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Vestibular Toxicity: Causes, Evaluation Protocols, Intervention, and Management

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Abstract

The loss of vestibular function, typically bilateral, due to chemical solvents and pharmacological agents is not rare and has been investigated and reported for many years. The successful treatment of bacterial infections and sepsis with IV antibiotics and cancer-fighting drugs like cisplatin makes the decision to use these life-saving drugs less of a debate, despite their potential deleterious effect on balance and equilibrium. The purpose of this article is to provide the reader with an overview of the more common substances found in industry and medicine which may decrease or permanently destroy peripheral and/or central vestibular function. A review of bedside and clinical evaluation protocols will be discussed as well as best practice intervention with balance retraining therapy. Finally, the role of the audiologist and opportunities for participation in an interdisciplinary approach to evaluation and management will be presented.

Keywords: vestibular, vestibulotoxic, balance retraining, fall-risk management

Whether encountered on the floor of a manufacturing plant or in life-saving cancer treatment, exposure to vestibular toxic chemicals or medications can be life-altering. Patients commonly suffer deficits in hearing and balance, but ototoxic chemicals also can disrupt central auditory and vestibular function and may be the genesis of tinnitus. [1] Although exposure to ototoxins may cause either auditory or vestibular loss, or both, this article will focus on vestibular toxicity.

Human equilibrium has been referred to as the sixth sense. When operating properly, this elegant system comprises three sensory modalities: vestibular, vision, and somatosensory, which provide accurate information, processing, and motor output responses to allow for navigation through the environment along with musculoskeletal control in response to gravity. Carefully coordinated movements for everyday living or challenging activities, such as balancing on a step-stool, or playing sports are managed through complex involuntary reflexes which require no thought or action. The paired vestibular sensory organs are recognized as being the most influential of these three sensory modalities. Responsible for at least twothirds of the information that the brain requires to make accurate responses to coordinate our head and eye movements and maintain our center of gravity (COG) over a moving and dynamic base of support (BOS) as occurs with normal ambulation.

When otologic disorders of the vestibular system arise, such as vestibular neuritis, Meniere's disease, or labyrinthitis, typically only one inner ear is affected. It is the sudden and significant drop in afferent firing from the involved ear that causes the debilitating vertigo. After an acute phase lasting perhaps 30 minutes to hours, the patient's return to normalcy may be based on a combination of recovery of inner ear and nerve function, predisposition to motion intolerance, and neural plasticity. When individuals cannot recover through a process known as central compensation, then nonmedical management with vestibular rehabilitation therapy (VRT) or balance retraining therapy (BRT) has been accepted as the gold standard of treatment, with excellent measurable outcomes. [2] Most often the individual is able to return to their normal activities without any residual symptoms. This is based on the brain's ability to adapt and operate with information only available from one functioning vestibular mechanism. Unfortunately, vestibular toxicity creates a more complicated deficit, which cannot typically be remedied as easily or fully by therapeutic intervention and is why a discussion of vestibular toxicity is of great importance. The purpose of this article is to provide the reader with an understanding of the causes, bedside and clinical evaluation protocols, as well as intervention and management strategies currently available for those individuals experiencing vestibular toxicity.

Causes of Vestibular Toxicity

There are two primary categories of causation of vestibular toxicity: chemicals and solvents used in manufacturing and industry and pharmacological agents employed to treat serious and oftentimes life-threating medical conditions. The impact of the toxicity may be amplified by several variables including exposure time, concentrations or dosage, influence of polypharmacy, as well as complicating medical comorbidities (e.g., diabetes). Although vestibular toxins may cause either unilateral or bilateral vestibular loss or hypofunction, the majority of dysfunction is bilateral due to the systematic nature of the toxins. Unlike acquired peripheral otologic-based vestibular disorders, affecting only one ear, bilateral losses tend to be more debilitating. With an inability of the brain to accommodate to the loss of both vestibular mechanisms and its central connections, the individual becomes visually surface dependent. They keep their balance with their eyes and sense of touch. By virtue of this, it is impossible to regain true normal equilibrium function and it is further complicated by any comorbidities (e.g., glaucoma, macular degeneration, and peripheral neuropathy) affecting vision or sense of touch.

Chemicals and Solvents

The association between industrial and occupational encountered chemicals and solvents and vestibulotoxicity has long been known. [3] There are a variety of frequently used agents in the workplace, especially grease cutting agents such as toluene and styrene, a by-product of fiberglass production. Workers in these industries, such as mechanics and repair personnel who use toluene to clean their hands, may ingest the solvents through osmosis as well as an inhalant. Many such chemicals and solvents may cause either peripheral end-organ hair cell destruction or neurologic damage to the balance centers in the brain. Table 1 lists commonly encountered known vestibulotoxic chemicals and solvents.

Pharmacological Agents

The two most commonly encountered vestibulotoxic medication groupings are in the aminoglycoside antibiotic and cisplatin families, [4] as shown in Table 2 . This family of drugs is used increasingly to combat difficult-to-treat and even life-threating bacterial infections. This often is a result of sepsis, often acquired during a hospital or nursing home stay. According to the Centers for Disease Control and Prevention, sepsis accounts for one in three hospital deaths. [5] Sepsis may be either bacterial or viral but is most usually bacterial and that is the reason for the use of strong antibiotics. The sepsis may spread throughout the body through the bloodstream damaging the vital organs.

Cisplatin is an effective and commonly used anticancer drug used in the treatment of tumor malignancies. It is delivered only through IV and does not exist in a pill form. While it is more associated with hearing loss and tinnitus, it may cause neuropathy, which will affect the individual's balance.

Evaluation Protocols

When evaluating the peripheral and central vestibular system, it is advisable to consider examination of the full system and critically important reflex arc: vestibulo ocular, vestibulo spinal, and vestibulo colic. The feasibility and ease of providing basic screening protocols must be considered, especially for those individuals receiving medical care, who may already be in hospital or debilitated, weak or deconditioned, or may simply not have access to more comprehensive testing facilities. Fortunately, there are several highly sensitive, easily administered bedside screening protocols which have good correlation with the more advanced clinical tests.

Bedside Evaluation Protocols

Dynamic Visual Acuity

A common indication of abnormal vestibular function is the presence of oscillopsia. Best described as the inability to have stabilized vision during active head movement in the frequency range of the vestibular ocular reflex (VOR) 0.5 to 6 Hz. Individuals with bilateral loss resulting in oscillopsia often report “I feel like my eyes need shock absorbers.” It may be exacerbated by trying to focus while walking on uneven surfaces or when walking or jogging at faster speeds, due to increased vertical head pitch with heel strike. Oscillopsia may be tested rather easily with the use of a Snellen chart, wall mounted or hand-held, and a metronome (can be downloaded as an app on a smartphone) to monitor frequency. Numerous investigators [6] have reported patterns of oscillopsia associated with unilateral and bilateral vestibular losses, with greater degrees of impairment for individuals with the bilateral loss. A baseline score is established by asking the patient to read the smallest/lowest line on the chart, without head movement. The test is then repeated, with the patient moving their head, first in the horizontal plane, followed by vertical head movement. If the patient's vision is blurred and he or she requires to go up three lines or more, to the larger font, it is considered a positive finding for oscillopsia in that particular plane of head movement. Researchers have shown that horizontal oscillopsia is more prevalent in peripheral losses, with bilateral losses showing degradation of vision in both the horizontal and vertical planes (Table 3).

Head Thrust Test

When the VOR is not functioning properly, the eyes cannot react correctly to the movement of the head within the frequencies of the VOR. The abnormal response is called the corrective saccade. The head thrust test has been long recognized as among one of the most sensitive bedside tests, first described by Halmagyi and Cuthroys. [7] In cases of acquired unilateral dysfunction, the correction, referred to as an overt saccade, will be observable when the head is moved toward the sick or affected ear. This corrective saccade, however, disappears days or weeks after the acute event and requires a computerized version of the test to see the unobservable to the naked eye covert saccade. This will be discussed in the Clinical Protocols section. In most cases of vestibular toxicity, because the loss is bilateral, the corrective saccade will persist and be observable with bidirectional head thrust.

Gans Sensory Organization Test with Clinical Test of Sensory Integration of Balance

The vestibulo spinal reflex (VSR) has been shown by investigators for more than 35 years to be one of the most consistent indicators of vestibular loss. [8] Using the simple premise, reported by Horak et al [9] that when there is vestibular dysfunction, the individual becomes visually and surface preference, using vision and touch to maintain balance. These patients were unable to maintain their COG over a dynamic BOS with eyes closed. The standardized result of individuals aged from 3 to 79 years indicates that other than attributing to other comorbidities, they should be able to keep their balance with vision denied.

Clinical Protocols

Computerized Dynamic Visual Acuity

The presence of oscillopsia is among the most common complaint of individuals with bilateral vestibular loss or acute onset unilateral loss or hypofunction. There are numerous standardized tests of dynamic visual acuity, using ototypes, numerals, or other visual targets. [10] These computer-based systems typically have audible metronomes or velocity detector headsets. The equipment will not run the test if the patient's head velocity is not moving in the correct direction or speed. In addition to providing a precise picture of the functional impairment, this evaluation can assist in the serial testing of the patient to demonstrate a cessation of further loss, as well as improvement in function during or after therapy (Table 4).

Video Head Impulse Test

Recently, a computerized version of the head thrust test has emerged and offers one of the most sensitive, comfortable, noninvasive protocols which is also portable and may be administered bedside or chairside. Standing behind the patient, the test is administered while the patient looks at a target directly in front of them while the tester holds their head comfortably in both hands and applies quick head impulses. It is well tolerated by children as young as 10 months of age as well as elderly individuals. There are versions which test only the horizontal plane, but most commercial systems also test the vertical plane. This allows for the evaluation of all six semicircular canals. The ability to demonstrate the presence of corrective covert saccades is a sensitive indicator of abnormality, but also may be used as a serial monitor and an indicator of improvement, recovery of the VOR function posttherapy.

Fig. 1 shows the video head impulse test (vHIT) with corresponding data presentation.

Rotation Testing

There are two widely accepted methods of rotation testing: active and passive. The term active means the patient will actively participate in the test, while passive indicates they will be seated during the test in a rotary chair and will not be asked to participate other than to keep their eyes open. Active rotation testing allows the patient to volitionally move their head at higher frequencies more consistent with everyday activities (1–6 Hz), while wearing a video-goggle with a velocity sensor. This provides a computerized analysis, across the VOR frequency range, of the gain (amplitude) and phase (timing) of eye movement relative to head movement. The anticipated abnormality with vestibular loss is low gain and high phase, meaning the eyes do not move far enough relative to head position but move too quickly. The benefit of this system is that it is less expensive than rotary chair, and highly portable. It requires only the video-goggle and laptop computer, and testing may be accomplished at bedside. It is also an excellent method of serial monitoring and documentation of recovery of function during or after therapy and may be used for young children and the older adult. The caveat is that it does require some degree of coordination, which on occasion is difficult for some patients to complete the full range of frequencies.

Rotary chair testing (RCT) is the traditional passive rotation test and is among the most reliable and objective. [11] It, like the active test, evaluates gain and phase with bidirectional rotation, but, of course, is limited to horizontal plane of acceleration. The benefit of all rotation testing is that it exerts a true physiologic stimulus, unlike the caloric test. Caloric testing is based on a thermal convection (warm or cool) using air or water irrigation, stimulating only the horizontal canal. This stimulus is aphysiologic and at an ultra-low frequency (0.003 Hz), well below the vestibulo-ocular reflex (VOR). RCT at 0.64 Hz is much closer to the lower limit of the VOR. Fig. 2 depicts a patient in a rotary chair with infrared video-goggle.

Videonystagmography with Calorics

Although videonystagmography has long been considered the keystone of vestibular assessment tools, the recent advances of rotation tests, vHIT, and cervical vestibular evoked myogenic potential (cVEMP) have added a great deal to the diagnostic armamentarium. The caloric test is now less desirable than in past decades for the determination of true bilateral vestibular loss. Numerous investigators have shown this in recent studies. The caloric test is subject to great inter- and intrasubject variability because of its dependence on the delivery of heated and cooled air or water across the ear, changing the temperature of the inner ear fluids within the horizontal canals.

Computerized Dynamic Posturography

The use of computerized and standardized postural stability tests is among the most sensitive in revealing the functional impairment caused by unilateral and bilateral vestibular loss. [11] Individuals with vestibular loss manifest with strong visual and surface preference. Simply put, they use their eyes and touch to manage their COG over a dynamic BOS. Computerized dynamic posturography (CDP) also has an additional sway-reference challenge which requires the patient to maintain their balance with a moving platform and visual surround which is responding to their movement. These standardized patterns can identify and differentiate normal versus vestibular and neurological descending motor tract disorders secondary to stroke, Parkinson's disease, etc. One component of the tests, Adaptation, evaluates the patient's ability to recover from a range of perturbations, as what may occur when someone is unexpectedly bumped or jostled. This helps better identify the individual's functional impairment and at what level of fall-risk they present. Likewise, it may serve as a valuable measure posttherapy to document successful treatment outcomes and prognosis. Fig. 3 is a photograph of a patient during CDP test.

Therapy and Activities of Daily Living

The loss of vestibular function may present the individual with life-altering decisions. For a younger individual, it may preclude their ability to engage in activities such as riding a bicycle at nighttime, playing an aggressive game of tennis, or continuing to work safely as a carpenter or roofer. For the older adults, it may no longer be safe for them to live alone and age in place, with a greater concern over fall-risk. This is of particular importance for individuals with comorbidities affecting sight and touch, which become the two-primary backup systems when the vestibular system becomes impaired. Unlike an acquired unilateral vestibular dysfunction, secondary to vestibular neuritis, where patients may recover their functional abilities, a bilateral loss of peripheral or central function will create additional challenges for individuals, as they will not have full capabilities even with the best therapy. The goal of therapy is to increase through substitution their ability to utilize the remaining sensory modalities of vision and proprioception to maximum capacity. This therapy may include both balance and gait training which focuses on improving function when in challenging environments. As can be seen in Figs 4 and 5 , the use of technology providing feedback on maintaining their COG over a dynamic BOS forces improved postural stability and ability to ambulate safely. The recent introduction of virtual reality therapy, which provides a realistic and safe environment for the patient, is showing great promise as a successful intervention tool. [12] Fig. 6 shows an individual participating in a virtual reality session as part of their balance therapy program.

The Role of Audiology

Audiologists can play a role in every facet of a patient's evaluation and treatment regimen. This important role is too often unfilled. For the most part, audiologists have not yet integrated themselves into the clinics, hospitals, and outpatient centers that serve as venues for chemotherapy and other cancer treatments. The fit, however, into these venues is potentially an easy one for all providers. During a cycle of treatment in a cancer center, patients undergo several sessions of drug administration that can last for hours at a time. During these treatment sessions, patients are very much a captive audience. Nurses, physicians, physical therapists, dieticians, and counselors alike take advantage of the nature of chemotherapy sessions to meet and see patients. In this way, the health care providers go to the patient, rather than having the expectation that the patient will know to schedule with the various health care providers. It follows that audiologists ought to make appearances during these midtreatment rounds as well.

The work of an audiologist in the context of ototoxicity, especially as the result of deliberate treatment for life-threatening diseases, is often referred to as *monitoring* . It is true that diagnostics for hearing and balance inform our understanding of the adverse side effects of the treatment methods used to address the patient's illness. But an audiologist can do much more for the patient with ototoxicity than follow a debilitating progression. Although changes in hearing, tinnitus, or vestibular function may encourage a review of drug dosage when reported to the managing physician, it is uncommon that the drug regimen will be altered significantly because of the lifesaving nature of the treatment plan. It is unlikely that questions about the health of someone's inner ear will prompt a physician to stop the administration of potentially lifesaving treatments altogether. Audiologists should thus avoid promoting their contribution to the treatment of patients undergoing ototoxic medications as monitoring, and instead opt for *management* . Semantically, management conveys action and perhaps most importantly an ongoing relationship. Management also more accurately accounts for the entire spectrum of an audiologist's potential contribution to a care team.

Audiologists play an important role in an interdisciplinary team, which will likely include physicians and physical therapists. The diagnostic protocols administered by the audiologist can identify the nature of a patient's imbalance and then facilitate the triage and intervention to help fortify a patient's safety and continued independent mobility. We propose that patients with ototoxicity, specifically due to cancer treatment, represent a population that is currently underserved by audiologists. By integrating into cancer treatment centers and working with local oncologists, audiologists can contribute to the treatment and recovery of patients.

Summary

The prevalence of vestibulotoxins in the workplace and in pharmacological treatments suggests a growing need for audiologists to be aware of their role in the evaluation, triage, and management of this population. The successful use of antibiotics and cancer-fighting drugs means that individuals will be living longer and more active lives post–medical treatment. Many of these individuals, however, will be living with significantly disrupted equilibrium, and will need the care of an interdisciplinary team composed of audiologists, physicians, and physical therapists who understand the best protocols for evaluation and successful therapeutic and interventional management.

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Footnotes

Conflict of Interest None.

References

1. Frisina R D, Wheeler H E, Fossa S D et al.Comprehensive audiometric analysis of hearing impairment and tinnitus after cisplatin-based chemotherapy in survivors of adult-onset cancer. *J Clin Oncol.* 2016;34(23):2712–2720. [PMCID: PMC5019759] [PubMed: 27354478]

2. Gans R, Katz J, Chasin M, English K M, Hood L J, Tillery K L.Vestibular rehabilitative therapyIn: Handbook of Clinical Audiology Seventh Edition., eds.Lippincott William & Wilkins; 2015425–433.

3. Arlien-Søborg P, Zilstorff K, Grandjean B, Milling Pedersen L. Vestibular dysfunction in occupational chronic solvent intoxication. *Clin Otolaryngol Allied Sci.* 1981;6(04):285–290. [PubMed: 6974623]

4. Campbell K CM, Le Prell C G. Drug-induced ototoxicity: diagnosis and monitoring. *Drug Saf.* 2018;41(05):451–464. [PubMed: 29404977]

5. Sepsis. Centers for Disease Control and Prevention. Available at:https://www.cdc.gov/sepsis/index.html. Published July 20,2018. Accessed December 10, 2018

6. Roberts R A, Gans R E. Comparison of horizontal and vertical dynamic visual acuity in patients with vestibular dysfunction and nonvestibular dizziness. *J Am Acad Audiol.* 2007;18(03):236–244. [PubMed: 17479616]

7. Halmagyi G M, Curthoys I S. A clinical sign of canal paresis. *Arch Neurol.* 1988;45(07):737–739. [PubMed: 3390028]

8. To-Alemanji J, Ryan C, Schubert M C. Experiences engaging healthcare when dizzy. *Otol Neurotol.* 2016;37(08):1122–1127. [PubMed: 27525623]

9. Horak F B, Jones-Rycewicz C, Black F O, Shumway-Cook A. Effects of vestibular rehabilitation on dizziness and imbalance. *Otolaryngol Head Neck Surg.* 1992;106(02):175–180. [PubMed: 1738550]

10. Schubert M C, Herdman S J, Tusa R J. Vertical dynamic visual acuity in normal subjects and patients with vestibular hypofunction. *Otol Neurotol.* 2002;23(03):372–377. [PubMed: 11981398]

11. Gans R E, Yellin M W. New York: Thieme; 2007. Assessment of vestibular function; pp. 540–566.

12. Neri S G, Cardoso J R, Cruz L et al.Do virtual reality games improve mobility skills and balance measurements in community-dwelling older adults? Systematic review and meta-analysis. *Clin Rehabil.* 2017;31(10):1292–1304. [PubMed: 28933612]

Figures and Tables

Table 1

Chemicals and Solvents with known Vestibulotoxicity

Toluene
Styrene
Xylene
Trichloroethylene
Ethyl benzene

Table 2

Pharmacological Agents with known Vestibulotoxicity

Aminoglycoside
Gentamicin
Cisplatinum
Tobramycin
Dibekacin
Streptidine
Carboplatin

Table 3

Bedside Vestibular Protocols for Assessment of Bilateral Dysfunction and Corresponding Predictive Value

Evaluation protocol	Anticipated results with bilateral vestibular dysfunction	Predictive value
Dynamic visual acuity test with Snellen chart	Oscillopsia in horizontal and vertical planes with head movement at 0.5 Hz and above. Requires the patient to go up 3 lines on eye chart	Moderate
Halymagi's head thrust test	Observable corrective saccades with bidirectional thrusts	Moderate
Gans Sensory Organization Performance test with clinical test of sensory integration of balance	Vestibular loss pattern—abnormal sway or fall on all conditions with eyes closed on dynamic surface and stepping Fukuda	Strong

Table 4

Clinical Vestibular Protocols for Assessment of Bilateral Dysfunction and Corresponding Predictive Value

Evaluation protocol	Anticipated results with bilateral vestibular dysfunction	Predictive value
Computerized dynamic visual acuity test	Oscillopsia in horizontal and vertical planes with head movement at 0.5 Hz and above	Strong
Video head impulse test	Presence of overt corrective saccades in all planes	Strong
Rotation testing	Rotary chair (passive rotation testing) results will indicate low gain and high phase for bidirectional rotation VORTEQ (active rotation) will show low gain and high phase beginning at the higher frequencies of the Vestibulo-ocular reflex and extending downward 2–6 Hz	Strong
Videonystagmography calorics	Bilateral weakness. Total of four bithermal calorics < 24 deg/s	Moderate
Computerized dynamic posturography	Vestibular loss or dysfunction pattern consistent with postural control utilizing vision and surface dependence	Strong

Figure 1

Video head impulse test (vHIT) is highly sensitive for bilateral and unilateral vestibular dysfunction.

Figure 2

Rotary chair testing provides a true physiologic stimulus and is a more reliable indicator of peripheral vestibular function than are calorics.

Figure 3

Postural stability testing with computerized dynamic posturography (CDP) provides a comprehensive assessment of functional balance impairment and fall-risk.

Figure 4

Gait therapy for patients with bilateral vestibular loss often is used in reducing fall-risk.

Figure 5

The use of interactive balance therapy protocols may accelerate the patient's ability to ambulate safely post–vestibular loss.

Figure 6

The use of virtual reality therapy plays an important role in helping patient's regain independence in everyday situations.