

Abstract

Title

Understanding Ototoxicants & Hearing Impairment

Background

Most of the **Ototoxicants** are SVHCs in the global supply chain. These substances are hazardous to health if used as antibiotics, pain killers, anti-anxiety, anti-depression, anti-cancers, and blood pressure controlling.

Animal and human study shows their effects on hearing process resulting in hearing impairment or hearing temporary or permanent loss. It may happen alone or in combination of occupational environmental exposures (synergistic). Chemicals like mercury, lead, gas like carbon monoxide and medicinal use of aspirin, quinine, loop diuretics, streptomycin, and chemotherapy like cisplatin could damage hearing organs structurally or the nerves system resulting in tinnitus including like dizziness, nausea, and imbalance.

Objective

Knowing more on ototoxicants as SVHCs, exposures and hearing problem developed by their use. Physicians should know the conditions of their specific use and data on each substance prescribed.

Method

This article is a review of the literature on ototoxicants as SVHCs available in the global supply chain. The author is interested in regulatory affairs; classification based on occupational exposures limits (OELs) while monitoring SVHCs as a class of ototoxicants and their dose (toxicity).

Results:

Ototoxicants as chemicals or their mixtures have potential to hearing loss and impairment of inner ear (cochlea) as a result of study on human and animals. There is a need of further study to classify ototoxicants as separate class of SVHCs, risk evaluation, usage, data, thereby, establishing OELs or PELs like US OSHA or the recommended values by the ACGIH or NIOSH.

Conclusions:

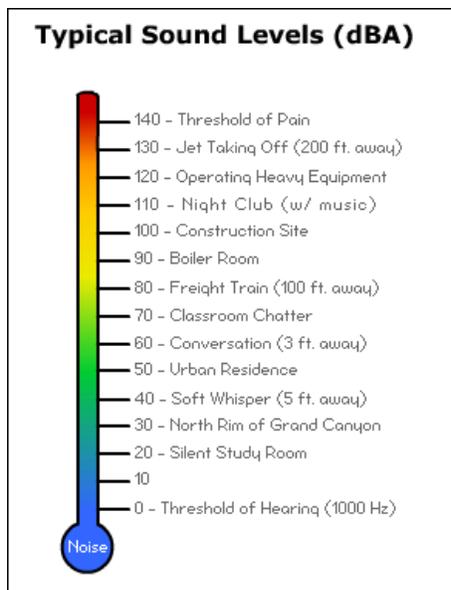
Health care providers should review:

- The data available on ototoxicants in the global supply chain.
- Diagnose from knowing the individual's history, symptoms, and test results.
- Advise patients on the use of these substances; use of hearing protection, avoiding high noise sources, stayed hydrated while monitoring patients' hearing.
- Audiologists or otolaryngologist to identify the ear damage; diagnose treatment options for patients on ototoxicants.
- Education, minimum use of these SVHCs, monitoring and continued research on the replacement of these substances by non-ototoxicants recommended.

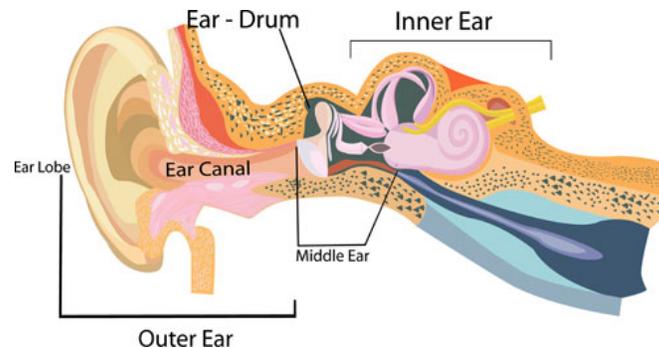
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Our Ears



Understanding Ototoxicants & Hearing Impairment

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Hearing loss could be temporary or permanent. Everyone experience more or less temporary hearing loss while or after flying. Permanent hearing loss could be as part of the aging process or by ototoxicants which are chemicals that could damage some parts of ears, eardrum, or the auditory canal resulting in hearing impairment alone or in combination with excessive noise (synergistic exposure).

All outer and middle ear causes of hearing loss result in conductive hearing loss; nearly all inner ear causes result in sensorineural hearing loss. Though hearing loss occurs with steadily increasing age which is 3% at ages 21-34 and increase to 43% at ages 65-84. Worldwide, estimates from the World Health Organization are that hearing loss affects 538 million people.

Hearing loss could be related to any part of the ear apparatus. Most common causes affecting these parts of the ear apparatus are congenital defect, infection, acoustic trauma, presbycusis, sociococcus, noise induced, vibration health effects, and tumor. This article concentrate on substances of very high concerns (SVHCs) or toxic substances of routine life use that lead to ototoxicity.

The effect of these substances could be temporary only restricted to the period of their use and sometimes these effects appear after their use and could be permanent.

The aim of this article is to educate the reader regarding ototoxicants and to abstain from these chemicals as for as possible.

Literature research shows that some of these are substances of very high concerns (SVHCs) such as pharmaceuticals, certain pesticides, solvents; metals may harm the hair cells, if repeated, the exposures could result in permanent or temporary noise-induced hearing loss or other types of hearing losses. **European Union (EU)'s Chemical Agency (ECHA) has systems for database for substances of very high concern (SVHCs) in products containing ototoxicants in the global supply chain.**

The risks of hearing losses are more when people are allowed to use these chemicals at the same time working or living near the potentially high or elevated noise levels. The US Occupational Safety and Health Administration(OSHA) has a noise occupational standard under 29 CFR 1910.95 that requires employers to have a hearing conservation program in place if workers are exposed to a time-weighted average (TWA) noise level of 85 decibels (dBA) or higher over an 8-hour work shift. See the above figure, typical sound levels as dBA by the US OSHA. 90 dBA is the action level, above this level; it violates the OSHA Occupational Noise Standard. See above figure for three parts of the ear: external, middle, and the inner ear.

Types of Hearing Loss

Known types of hearing losses are:

- **Conductive:** outer and middle ear, generally lose loudness only.
- **Sensori neural:** Occurs in the inner ear
- **Mixed** may be the combination of above a and b
- **CNS:** between the inner ear and brain

- **Psychogenic:** Functional or non-organic hearing loss
- **Chemicals (Ototoxicants):** Pharmaceuticals, certain pesticides, solvents, metals etc.

Chemicals as Known Ototoxicants

Ototoxins can also cause hearing loss by damaging the cochlear hair cells caused by combination of chemicals and high noise. Combination with high noise levels and exposures of long time use of chemicals may result in hair impairment.

Organic solvents are the most commonly identified chemicals, but others may also be involved for example metals and chemical asphyxiants. The hearing frequencies affected by solvent exposure are different than those affected by noise. Research suggests that solvents may interact synergistically with noise. **Even when noise and chemicals are at permissible exposure levels (PEL), the impact of a combined exposure can do more damage than a higher exposure to either hazard alone.**

Chemicals in Association with High Noise Levels

Benzene, carbon disulfide, carbon monoxide, ethyl-benzene, hydrogen cyanide, lead, mercury, n-hexane, solvent mixtures, styrene, trichloroethylene, toluene, xylene, organic solvents are ototoxicants. They are widely used in automotive and aviation fuels; in plastics industries; as thinners for paints, lacquers and dyes; in the manufacture of detergents, medicines, perfumes, fabric and paper coatings, printing inks, spray surface coatings; and in insect repellents.

The ACGIH notes on the 2019 TLVs BEIs Booklet-Audible Sound also referenced arsenic, carbon disulfide, chlorobenzene, mercury, nitriles, n-hexane, pesticides and trichloroethylene as ototoxicants under investigation.

European Union Chemical Agency (ECHA)

ECHA still working on several steps to be taken before going through the implementation of submitting notifications to the agency, and the strong role that member states have to play in this respect. There is also need look at the involvement of national authorities and how they will interpret this legal text, which they will need to translate into their national law, as well as how it could be process in harmonizing across the EU. **Rule making process definitely takes time before becoming the part of regulations.**

Medical review and Ototoxiciry

The types of hearing loss described above due to the ototoxicants are well known having effects to the auditory hearing loss due to damage to the inner ear or the hearing nerve resulting to hearing loss from very mild to very severe loss.

Ototoxicity is the property of being toxic to the ear (oto-), specifically the cochlea or auditory nerve and sometimes the vestibular system, for example, as a side effect of a drug. The effects of ototoxicity can be reversible and temporary, or irreversible and permanent. Common signs of ototoxicity are the ringing or buzzing sounds in ears (tinnitus), dizziness or loss of balance

It is very important to maintain and keep the ears functioning properly. We should be aware of which medications and treatments have been found to cause hearing loss in some patients while knowing which medications ototoxic and could damage ears. According to the American Speech-Language-Hearing Association, there are currently more than 200 of them on the market. It is important to consult a doctor of the hearing care professional immediately if you are on medication and notice the symptoms of hearing loss such as tinnitus, or vertigo immediately to prevent further damage or complication due to the long term use of medications. The most common medications known to cause hearing loss are:

- Large quantities of aspirin (usually 8 to 12 pills a day)
- Quinine, which is found in muscle relaxants for night cramps and some malaria medications
- Loop diuretics intended for high blood pressure and heart problems
- Certain antibiotics used to treat kidney disease and similar conditions, usually the group known as aminoglycosides. Erythromycin and tetracyclines are also ototoxic.
- Certain antidepressants, including the SSRIs Celexa, Luvox, Paxil, Prozac, and Zoloft, as well as the tricyclics Clomipramine and Amitriptyline
- Some methods of chemotherapy, such as cisplatin, carboplatin, 5FU, nitrogen mustard or bleomycin
- Heavy metals like lead, mercury, cadmium and arsenic.

Nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most common pain relief medicines in the world. NSAIDs such as naproxen and ibuprofen particularly in adult men may be ototoxic and contribute to hearing loss. For more info, visit the web page at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2831770/>.

With so many potential risks for your hearing, it is important to keep a record of how your hearing changes when beginning a new medication.

Have a baseline test of your hearing performed before and after starting treatment of known ototoxic drugs to determine whether hearing loss has occurred. This will make it easy to decide how to proceed without having to sacrifice your hearing health, though you should plan to have regular hearing tests performed as you monitor your progress. It is up to your doctor to determine the hearing loss due to the specific medicine that is causing hearing loss while suggesting some steps for improving or restoring your hearing. It is hard to diagnose hearing loss due to ototoxicants but there are some factors you can watch for:

- Long-term, high-dose exposure to ototoxic chemicals
- Cumulative lifetime dose of drugs that could have ototoxic effects
- Impaired kidney function
- Simultaneous ingestion of multiple ototoxic drugs
- Age
- Existing hearing loss or ear damage
- Pregnancy
- Previous exposure to head and neck radiation
- Genetic pre-disposition or family history of ototoxicity

For further information on ototoxicants, consult your personal physician or a doctor of the hearing care professional immediately if you are on medication and notice the symptoms of hearing loss such as tinnitus, or vertigo immediately to prevent further damage or complication due to the long term use of ototoxicants.

It is a good idea review the Safety Data Sheet (SDS) once identified and confirmed by your doctor. Your doctor may prescribe some non-ototoxicants medication to avoid any further hearing loss.

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- US OSHA News Release on Preventing Hearing Loss Caused by Chemicals (Ototoxicity) and Noise Exposure, web page at:
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Very Respectfully,

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