines with age, if this trend does not follow for an individual, an underlying vestibular asymmetry or metabolic disorder should be investigated. In contrast, visually induced motion sickness may increase with age. When severe, however, an underlying ocular motility issue or other cause of increased eyestrain should be investigated.

Treatment

Both motion sickness and visually induced motion sickness can be treated with habituation exercises to slowly increase the threshold for developing symptoms with motion exposure. Oral treatments include anticholinergic, antimuscarinic, benzodiazepine, and antihistaminergic medications. Common options include meclizine, dimenhydrinate, promethazine, prochlorperazine, diazepam, and scopolamine.[49] Scopolamine can be given in oral form for rapid action or as a patch placed on the mastoid and changed every 72 hours. No agent should be used chronically, however, because they interfere with vestibular compensation and can be associated with side effects such as sedation, confusion, dry eyes, dry mouth, and urinary retention. If medications cannot be taken and exposure to motion is inevitable, controlled breathing exercises, listening to music, or exposure to pleasant smells can be helpful.[50–52]

BILATERAL VESTIBULOPATHY

This section reviews the clinical features, diagnostic criteria, causes, time course, and treatment for bilateral vestibulopathy. Although this is an uncommon disorder, it is important to recognize because of the extremely high degree of morbidity, the lack of effective treatments, and the wide range of causes.

Clinical Syndrome

Bilateral vestibulopathy refers to significant impairment of both peripheral vestibular systems. It may occur with or without hearing loss. The typical patient with bilateral vestibular loss experiences chronic unsteadiness in the upright position that is absent when sitting or lying down. Imbalance is particularly severe in low-light settings and walking on uneven surfaces when other body position–orienting sensory inputs (eg, vision, somatosensory) are challenged (CASE 6-4).[53]

Patients may report that their "eyes are not keeping up with my head," which relates to impaired conduction of head acceleration information through a slowed vestibulo-ocular reflex (VOR). Oscillopsia ("bouncing vision") with walking or blurred vision with head movement may occur. Even though oscillopsia is most severe with walking, milder symptoms may be present in the seated position and induced by a strong heartbeat or head movement during speaking or chewing. Patients may prefer to keep their hand on their chin to stabilize the head during these situations.

Imbalance can be compounded by the loss of vestibulospinal reflexes that are critical in translating head position information into spinal reflexes that maintain balance in the upright position. Chronic loss of vestibular input can also lead to degeneration of central vestibular projections to the hippocampus that are involved in spatial navigation.[54]

Reduced ability to stabilize vision from a weakened VOR, diminished postural reflexes from a weakened vestibulospinal reflex, and degraded spatial orientation sense from reduced vestibular input to the hippocampus can synergistically worsen balance impairment and risk for falls in bilateral vestibulopathy.

Criteria

Diagnostic criteria for bilateral vestibulopathy were established by the Bárány Society in 2017 and are presented in TABLE 6-3.[55] Individuals with bilateral vestibulopathy are diagnosed by a combination of symptoms as well as diagnostic vestibular function metrics. Because the angular vestibular ocular system operates at different velocities and testing procedures are tuned for different frequencies, each testing procedure has different criteria. Video head impulse testing is tuned for high-acceleration head movements, rotational chair testing detects medium-frequency head movements, and caloric testing detects very-low-frequency activity. In recognition of these differences, the criteria for definite bilateral vestibulopathy as set forth by the Bárány Society allow for a diagnosis based on any of these measurements. A diagnosis of probable bilateral vestibulopathy can be made if the clinical symptoms are met and only an abnormal bedside head impulse testing response is present.

Rotational chair testing is the most physiologic method of assessing bilateral vestibulopathy because both vestibular systems are tested at the same time. It is not affected by structural issues such as a narrowed external ear canal, a perforated eardrum, middle ear fluid, or a temporal bone abnormality (all of these abnormalities can affect caloric irrigation studies). A reduced gain of the VOR

KEY POINTS

- Certain disorders such as migraine, vestibular migraine, and Ménière disease can increase susceptibility to motion sickness. Motion sickness susceptibility can increase with vestibular neuritis but return to normal if the vestibular paresis is compensated. Individuals with bilateral vestibulopathy have very low motion sickness susceptibility.
- Habituation exercises, medications (antimuscarinic, anticholinergic, antihistaminergic, or diazepam), controlled breathing, music, or pleasant smells can modify motion sickness severity.
- Core symptoms of bilateral vestibulopathy include gait unsteadiness, postural instability, visual blurring with head movement, and sometimes oscillopsia.
- Bilateral vestibulopathy can be diagnosed by rotational chair testing, caloric irrigation, or video head impulse testing; the most reliable method is rotational chair testing.

CASE 6-4

A 70-year-old man had a history of Ménière disease about 20 years prior that had left him with poor hearing and a compensated vestibular deficit in his right ear. One morning, he woke up with severe rotational vertigo, left ear tinnitus, and aural fullness. The symptoms lasted about 5 hours. Over the next year, he had three more episodes of similar vertigo. He noticed gradually reduced balance function in between each spell of vertigo. In particular, he noticed difficulty walking at night. He also felt that when he turned his head quickly, his vision had a short lag catching up to his head movement. He noted that his vision kept "bouncing" whenever he walked.

His examination was remarkable for normal visual acuity in both eyes. Hearing was absent in the right ear. He could detect conversational speech in the left ear but required frequent repeating. Bilateral catch-up saccades were present on the head impulse maneuver. His baseline gait was widened, and he had a positive Romberg sign.

He started a vestibular rehabilitation program to help with the visual blurring, was referred to otorhinolaryngology for a cochlear implant evaluation, and was counseled on taking additional precautions when walking at night or on uneven surfaces.

COMMENT

Because each peripheral vestibular system can detect motion in both directions, the loss of one vestibular system can be compensated for readily. However, when both peripheral vestibular systems are damaged, leading to bilateral vestibulopathy, the functional consequences can be severe. The dysfunction occurs because of the loss of the vestibulo-ocular reflex that drives compensatory eye movements for head motion and vestibulospinal reflexes that adjust posture for head motion. Thus, symptoms of bilateral vestibulopathy include imbalance, visual lag, and oscillopsia when severe. Bilateral vestibulopathy has many causes, such as sequential inner ear dysfunction, which can occur in Ménière disease, like in the case above. It can also happen with sequential vestibular neuritis, vestibulotoxic medications, or infiltration of the inner ear space from contents of the intracranial space such as blood (eg, subarachnoid hemorrhage), inflammatory cells (eg, meningitis), or cancerous cells (eg, carcinomatous meningitis). It can occur idiopathically, in combination with other peripheral neuropathies, or in CANVAS (cerebellar ataxia, neuropathy, vestibular areflexia syndrome). When some residual vestibular function remains, vestibular therapy can be helpful, but the mainstay of treatment is to protect other systems that contribute to postural control (ie, vision, proprioception, cognition, physical conditioning) and to be aware of situations that challenge these other pathways and create dangerous circumstances (eg, walking in low light).

(eye movement velocity relative to chair movement velocity in sinusoidal harmonic acceleration) and a phase lead of eye position relative to chair position are indicative of vestibular impairment. Caloric testing is the most widely available test of inner ear function but is the least relevant because activation of one vestibular system at a time with a temperature stimulus is not physiologic and only corresponds to a natural stimulus frequency of 0.003 Hz. It can also be limited by structural abnormalities of the external and middle ears, as noted earlier. Abnormal caloric testing that is suggestive of bilateral vestibulopathy should be verified with rotational testing because spuriously low-caloric-induced responses are common. Video head impulse testing has gained in use in some clinical contexts, but the limitations in reimbursement for incorporating video head impulse testing into a regular vestibular function testing battery has curtailed more widespread clinical use.

Bedside screening for bilateral vestibulopathy can be done by either performing the head impulse test or checking dynamic visual acuity. The head impulse test maneuver is a test of the VOR. During a head impulse test, the patient's head is held by the examiner with both hands and the patient is instructed to focus on a point on the examiner, such as his or her nose. The patient's head is then thrust to either side with short-excursion (10 degrees) high-acceleration movements. If the VOR is intact, the patient's eyes should be focused on the examiner at all times. If the VOR is impaired, the patient's eyes will passively follow the head movement during testing due to slowed conduction through the vestibular system. The patient will then make a corrective saccade back to midline to refocus on the examiner. The head thrusts must be done in a random manner so that the patient does not make predictive saccades ahead of the corrective saccade. The head impulse test is most sensitive for new-onset vestibular dysfunction and for severe

Diagnostic Criteria for Bilateral Vestibulopathy[a,b] TABLE 6-3

A Chronic vestibular syndrome with the following symptoms:

- **1** Unsteadiness when walking or standing plus at least one of 2 or 3 below
- **2** Movement-induced blurred vision or oscillopsia during walking or quick head/body movements and/or
- **3** Worsening of unsteadiness in darkness and/or on uneven ground

B No symptoms while sitting or lying down under static conditions

C Bilaterally reduced or absent angular vestibulo-ocular reflex (VOR) function documented by:

Bilaterally pathologic horizontal angular VOR gain <0.6, measured by the video head impulse test or scleral-coil technique and/or

Reduced caloric response (sum of bithermal maximum peak slow phase velocity on each side <6 degrees per second) and/or

Reduced horizontal angular VOR gain <0.1 upon sinusoidal stimulation on a rotatory chair (0.1 Hz, maximum velocity = 50 degrees per second) and a phase lead >68 degrees (time constant <5 seconds)

D Not better accounted for by another disease

[a] Modified with permission from Strupp M, et al, J Vestib Res.[55] © 2017 IOP Press and the authors.
[b] Probable bilateral vestibulopathy may be diagnosed if criteria A, B, and D are met but only if the pathologic horizontal bedside head impulse test is abnormal and no laboratory testing is available.

deficits in which the angular VOR gain is less than 0.4.[56] The overall sensitivity (84%) and specificity (82%) are fairly good for diagnosing bilateral vestibulopathy.[57] Over time, however, the corrective saccade can occur so early that it partially overlaps with the head thrust maneuver and is thus not visible to the naked eye.[58,59] Therefore, when suspicion for a vestibulopathy is high but the head thrust maneuver appears to be normal, follow-up with video head impulse testing or rotational testing should be performed.

Dynamic visual acuity can be checked at the bedside to screen for bilateral vestibulopathy. The patient is asked to read a Snellen chart with both eyes open,

TABLE 6-4

Etiologies of Bilateral Vestibulopathy

Primary inner ear

- Sequential or concurrent bilateral Ménière disease
- Sequential or concurrent bilateral labyrinthitis
- Sequential vestibular neuritis (rare)

Infectious

- Meningitis
- Encephalitis
- Cerebellitis
- Note common infectious agents: herpes simplex, varicella, mumps, *Treponema pallidum* (syphilis), *Borrelia burgdorferi* (Lyme disease), Creutzfeldt-Jakob disease

Autoimmune

- Cogan syndrome
- Susac syndrome
- Antineutrophil cytoplasmic antibody–associated vasculitides
- Polyarteritis nodosa
- Relapsing polychondritis
- Neuro Behçet disease
- Neurosarcoidosis
- Sjögren syndrome
- Systemic lupus erythematosus
- Antiphospholipid syndrome
- Graves and Hashimoto thyroid disease
- Vogt-Koyanagi-Harada syndrome

Genetic

- Neurofibromatosis 2
- CANVAS (cerebellar ataxia, neuropathy, vestibular areflexia syndrome)
- *COCH* (*DFNA9*), *MYO7A* (*DFNA11*), *ESPN* (*DFNB36*), *PTPRQ* (*DFNB84A*)
- Spinocerebellar ataxia 3

CONTINUED ON PAGE 437

and the best level of acuity is assessed. The patient's head is then passively oscillated at 2 Hz, and acuity is reassessed. Losing more than two lines of acuity suggests an impaired VOR with specificity going up with more lines of acuity lost.[60]

Causes

Bilateral vestibulopathy may be idiopathic in 20% to 50% of cases or may be caused by a variety of identifiable inner ear–specific or systemic disorders that involve the vestibular system (TABLE 6-4 and TABLE 6-5).[61–69] Intracranial

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- Spinocerebellar ataxia 6
- Episodic ataxia 2
- Hereditary sensorimotor neuropathy
- MELAS (mitochondrial encephalomyopathy, lactic acidosis, and strokelike episodes)

Degenerative

- Superficial siderosis
- Multiple system atrophy

Toxic/metabolic

- Medication-related ototoxicity (see TABLE 6-5)
- Wernicke encephalopathy (partially reversible)
- Vitamin B_{12}/folate deficiency
- Hypothyroidism
- Phenobarbital, phenytoin
- Miscellaneous: styrene, Jet Propellant-8 jet fuel, butyl nitrate, carbon disulfide, lead, mercury, manganese, tin

Oncologic

- Vestibular schwannomas
- Carcinomatosis–metastatic disease
- Paraneoplastic syndromes (anti-Yo, anti-Hu)
- Lymphoma

Congenital

- Usher syndrome
- Pendred syndrome
- Enlarged vestibular aqueduct syndrome
- CHARGE (coloboma of the eye, heart defects, atresia of the choanae, renal abnormalities and retardation of growth and/or development, genital abnormalities, and ear abnormalities) syndrome
- Other congenital malformations (eg, Mondini dysplasia)

Iatrogenic

- Surgical vestibular injury (eg, cochlear implant)

processes that involve blood, inflammatory mediators, tumor cells, or iron in the subarachnoid space can lead to passage of these elements through the cochlear and vestibular aqueducts into the inner ear, leading to hearing loss and vestibular dysfunction. Metabolic abnormalities (eg, deficiencies in vitamin B_1, vitamin B_{12}, folate, thyroid) can affect both the peripheral and central vestibular systems. Thus, although bilateral vestibulopathy is defined by its peripheral vestibular diagnostic abnormalities, it can be associated with systemic and central nervous system disorders with all contributing to balance dysfunction.

Vestibulotoxicity from aminoglycoside antibiotics should be suspected when an insidious onset of balance problems occurs after their use (TABLE 6-5). Of particular relevance is gentamicin, which is strongly vestibulotoxic and widely used to treat gram-negative bacterial infections for prolonged periods of time. The lack of auditory warning symptoms (eg, tinnitus or hearing loss), the systemic accumulation of gentamicin with prolonged use, and concurrent nephrotoxicity have been recognized as contributors to the high risk of gentamicin-related vestibular damage.[69] Other aminoglycosides to be aware of include streptomycin and amikacin, which are used to treat tuberculosis, and tobramycin, which is used to treat infections common in cystic fibrosis (eg, *Pseudomonas aeruginosa*).[70] Commonly used antibiotics in the penicillin, cephalosporin, macrolide, or fluoroquinolone classes are rarely vestibulotoxic.[71] Several other drug classes are known to cause ototoxicity but cause significantly greater hearing loss and tinnitus than vestibular loss. These drug classes

TABLE 6-5 **Vestibulotoxicity of Antibiotics**

Strongly vestibulotoxic

- Gentamicin
- Streptomycin
- Tobramycin[a]

Weakly vestibulotoxic

- Neomycin[a]
- Kanamycin[a]
- Amikacin[a]
- Netilmicin
- Vancomycin

Rarely vestibulotoxic

- Penicillins
- Cephalosporins
- Macrolides
- Fluoroquinolones
- Metronidazole

[a] Also cochleotoxic.

include loop diuretics, salicylates, quinine, cisplatin (which causes permanent hearing loss), carboplatin, paclitaxel, and nitrogen mustard.

Regular screening for vestibulopathy, such as with the head impulse, the video head impulse, or dynamic visual acuity testing, should be done for a patient who is put on repeated doses of vestibulotoxic medications. Because some vestibulotoxic medications can cause concurrent peripheral neuropathy and exacerbate imbalance (eg, platinum-based chemotherapeutics), vigilance should be particularly high in patients receiving these agents. Other medications such as vincristine, nitrogen mustard, loop diuretics, salicylates, and nonsteroidal anti-inflammatory drugs are also potentially ototoxic but generally cause more hearing loss and tinnitus than vestibular dysfunction and are thus more readily detected as a cause for ototoxicity.

In 2011, a disorder called *CANVAS* (cerebellar ataxia, neuropathy, vestibular areflexia syndrome) was described in 27 patients with late-onset cerebellar ataxia, bilateral vestibulopathy, and a non–length-dependent sensory neuropathy.[72] Histopathology showed cerebellar Purkinje cell and dorsal root ganglion loss. Clinical cerebellar abnormalities included the presence of downbeat and gaze-evoked nystagmus, poor visual suppression of the VOR, rebound nystagmus, saccadic dysmetria, and greater axial compared with limb dysmetria. Brain MRI showed atrophy of the vermis as well as crus I of the cerebellar hemisphere. Most cases of CANVAS present later in life (in the sixth decade), but the range of age at onset of initial symptoms has subsequently been reported to be as wide as 19 to 76 years.[73] The earliest symptom is a chronic cough, with unsteadiness, sensory loss, and dysautonomia as subsequent symptoms. The phenotype can be incomplete and the order of onset of symptoms variable among patients, however. An autosomal recessive inheritance pattern was confirmed to be a biallelic pentameric repeat expansion (AAGGG) that was observed in 90% of cases in which all three systems were involved (sensory, vestibular, cerebellar) and in 14% of cases in which the phenotype was incomplete. Of the individuals for whom the clinical information was known, the sex distribution was 55% female and 45% male; 45% of the cases were familial, and 55% were sporadic. All cases were in patients of Caucasian origin, which raised the possibility of a commonly shared distant ancestor.[73]

Time Course

Patients with inner ear disorders, such as Ménière disease or vestibular neuritis, may do fine with a unilateral vestibulopathy because one vestibular system can detect head motion in both directions, but if the second inner ear function is lost, the clinical effects can be quite devastating. Vestibulopathy can also occur insidiously and may be asymptomatic until significant dysfunction is present. This is particularly true for idiopathic cases and those occurring after exposure to ototoxic medications.

Treatment

Currently, no standardized treatments can reverse damage to the inner ear due to the causes of bilateral vestibulopathy. Intensive research on vestibular implants is in preliminary stages at the time of this writing.[74] Patients with bilateral vestibulopathy may respond well to vestibular rehabilitation measures, especially if they have some residual vestibular function left. Protecting vision, treating potential causes of peripheral sensory loss, staying cognitively intact, and

KEY POINTS

- **Bilateral vestibulopathy may occur after sequential inner ear injury such as from Ménière disease, vestibular neuritis, or vestibular schwannomas, from extension of intracerebral processes such as meningitis, carcinomatosis, or other processes in the subarachnoid space into the inner ear, or secondary to vestibulotoxic medications such as aminoglycoside antibiotics.**

- **Vestibular rehabilitation, protecting vision, and avoiding deconditioning are helpful in reducing morbidity from bilateral vestibulopathy. Safety measures should emphasize care in low-light settings.**

maintaining good muscle tone are important for reducing morbidity from bilateral vestibulopathy. Patients should also be warned not to swim alone because they can become easily disoriented when their eyes are closed and may swim the wrong way. They should be particularly vigilant in low-light settings in all circumstances.

PERSISTENT DIZZINESS AFTER MILD CONCUSSION

This section reviews the clinical features, time course, and treatment for persistent dizziness after a mild concussion. This clinical syndrome represents a

CASE 6-5

A 20-year-old woman who played collegiate hockey was knocked particularly hard against the wall of the ice rink and felt a bit dazed after the impact. She continued to play the rest of the game but felt that she couldn't quite predict the position of the puck as well as she used to. In the days after the game, she developed a persistent headache, difficulty with shifting from reading the blackboard to reading her notebook, and a feeling of lightheadedness and "wooziness" when running. When she was particularly tired, she noticed slight double vision. She had a difficult time watching movies with her friends because the motion on the screen made her feel like she was moving.

She saw a neurologist when she was still symptomatic after a month. On examination, she had a slight slowness of response to questions but with normal informational content. Visual acuity was normal, but she had a convergence insufficiency. Hearing and head impulse testing were normal. Baseline gait was normal, but she had difficulty balancing on one foot. This was abnormal given her age and high baseline athleticism. She did not develop vertigo or nystagmus on positional (Dix-Hallpike) testing. Her neurologist started her on nortriptyline for the headaches and referred her for visual and vestibular rehabilitation therapy. The vestibular therapist started her on a graduated exercise program of increasing head movement and physical exertion. An optometrist with experience in vision rehabilitation helped her with eye muscle–strengthening exercises. She stayed off the ice that season but did train in the gym. Her symptoms gradually improved over the next 3 months until she was able to play hockey again.

COMMENT

Although concussions are otherwise known as *mild traumatic brain injury*, the symptoms can be quite debilitating. Benign paroxysmal positional vertigo, vestibular migraine, exertional dizziness, spatial disorientation, and visual dysfunction can follow concussions. Severe structural injury to the inner ear is uncommon after concussions, but a screen for benign paroxysmal positional vertigo with the Dix-Hallpike test should always be performed after a concussion because it is common and treatable. Vestibular rehabilitation, ocular motor rehabilitation, treatment of headaches, and graduated return to activity are the mainstays of treatment.

major public health issue because it affects every age group, has a wide number of potential causes, and can manifest with a variety of both visually triggered and head motion–triggered symptoms.

KEY POINT

● Postconcussion dizziness includes categories such as positional vertigo, exertional dizziness, vestibular migraine, spatial disorientation, and visual disorders.

Clinical Syndrome

The term *concussion* refers to mild traumatic brain injury in which biomechanical insult from blunt head trauma leads to brain dysfunction. Blunt head trauma occurs in combat, sports, whiplash, motor vehicle accidents, altercations, falls, and various accidents. Dizziness is a frequent symptom of concussion, affecting between 59% and 98% of patients depending on the mechanism and time since injury; it can accompany headaches, cognitive dysfunction, emotional dysregulation, and ocular-motor problems.[75,76] Concussions can lead to both peripheral and central vestibular dysfunction as well as dizziness due to a variety of ocular and visual processing problems (CASE 6-5). Penetrating head injuries or blast injuries are more likely to be associated with hemorrhages and structural brain problems, causing additional symptoms that are beyond the scope of this article.

The most common categories of dizziness after concussion are positional vertigo, exertional dizziness, vestibular migraine, spatial disorientation, and dizziness secondary to visual disorders.

POSITIONAL VERTIGO. BPPV can occur after a concussion due to mechanical dislodgement of otoliths from the utricle and can be present in up to 61% of individuals after head trauma.[77] This results in typical BPPV as occurs from nontraumatic causes. However, when BPPV follows head trauma, care should be taken to rule out bilateral and multiple canal involvement. BPPV is treated with the canalith repositioning maneuver appropriate to each canal (ie, the Epley head-hanging roll maneuver for posterior canal and the Lempert roll maneuver for horizontal canal).

EXERTIONAL DIZZINESS. Patients with concussion can experience dizziness during and after exercise. This is treated with graduated increases in exercise duration to build up tolerance.

VESTIBULAR MIGRAINE. Headache is one of the most frequent symptoms of concussions and can be associated with light and sound sensitivity and dizziness. General migraine therapies are effective (adequate sleep, exercise, stress moderation, healthy diet) as well as vestibular rehabilitation. Preventative migraine medications may be added in cases that become chronic.

SPATIAL DISORIENTATION. This symptom is typically the most protracted because it can be associated with abnormalities in the VOR. Patients can experience unsteadiness of gait, postural instability, and even symptoms when they are lying down. Gentle graded vestibular therapy is the mainstay of therapy, but symptoms can become chronic (ie, lasting more than 3 months).

VISUAL DISORDERS. Patients who develop ocular or visual-processing dysfunction after concussion may describe their symptoms as "dizziness." The most common concussion-related visual disorders include convergence insufficiency (inability to move eyes inward, required for near work), accommodation dysfunction (inability to flexibly change focus), stereopsis (depth perception), and heterophorias (latent misalignment of the visual axes). Higher-order visual

processing can be affected in concussions because much of the cerebral cortex is dedicated to visual function or ocular motility. After concussion, basic problems with smooth pursuit and saccadic control can occur, leading to problems with reading and a propensity for eyestrain. Susceptibility to visually induced dizziness and visually induced motion sickness can occur, as well as reduced figure-ground segregation ability (difficulty separating visual targets of interest from the background). With sufficient head trauma, more severe ocular motility disorders caused by injury or entrapment of the oculomotor, trochlear, or abducens nerves can lead to diplopia.[78]

Mild traumatic brain injury is typically not associated with severe structural damage to the inner ear, but concern should be raised when concussions are associated with severe prolonged spells of vertigo or hearing loss. In these cases, the following less common but more serious disorders should be considered.

SUPERIOR CANAL DEHISCENCE. Superior canal dehiscence is a disorder in which a likely congenitally thin roof of the superior (also called *anterior*) semicircular canal that separates the labyrinth from the intracranial space is dehisced. About half of cases of superior canal dehiscence occur after head trauma or barotrauma. Superior canal dehiscence symptoms include sound-induced spells of vertigo (ie, Tullio phenomenon), conductive and/or sensorineural hearing loss, tinnitus, and autophony. In rare cases, superior canal dehiscence can be caused by fracture of the temporal bone, but this is usually in the setting of severe head injury rather than concussion.[79]

PERILYMPHATIC FISTULAS. Perilymphatic fistulas are difficult to diagnose but should be suspected when head trauma leads to sensorineural hearing loss, vertigo, and tinnitus. They occur when the inner ear is connected to the middle ear through a ruptured oval or round window.[80]

ENDOLYMPHATIC HYDROPS. Primary endolymphatic hydrops is referred to as *Ménière disease*. Secondary or delayed endolymphatic hydrops can occur after head trauma when the force is strong enough to disrupt the membranous labyrinth and affect fluid pressure. Delayed endolymphatic hydrops symptoms include vertigo spells associated with hearing loss, tinnitus, and aural pressure.[81]

Criteria

Efforts are undergoing to categorize the different components of posttraumatic dizziness into symptom domains, and these categories may help focus therapy.

Causes

Concussion-related dizziness is diagnosed by the temporal profile of symptoms following the acute event, keeping in mind that multiple concurrent contributors to symptoms may be present. Unwitnessed events or associations made with a long temporal delay can make attribution of chronic symptoms difficult, however. Some symptoms from concussion may not be apparent at the time of injury but may occur after a period of posttraumatic inflammation.

Time Course

Balance problems generally resolve in a few days after a concussion, but abnormalities in the VOR predict longer recovery.[82] Dizziness that occurs

immediately upon impact, the presence of migraine headaches, preexisting mood or anxiety disorders, and impending litigation are predictors of slower recovery.[83] Symptoms that last beyond 4 weeks are considered part of the postconcussive syndrome, and the most difficult vestibular symptoms to treat are persistent spatial disorientation and unsteadiness.

Treatment

After a concussion, all patients should undergo positional testing for BPPV, a screen for auditory dysfunction, and an assessment for migraine headaches. Treatment should be tailored for these initial high-yield areas. Structural injury to the inner ear is uncommon, but red flags such as sound-induced vertigo and hearing loss should be ruled out. In most cases, concussions will not be associated with any measurable abnormalities despite severe symptoms. Vestibular rehabilitation should be offered to patients with persistent symptoms, particularly those with abnormalities in the VOR.[84,85] An optometrist trained in vision rehabilitation can help with ocular motility issues. Concussions can lead to complicated symptoms, including cognitive slowing, irritability, and chronic pain, all of which can impact recovery from dizziness. These additional symptoms can require management assistance from other specialties.

KEY POINTS

- **Concurrent ocular motor dysfunction and visual processing disorders may occur with postconcussion dizziness and can significantly add to morbidity.**
- **It is important to rule out structural injury to the inner ear after head trauma, particularly if severe vertigo or concurrent hearing loss is present.**
- **Graded vestibular rehabilitation is generally required for postconcussive dizziness along with a multipronged approach to address concurrent cognitive slowing, headache, anxiety, and mood dysregulation.**

CONCLUSION

Chronic dizziness can be caused by homeostatic perturbations, prolonged motion exposure, concussion, impaired vestibular function, or innate difficulties with habituation to motion. Although symptoms may initially seem intractable, methodically identifying modifiable factors can make untenable problems more manageable. Many of these chronic disorders can be treated with education, lifestyle modifications, vestibular rehabilitation, serotonergic antidepressants, and treatment of concurrent maladaptive thought processes. Giving patients a clear diagnosis, educating them on the nature of these disorders, and communicating reasonable expectations for the tempo of recovery are critical factors in the successful management of chronic dizziness.

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