



## VESTIBULAR TOXICITY

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*This handout is intended as a general introduction to the topic. As each person is affected differently, speak with your health care professional for individual advice.*



### Key points

- Temporary or permanent damage to the balance system from certain drugs and chemicals. Fortunately, rare.
- Unborn babies, very young children, hearing impaired, and the elderly are most at risk.
- Well-known vestibular toxins include aminoglycoside (AG) antibiotics, platinum-based chemotherapeutic drugs, mefloquine, solvents, organophosphates, and heavy metals.
- Exposure may be unavoidable when treating potentially life-threatening conditions such as malignant tumours and severe infections.
- In other cases, equally effective non-toxic alternatives can prevent damage.
- Some toxins damage both the balance and hearing parts of the inner ear.
- Others damage only the balance parts or only the hearing parts.
- Lost vestibular or hearing function cannot be brought back. Early diagnosis may prevent permanent damage.

### What is vestibular toxicity?

The term “vestibular toxicity” is used on this page to describe damage to the vestibular system from toxic (poisonous) drugs and chemicals. Vestibular toxicity can damage the balance structures in the inner ear (semicircular canals and otoliths), the vestibular nerve (8th cranial nerve) and/or neurons in the parts of the brain that help control balance. The damage may be temporary or permanent. Although not a life-threatening condition, the effects of vestibular toxicity can have a major impact on quality of life.

The use of drugs toxic to the vestibular system is relatively common, particularly in patients with potentially life-threatening conditions such as malignant tumours and severe infections. Sometimes there is no alternative medication. In these cases, the risk of not using the drug can be far greater than the risk of possible damage to the vestibular system.

One or more side effects of thousands of medications can impair balance. Some of these medications suppress the vestibular system and may do so in a way that causes dizziness and imbalance. Others lower blood pressure and cause light-headedness. These effects are temporary and are not considered vestibular toxicity.

Some drugs and chemicals that harm the vestibular system also damage the hearing part of the ear (cochlea). Hearing loss and tinnitus (ringing in the ears) may result. However, some toxic substances are highly selective, damaging only hearing or balance.

Vestibular toxicity has not been widely investigated. It is likely the number of people affected is underestimated. Patients who have balance problems or dizziness but no hearing loss after

exposure to a toxic substance may have their unsteadiness or dizziness attributed to different cause. This is particularly true of very sick or frail patients. They may have no awareness of imbalance when they are bedridden. It is only when they return to walking that they notice problems with balance. By then, the damage may be severe and permanent.

Damage to the vestibular system from toxic substances is rare. While it affects all age groups, the overall number of people affected is unknown. Unborn children, babies, young children and people over the age of 65 are most at risk.

### Risk factors

The incidence and severity of damage to the vestibular system is dependent on the dosage and properties of the toxic substance itself. Heightened risk factors for damage may include:

- Length of time the drug or substance is in the body.
- Amount of exposure.
- How the substance enters the body (orally, drops into the ear, intramuscular injection, intravenously, absorption into the skin, or inhalation).
- Interaction and other types of interference from other drugs or substances.
- Exposure to more than one vestibular toxicant at the same time.
- Multiple incidences of exposure.
- Pre-existing vestibular disorder.
- General physical state.
- Other medical conditions such as congestive heart failure, pancreatic insufficiency, diabetic retinopathy and peripheral neuropathy, kidney failure, cirrhosis of the liver, and high blood pressure (hypertension).
- Reduced ability to eliminate the substance because of poor kidney function.
- Genetic susceptibility or allergic reaction.

- Exposure to both noise and toxic substance at the same time.

Older people are at particular risk. They often take multiple medications and tend to metabolize them more slowly. As a result, drugs tend to remain in the body for a longer period of time.

Medications toxic to the vestibular system should not be given to:

- pregnant women
- people who are hearing impaired and/or elderly if a non-toxic alternative is available

### What are the causes?

Medications and other substances known to cause significant vestibular toxicity include:

#### Aminoglycoside (AG) antibiotics

AG antibiotics have been used to treat some serious bacterial infections since the 1940s. Of all drugs, they are most toxic to the vestibular system. AGs work by stopping bacteria from making proteins needed for their survival. They are usually given into the veins of the body (intravenously). They can also be taken orally or as eardrops. Studies suggest no dose is safe no matter how AGs are administered.

Damage to the vestibular system happens in up to 15% of patients taking AGs. They are used in about 3% of patients admitted to hospitals. Patients with cystic fibrosis, immune dysfunction and certain chronic infectious diseases are more likely to be treated with AGs. Some people have mitochondrial DNA mutations that make them more susceptible to AG toxicity.

AGs can cause both temporary (reversible) and permanent damage to the balance structures in the inner ear. Damage happens first to hair cells in the semicircular canals and later in the saccule and utricle. An early sign of toxicity may be positional nystagmus (uncontrollable rapid eye movement). There is little damage to the vestibular nerve. The toxic effect gradually builds up over several weeks and is eliminated slowly. There may be a delay in

vestibular symptoms. In some patients treated with AGs for over 10 days, damage to the vestibular system may not be apparent until 1 to 10 days after treatment stops. It is important to monitor patients for vestibulotoxic effects for up to 6 months after stopping taking an AG.

Severe AG toxicity usually causes symmetric bilateral vestibulopathy. In some cases, hair cells may remain undamaged in the otoliths (utricle and saccule) either in one or both ears.

The likelihood of AG toxicity increases along with the use of several commonly used medications including:

- vancomycin (an antibiotic used to treat some serious bacterial infections)
- loop diuretics, such as bumetanide, ethacrynic acid, furosemide and torsemide (used to treat high blood pressure)
- cisplatin
- metronidazole (an antibiotic used to treat certain bacterial and parasitic infections)
- Of the AGs approved for use in Canada, two are highly toxic to the vestibular system:
- Streptomycin – in one study, 15% of patients treated with 1g of streptomycin daily for tuberculosis developed vestibulotoxicity.
- Gentamicin toxicity accounts for between 15 to 50% of people with bilateral vestibulopathy.

Gentamicin is more likely to be toxic when given in combination with vancomycin and/or along with exposure to noise.

Injection of gentamicin into the middle ear is an effective treatment for some people with Ménière's disease. It can completely eliminate dizziness. A downside is that about 20% of people have additional hearing loss after treatment.

Gentamicin given as eardrops appears to be toxic to the vestibular system when given over long periods of time. The use of eardrops containing gentamicin (Garasone<sup>®</sup>) has been banned in Canada for people with perforated eardrums. The drug can

enter the inner ear where it is absorbed into inner ear fluid, damaging both hearing and balance.

### Platinum-based chemotherapeutic (antineoplastic) drugs

These drugs are effective at inhibiting or preventing the growth and spread of tumours and malignant cells (cancers). A number of studies show a connection between platinum-based chemotherapy, especially cisplatin (Platinol<sup>®</sup>, Platinol-AQ<sup>®</sup>), and vestibular toxicity in some patients. Research suggests that patients with pre-existing loss of vestibular function are more likely to have vestibular toxicity after exposure to cisplatin. The toxicity of cisplatin varies significantly from patient to patient. Research suggests this is partly related to genetic variations.

### Solvents

Solvents are a group of compounds routinely used in commercial industries. Solvents have a toxic effect on the parts of the brain that process information about balance rather than the balance structures in the inner ear. Solvents influence the brain areas that control eye movements in response to head movements. The effects of solvents on the vestibular system are not as well documented as their effects on hearing. Combined exposure to noise and solvents is worse than solvent exposure alone. The following commonly used solvents are known to be vestibular toxicants:

- **Toluene diisocyanates (TDI)**  
An estimated 24,000 Canadians are exposed to TDI, mainly through inhalation, in their workplaces. The main occupational groups exposed include plastic processing machine operators, followed by labourers in rubber and plastics manufacturing, automotive service technicians, plastic product assemblers, finishers, and inspectors, and motor vehicle assemblers.
- **Styrene**  
An estimated 89,000 Canadians are likely exposed to styrene, mainly through inhalation,

in their workplaces. The main occupational groups exposed include automotive service technicians, plastics processing machine operators, and furniture finishers and refinishers.

- **Trichloroethylene (TCE)**

An estimated 9,800 Canadians are exposed to TCE, mainly through inhalation and skin contact, in their workplaces. The main occupational groups exposed are metal product machine operators, plating, metal spraying and related operators, and labourers in metal fabrication.

## Mefloquine

Mefloquine is one of the quinolone-class of drugs. Health Canada warns that mefloquine can cause permanent dizziness, vertigo, tinnitus and loss of balance in some people. Serious side effects not related to balance and dizziness include anxiety, paranoia, depression, hallucinations, psychotic behaviour and thoughts of suicide.

Mefloquine was formerly sold in Canada under the brand name Lariam®. It was commonly prescribed to travellers and members of the Canadian Armed forces deployed overseas during the 1990s. The generic version continues to be available but is now seldom prescribed. Mefloquine may be used when there are contraindications to prescribing non-quinolone malarials such as atovaquone/proguanil (Malarone®).

## Organophosphates

Organophosphates are the most widely used insecticides. They are used in agriculture, homes and gardens, as well as in veterinary practice. Very limited data suggests that organophosphates may damage the vestibular system.

## Heavy Metals

Research suggests there may be a link between lead and cadmium in the blood and vestibular dysfunction.

## What are the symptoms?

Symptoms vary from person to person, the nature of the exposure, whether one or both sides are affected, and whether the injury is mild or severe.

Signs of damage to the balance structures in the inner ear may include:

- \* Imbalance (disequilibrium) particularly in situations where vision is limited (such as with eyes closed, in dimly rooms or at night) or while walking on uneven ground.
- Oscillopsia (visual blurring with head movement). This symptom is caused by the loss of vestibular input on both sides (bilateral) to the oculomotor muscles. For example, head movement when walking may give a sense your surroundings are bobbing up and down. Turning the head to one side may give a sense your surroundings are whirling around. Severe oscillopsia can make clear vision impossible with even the slightest head movement. It makes it difficult to read and participate in activities of daily living.
- Spontaneous nystagmus (uncontrollable eye movements) or positional nystagmus.
- Ataxia (impaired coordination of voluntary muscle movements).

Vertigo (spinning sensation) and nystagmus are typically absent when the damage is to both inner ears at the same time, such when exposure to a vestibular toxin is systemic (whole body).

Symptoms of damage to the parts of the brain that process balance information sent from the inner ear include:

- increased postural sway
- positional nystagmus

If the toxic substance has also affected the hearing portion of the inner ear (cochlea), hearing loss and tinnitus may occur.

## How is it diagnosed?

If you suspect you or a loved one may have been exposed to a vestibular toxin talk to a doctor as soon as possible. Early diagnosis can prevent permanent damage.

A diagnosis of vestibular toxicity is usually a diagnosis of exclusion. The doctor will take a detailed history of your previous and current medical conditions as well as current symptoms. You will be asked about previous and current use of medications including ear drops. You may be asked to complete a questionnaire to assess how symptoms are affecting your quality of life.

You may be tested to confirm a deficit of the vestibulo-ocular reflex (VOR) if bilateral vestibulopathy is suspected. A diagnosis of BVW can be made at the bedside with the non-invasive head impulse test (HIT).

Depending on your symptoms, you may be referred to a specialist such as an otologist (ear nose and throat or ENT doctor), neuro-otologist, neuro-ophthalmologist or neurologist.

## How is it treated and managed?

Management emphasis is on preventing and limiting damage from vestibular toxicants. Strategies include:

- Trying to avoid exposure to vestibular toxicants. In many cases, a good non-toxic alternative can be used.
- Using the lowest therapeutic dose of vestibular toxic medication when it is medically necessary and there is no reasonable alternative.
- Limiting simultaneous exposure to multiple vestibular toxicants as well as noise to decrease the effect of damage.
- Exposure to toxic chemicals in some industrial processes may be unavoidable when elimination is not possible. Substituting the chemical or loud equipment with safer alternatives when possible.

- Taking steps to minimize the potential exposure to toxic chemicals by changing work processes, ventilation or protection (such as wearing hearing protection, protective clothing and masks).
- Reducing noise levels.
- Changing work schedules to avoid the hazards.

Unfortunately, once vestibular function is lost it cannot be brought back. It is up to the brain to learn to compensate for this deficit by using input from the eyes and proprioception (skin, muscles and joints). Patients with partial damage may have spontaneous improvement of symptoms.

Vestibular rehabilitation therapy, a type of exercise-based therapy, is the most effective treatment. Its goal is to help train your brain to relearn how to balance and how to respond to signals from the vestibular and visual systems. Results vary depending largely on:

- the severity of damage
- the health of the other parts of the balance system (visual and proprioceptive)
- whether one or both sides have been affected
- whether the damage was peripheral (inner ear) or central (brain)

People with one-sided vestibular loss will often make marked improvement in overall balance function with therapy aimed at improving habituation and substitution. Those with bilateral loss may be helped by vestibular rehabilitation therapy targeting adaptation and substitution.

Hearing amplification (hearing aids) or cochlear implantation may help people with hearing loss.

## What to expect in the future

Usually, damage is complete 6 months after exposure ends.

Most people with vestibular loss on one side (unilateral) will recover within a few weeks. About 20% will develop chronic unsteadiness and oscillopsia. Spontaneous compensation may occur,

or vestibular rehabilitation therapy can help people make significant improvement in overall balance function.

Vestibular loss on both sides (bilateral) is usually permanent. Unfortunately, hair cells in the inner ear do not regrow. People with bilateral loss are prone to falls. They are unlikely to return to their former physical activities, and their ability to function independently is impacted significantly.

Research is continuing into strategies and treatments that may help patients in the future.

These include:

- Identifying genetic variations to predict the severity of vestibular toxic effects.
- Identifying drugs with protective effects that can be used along with known vestibular toxicants to reduce the harmful effects of treatment.
- Vestibular implants are a promising technical solution to restore balance for those with bilateral vestibular loss.

## Visit our website

View this and other articles about vestibular disorders – [www.balance&dizziness.org](http://www.balance&dizziness.org).

In addition, find information about how the balance system works, the journey from diagnosis to treatment, building a wellness toolkit, and more.

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If you find the information in this handout helpful, we ask for your help in return. The cause of supporting those affected by balance and dizziness disorders with ad-free, up-to-date, evidence-based information written for Canadians needs you. Please become its champion – [donate to Balance & Dizziness Canada](#).

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