

# Preventing ototoxicity and its effects



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The term ototoxicity is used to refer to temporary or permanent damage to the audiovestibular system as a result of medicines or chemicals. The ototoxic substances may target:

- The vestibular system, which is important for balance
- The cochlea, which is the organ of hearing
- The auditory pathways, which convey signals from these structures to the auditory cortex/vestibular cortex
- A combination of these.

Although studies from many countries have shown that ototoxicity is not a major cause of hearing loss or balance problems, it is important as it is potentially preventable. It is more prevalent in low- and middle-income countries (LMICs) due to a lack of understanding amongst health workers and insufficient resources to identify improper use of medicines and chemicals. Health workers may not have come across ototoxicity in their training. Laboratories in hospitals may lack the facilities to monitor the blood levels of ototoxic drugs and industrial use of ototoxic chemicals may not be recognised as a cause for concern by those responsible for the care of the workers exposed.

## Causes of ototoxicity

Ototoxic substances can be medicines or environmental agents. A list of the more common ones can be seen in Table 1.

### Medicines

Ototoxic medicines could be administered by oral, intramuscular, intravenous routes and also given topically (e.g. eardrops when there is an eardrum perforation).

The most frequently used ototoxic medications are antibiotics (e.g. aminoglycosides such as gentamicin in Neonatal Intensive Care Units) and cytotoxic drugs (e.g. platinum-based chemotherapy regimes for specific cancers). Antimalarials such as quinine and its derivatives are still being used in certain countries and can occasionally be ototoxic.<sup>1</sup>

Factors which influence the effects of ototoxic medication are listed below:

- **Dosage:** ototoxic antibiotics such as gentamicin are often life-saving and can be used safely as long as the dosage is not too high. Blood levels would need to be monitored to ensure this.
- **Duration of treatment:** medication given at normal dose levels can be cumulative (e.g. aminoglycosides).<sup>2</sup>
- **Synergism:** combination medications can potentially be more ototoxic.<sup>3</sup>
- **Susceptibility:** some individuals may be genetically more likely to develop a hearing loss as a result of aminoglycoside medication. A change in one or more genes can render family members more likely to develop a sensorineural hearing loss. A hearing loss may have occurred later in life anyway, but the medication hastened its onset.<sup>4</sup>



It is important for health workers to be aware of ototoxicity. **IVORY COAST**

- **Coexisting medical conditions:** these can increase the risk of ototoxicity occurring, e.g. in chronic kidney disease as a result of impaired elimination of the drug.<sup>5</sup> Where there is an ear perforation, eardrops, as a result of prolonged use or frequently repeated courses, could cause ototoxic damage in the affected ear as the amount reaching the inner ear is increased (see Box).
- **Past medical history:** pre-existing acoustic trauma<sup>6</sup> and previous radiation for head and neck cancer<sup>7</sup> can make it more likely that ototoxic medication given subsequently, even at normal dosage and usage, can result in damaging effects to the inner ear.

### Environmental agents

Ototoxic environmental agents, such as organic solvents or industrial chemicals (see Table 1), can be inhaled or absorbed through the skin and damage sensory cells in the inner ear. Ototoxic solvents are used extensively in the paint, dry cleaning engineering, printing, plastic and rubber industries. Ototoxic chemicals include arsenic, which is used in weedkillers and the tanning industry.

The ototoxic effects of organic solvents or industrial chemicals can be enhanced in workers who are also exposed to loud noise.

Many countries have legislation which regulates exposure to these environmental agents as well as exposure to loud noise.

## Preventative measures

It is preferable and possible to prevent ototoxicity. If it has occurred already, it is important to detect it early to prevent further damage and manage it effectively.

- Medical practitioners should avoid using ototoxic medication unless absolutely necessary, e.g. in treating neonates, especially where there is other, non-ototoxic, medication available.
- Health practitioners should be made aware of ototoxic substances (Table 1), of the risk factors for ototoxicity, as well as symptoms of ototoxicity and available methods of management (see next sections).
- In settings where there are no alternatives to ototoxic drug usage, there should be a personalised ototoxicity monitoring programme to allow for harm-minimisation and early detection.<sup>8</sup>

### TREATING DISCHARGING EARS: BEWARE OF OTOTOXICITY

Topical aminoglycosides are still often used as a first-line treatment of chronic suppurative otitis media (CSOM), although they carry a risk of ototoxicity, especially with longer-term or repeated use.

It has been suggested that, when possible, topical quinolones be used, as they do not carry the same risk.<sup>11</sup>

When topical aminoglycosides are the only available choice to treat CSOM, ENT-UK has issued the following guidelines for safer use:<sup>12</sup>

- Only use a topical aminoglycoside in the presence of obvious infection when suitable non-ototoxic antibiotics could not be used.
- Do not use for longer than 2 weeks.
- If possible or practical, baseline audiometry should be performed before treatment (at least bone conduction thresholds).
- The justification for using topical aminoglycosides should be explained to the patient.

**TABLE 1 MOST COMMON OTOTOXIC SUBSTANCES**

Aminoglycoside antibiotics	Loop diuretics	Anti-malarials	Anti-cancer drugs	NSAIDs*	Environmental agents	Eardrops
Gentamicin Amikacin Tobramycin Neomycin Kanamycin Streptomycin	Furosemide Bumetamide Ethacrynic acid Bumetamide Torsemide	Quinine Chloroquine	Cisplatin Carboplatin	Salicylate Naproxen Ibuprofen	Toluene Xylene Ethylbenzene Trichloroethylene Benzene Arsenic	Aminoglycosides Boric acid (prolonged use)

\*Non-steroidal anti-inflammatory drugs

Sodium thiosulfate is used in some hospitals to reduce ototoxicity from chemotherapy (cisplatin). Several other substances have been proposed in the prevention of ototoxicity on the basis of animal studies: these include glutathione, amifostine, N-acetylcysteine and steroid therapy.<sup>9</sup> The use of these agents in humans awaits robust clinical trials.

## Symptoms

Those affected by ototoxicity may notice:

- A hearing loss: this usually starts in the high frequencies and may not be noticed by the patient initially.<sup>8</sup> The loss in the high frequencies results in difficulty discriminating speech, but the more normal low frequencies makes the hearing loss more difficult to detect.
- Hyperacusis: a greater sensitivity to loud sounds.
- Tinnitus: noises in the ear not caused by an external sound. It is usually the first sign of salicylate ototoxicity.
- Dizziness: a feeling of being off-balance.
- Vertigo: a sensation of your surroundings moving.

There may be a single symptom or several occurring simultaneously, and onset may be rapid or gradual. Severity may be very mild to total incapacitation resulting in profound effects on communication and daily functioning. The effect may be permanent and progressive or reversible resulting in a short duration of symptoms (e.g. reversible symptoms due to salicylate, from physiological effects on outer hair cells rather than permanent cell loss).<sup>10</sup>

## Assessment of hearing, tinnitus and balance problems caused by ototoxicity

In a specialist department, the patient's history will be gathered, the ear and its related areas examined and hearing, tinnitus and balance assessed.

Hearing, including the main speech frequencies, is assessed in each ear separately using an audiometer. An audiometer can also be used to assess the nature and extent of tinnitus.

Balance problems can also be assessed clinically or by specialised equipment if available.

## Management of ototoxicity

Initial symptoms could be temporary and improve once the medication is reduced or stopped.

Where there is permanent hearing loss, various options can be offered to optimise communication and improve quality of life (e.g. hearing aids, cochlear implants, assistive listening devices etc.) and advice can

be given to avoid further damage. It is essential to follow up these patients, as hearing loss could progress.

Tinnitus may require management with psychological support, tinnitus maskers (wearable electronic devices) and medication.

Vestibular problems (imbalance) can be helped by specific exercises.

## How health workers can help identify ototoxicity

Ototoxicity is preventable and the earlier it is detected, the better the outcome. Non-specialist health workers can play an important role in early diagnosis. They can do the following:

- Maintain a high level of suspicion when seeing patients who have had potentially ototoxic medication.
- Be aware of the risk factors for ototoxicity.
- Understand that ototoxicity could occur rapidly or take months to appear, so continual vigilance is therefore needed.
- Be aware that early signs of hearing or vestibular dysfunction may not be noticed by patients, carers or professionals due to several reasons, including the severity of a patient's illness and the gradual deterioration of the function.

### Symptoms and signs to enquire about when seeing a patient

- Do they have noises in their ears (tinnitus)?
- Have they noticed any unsteadiness/difficulties in maintaining balance?
- Have they noticed difficulties with hearing, including hearing when they are in a noisy place? (Noise can mask out some elements of a sound/speech signal.)
- Have others noticed that the patient has poor hearing?
- Do they sometimes find it difficult to decide where a sound is coming from?

### Useful checks

- Health workers can use their voices to gauge whether a hearing loss is likely to be present to a moderate or severe degree.
- Check if whispered voice can be heard by the patient at a metre's distance from the ear without being able to lip-read, as this may be an indication that there could be a mild high-frequency hearing loss.
- Speak out of sight with the voice raised in steps until it is heard; this can indicate possible severity of the patient's hearing loss.

**Any patient suspected of ototoxicity must be referred to a specialist department where the patient can be tested and treatment discussed.**

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