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Drugs That Can Damage Your Ears (Ototoxic Drugs)

Ototoxicity—The Hidden Menace

Part II: Ototoxicity and the Practice of Audiology

© November 2003 by Neil Bauman, Ph.D.

[Part I](#) of this series presented an overview of the hundreds of ototoxic drugs currently available and how their potential side effects relating to hearing and balance turn countless lives upside down. Part I also detailed risk factors that predispose people to ototoxic effects and concluded with what individuals can do to reduce their risk.

In Part II, we'll examine things you, as an audiologist, can do to help your patients when their ears "butt heads" with ototoxic substances.

Think "Drugs" When Assessing Hearing Loss

As you know, when patients present for hearing evaluations, it is important to ask what medications they're taking. However, the importance of this questioning is not limited to a thorough and complete history. Rather, this knowledge may indeed impact their current status and future-based medical decision making.

If you look up their medications in [Ototoxic Drugs Exposed](#),¹ you'll quickly get an idea as to what may be happening to their ears. If ototoxic side effects started (or increased) around the time they began taking certain drugs, the ototoxic "index of suspicion" is elevated, and indeed, their current medications may be damaging their ears.

Given an elevated index of suspicion, and armed with objective data, you might contact the physician and suggest that perhaps alternative, non-ototoxic alternative medications might be an option.

For example, suppose a patient comes to you with severe hyperacusis which is disrupting her life. What do you do? Do you immediately think of something like Hyperacusis Retraining Therapy, or do you think "drugs?"

I suggest as a first step—think "drugs."

When patients ask me what they can do about their hyperacusis, among the first questions I ask is, "What happened in your life just before the hyperacusis began? Did you start taking new medications or was there

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a change in the dose of existing medications?" I ask for a complete list of their medications and I look them up in [Ototoxic Drugs Exposed](#) to see if any of them are known to cause hyperacusis. If any of them are known to cause hyperacusis, I suggest to the patient that he/she contact the doctor to investigate alternative drugs with the same benefits, but without hyperacusis as a known side effect. In certain situations, I may communicate directly with the physician on these issues.

Case 1:

A psychiatrist explained that a patient of hers had several psychiatric problems, but the one thing bothering the patient above all else was severe hyperacusis. The patient had tried hyperacusis remedies without improvement. The psychiatrist asked me if there was anything that might help her patient.

My first reaction was to "think drugs." I asked what medications the patient was on and what medications she had been on at the time the hyperacusis began. When I received the list of medications, I discovered that this patient was taking not just one, but three drugs known to cause hyperacusis! Of all the thousands of drugs on the market, only 38 are known to cause hyperacusis, yet this poor patient was taking three of them at the same time!

I suggested the psychiatrist consider taking the patient off those three particular medications (if medically possible) and then see whether the patient's hyperacusis was reduced or eliminated.

Case 2:

A man contacted me telling me had severe tinnitus and he wanted to know if there was anything he could do about it. Instead of suggesting a tinnitus masker or Tinnitus Retraining Therapy (TRT) or other treatments, I immediately thought "drugs." I asked if he had started any new medications about the time his tinnitus began.

He told me his doctor had recently put him on **Amitriptyline**. I suggested he ask his doctor to change his medication, if possible, as **Amitriptyline** is known to cause tinnitus. A couple of weeks later, he wrote me again, saying that 12 days after he stopped taking the **Amitriptyline**, his tinnitus went away. Again, the solution was simple and effective. Think "drugs."

Case 3:

A woman contacted me as she was experiencing annoying tinnitus and increasing hearing loss. As is my custom, I thought "drugs." I discovered she had been self-medicating-taking large doses of Aspirin each day for the nearly-constant headaches she often suffered.

I suggested to her that her hearing problems and her tinnitus were very likely a direct result of taking all that **Aspirin**. She stopped taking

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I especially encourage you all to leave comments about good ear specialists so others will know who is particularly good for the various ear conditions you have gone to a doctor for.

Do your part

to warn others of the bad doctors out there, and point them to the competent, caring, knowledgeable ear specialists that can best help them.

Aspirin. Six days later she wrote, "I have noticed that I am hearing better now. I have the TV volume set at level 18 instead of the usual 24. The ringing in my ears is still there but it is not as bad." Three days later she added, "Today when someone was talking behind me, I heard every word he said. My hearing still isn't perfect, but it is better than it was."

The people in the above examples didn't need expensive or extensive therapy or hearing aids. What they really needed was someone to help them see that they were damaging their ears due to medications they were taking. In many cases, you'll be able to help your patients more when you first think "drugs."

While You Are Thinking "Drugs," Think "Chemicals" Too

It is not only ototoxic drugs that damage our ears, there are at least 148 ototoxic chemicals that also give us grief.¹

Two of the more ototoxic classes of chemicals are the organic solvents and the heavy metals.

There are a number of organic solvents. Some of them are **benzene, benzyl alcohol, butyl alcohol, carbon disulfide, carbon tetrachloride, heptane, hexane, styrene, toluene, trichloroethylene** and **xylene**. Ototoxic heavy metals include arsenic, **cobalt, lead, manganese, mercury** and **trimethyltin**.

Most people likely have a number of ototoxic chemicals in or around their homes. Some of these ototoxic chemicals include adhesives, auto emissions, fungicides, glues, grease and spot removers, insecticides, insulation, lacquers, liquid correction fluid, organic solvents, paint, paint thinners, resins, room deodorizers, rug cleaners, spray paint, varnishes and wood preservatives to name a few.^{13, 14}

In addition, people may be exposed to ototoxic chemicals if they work in one of the many manufacturing plants and factories that use organic solvents or heavy metals. Such processes as electroplating, shoe manufacturing, dry cleaning, cold vulcanization, electronic battery manufacture and polyvinyl chloride manufacturing all use various ototoxic chemicals.¹⁴

Further, the pollutants in the air can also hurt peoples' ears. Depending on the type and severity of the air pollution, people can end up with hearing loss, balance problems or other damage to their ears.²

Most people probably think of air pollution as occurring outside. However, dangerous air pollution also resides within homes, offices and factories. Many of the indoor pollutants are organic solvents. When people inhale fumes from these solvents, they slowly but surely damage their ears.

One study of workers in a rubber factory revealed 47% had subclinical abnormalities in the auditory pathways and in their brainstems, due to solvents used in manufacturing rubber.¹⁶ One patient lost her hearing resulting from several years of using spray varnish in her garage without adequate ventilation. **Toluene** in the varnish was the culprit.

Sometimes, ototoxic damage from organic solvents is obvious—such as when it results in massive hearing loss or roaring tinnitus. However, in other cases (see above study) results can be insidious and subtle, presenting as impaired central auditory processing. Even though the chemical hasn't caused reduced "hearing" as might be expected on an audiogram, the person affected can't understand everything they hear.

A bit of probing may reveal that hearing loss is the result of exposure to an ototoxic chemical where you least expect to find it. Therefore, in addition to thinking "drugs," also think "chemicals."

Drug Interactions and Ears

Little is known about how ototoxic drugs adversely affect our ears. Dramatically less is known about ototoxic side effects when two or more ototoxic drugs are consumed at the same time. However, some interesting (and important) things have come to light in recent years.

Be Careful When Concurrently Taking Ototoxic Drugs

When a person takes two or more ototoxic drugs at the same time, or one immediately following the other, there are two likely outcomes. The ototoxic effects of each drug can either be additive, or the ototoxic effects can be synergistic.

In the first case, the total effect on the ears will be the sum of the effects of each drug as if they were taken separately. For example, if one ototoxic drug causes 2 "units" of damage and the second drug causes 3 "units" of damage, the resulting damage on the ear would be 5 "units" ($2 + 3 = 5$). This is the additive effect.

However, with some drug combinations, using the same example above, the result is not 5 "units" of damage as you might expect, but a larger number—say 10 "units" of damage. This represents a synergistic effect. With synergistic effects, the resulting damage is always greater than the sum of the damage of each individual drug.

To protect ears as much as possible, people should not take multiple ototoxic drugs at the same time, especially if they are known to have synergistic ototoxic effects.

The Order of Multiple Ototoxic Drugs Can Be Important

Researchers have discovered that the order a person takes certain ototoxic drugs can make an enormous difference as to whether they have much of a resulting hearing loss or not. With some drug

combinations, if you take the drugs sequentially, and not simultaneously, you can avoid the synergistic effect.

For example, in one medical treatment, doctors put their patients on two drugs, a LOOP DIURETIC (e.g., **Furosemide**) and an AMINOGLYCOSIDE antibiotic (e.g., **Tobramycin**). If the patient completes the course of the LOOP DIURETIC **before** he begins the AMINOGLYCOSIDE antibiotic, the resulting hearing loss from these two drugs is additive. However, if the patient takes both drugs simultaneously or if the AMINOGLYCOSIDE antibiotic is administered first, followed by the LOOP DIURETIC—the two drugs act synergistically to significantly damage the patient's ears.²⁵

The Synergistic Relationship Between Certain Drugs/Chemicals and Noise

Not only do certain ototoxic drugs react synergistically with each other, but they have another nefarious characteristic. Their ototoxic side effects can react synergistically with noise.

Certain ototoxic drugs when taken "normally" can result in a certain degree of hearing loss. However, if they are being taken while the patient is exposed to loud noise, the noise combines synergistically with the ototoxic side effects of the drug to cause even greater hearing loss than might otherwise be expected.

Some of the drugs that have this vicious effect include **Aspirin**,²⁰ the anti-cancer drug **Cisplatin**,²² the microbial antibiotic **Chloramphenicol**³ and AMINOGLYCOSIDE antibiotics such as **Gentamicin**¹² and **Kanamycin**.²³

This same synergistic effect on hearing loss between the ototoxic side effects of certain drugs and noise also occurs between certain chemicals and noise. Chemicals that make our ears more prone to hearing loss as a result of noise include organic solvents such as **carbon disulfide**, **dinitrobenzene**, **styrene**, **trichloroethylene**, **toluene** and **xylene** as well as the asphyxiant **carbon monoxide** and the heavy metal **lead**.^{4, 10, 17, 26}

Other chemicals with this same nefarious characteristic include **arsenic**, **butyl alcohol**, **butyl nitrite**, **heptane**, **hexane**, **manganese**, **mercury** and **trimethyltin**.¹⁹ This apparently is just the tip of the iceberg. Suspicion is already cast on **carbon tetrachloride**, various other metals and asphyxiants.^{17, 20}

Just how pronounced is this synergistic effect? Sometimes the results can be dramatic! In a study of Brazilian workers, those exposed to both noise and **toluene** had a 53% incidence of hearing loss. In contrast, those exposed to noise alone had a 26% incidence rate while the control group had an incidence rate of only 8%. When these results were adjusted for age, they showed that noise exposure increases the risk of

hearing loss by 4.6 times. When the noise was combined with exposure to **toluene**, the risk jumped a whopping 27.5 times!²¹

In another study, workers were grouped into one of four groups—those exposed to both noise and **toluene**, those exposed to **toluene** alone, those exposed to noise alone, and those not exposed to either **toluene** or noise (the control group). The hearing loss of those exposed to noise alone was 4 times greater than the control group; the hearing loss of those exposed to **toluene** alone was 5 times greater; and the hearing loss of those exposed to both noise and **toluene** was 11 times greater!¹⁷

Noise and Time Are Critical

One treacherous result of certain ototoxic drugs combined with noise is something you'd probably never suspect—the length of time a person's ears are still susceptible to the synergistic effects of ototoxic drugs and noise—**after** the drug has been discontinued.

If you tell a person not to take certain drugs while he is exposed to noise, he might think you are referring to the days he is actually taking the drug therapy. Surprise! Not true! A person has to avoid noise for much, much longer.

When a person takes AMINOGLYCOSIDE antibiotics or platinum anti-cancer drugs, such as **Cisplatin**, they are quickly transported to his inner ears. The problem is that, once there, these drugs persist in the inner-ear fluids long after they have disappeared from the bloodstream,¹¹ not just for a few days, but for several weeks to several months,¹⁵ and up to a year later!

During the time these drugs are present in peoples' inner ear fluids, they can be damaging their ears. More importantly, during this time, their ears are especially susceptible to the synergistic effects of loud noise.¹⁵ This means that if people have taken AMINOGLYCOSIDE antibiotics or **Cisplatin** and are now finished with this drug therapy, their ears are still in danger of even more hearing loss if they expose them to loud noise any time in the next few months or more, depending on their specific body chemistry.

This has important implications for the audiologist treating hearing aid patients with hearing aids and other amplification systems. Dr. James Kalkanis, M.D., recommends setting the gain and maximum power output (MPO) as low as possible in order to protect your patients' ears while their ears are very sensitive to the effects of noise, secondary to ototoxic medications. If a patient already wears hearing aids, you should instruct him to keep the volume down during this time also.¹⁵ The same is true for people exposed to ototoxic chemicals in the workplace. Workers exposed to ototoxic chemicals should be advised that it is in their best health interest to keep the volume down on their hearing aids, and to keep the work environment as quiet as is possible.

What is a safe level in such situations? The only thing known for sure is that current standards are not stringent enough. Researchers were surprised to discover that when noise and ototoxic agents team up to damage ears, this damage can occur even though exposure to both noise **and** chemicals are **within currently acceptable limits!**¹⁰

High Frequency Hearing Testing is Important

Many ototoxic drugs and chemicals begin destroying hearing at the highest frequencies first, and as exposure continues, lower frequencies become involved. Since hearing is traditionally only tested up to 8 kHz, most **initial** cases of hearing loss from ototoxic drugs and chemicals are **never** revealed by standard audiometric testing.

However, high-frequency audiometry is important if hearing loss from ototoxic drugs is to be minimized or prevented. High-frequency audiometry can reveal the early effects of ototoxic drugs before tinnitus appears or hearing damage is visible on a conventional audiogram (250 and 8,000 Hz).

In studies involving **Cisplatin**, the **first** indications of hearing loss **always** appeared between 10,000 and 16,000 Hz.²⁴ Of course, standard audiometric testing would not have revealed this hearing loss, as it impacts higher than typically tested frequencies.

Several ototoxic chemicals cause **initial** hearing loss in the high frequencies. For example, high-frequency hearing testing revealed that workers exposed to low concentrations of **styrene** fumes for 5 years had hearing losses in the high frequencies even though their hearing tests in the conventional frequencies were normal. If high-frequency hearing testing hadn't been done, **styrene** could have been given a clean bill of health—even though it is ototoxic.

Inhaling **styrene** fumes is known to cause a reduction in the upper limit of hearing. Researchers concluded that the upper limit of hearing is a sensitive indicator for early detection of ototoxicity in workers exposed to **styrene**¹⁸ and indeed, probably for many or most ototoxic drugs and chemicals.

One study demonstrated that audiometric testing across the conventional hearing range is the **least effective** method to determine initial hearing loss.⁵ Therefore, if you want to know whether drugs or chemicals are insidiously stealing your patients' hearing, you need to test their hearing up to the highest frequency possible.

Since ototoxic hearing loss typically begins at the highest frequencies and progresses through lower ones, audiologists should monitor the highest measurable frequencies in people with pre-existing hearing loss, to provide the earliest possible warning of further drug-related hearing loss.

Early detection does not, by itself, prevent further damage to a person's ears. However, it does give doctors time to adjust the dose or stop the medication altogether before hearing loss spreads to the conventional frequencies.⁶ If monitoring is restricted to frequencies below 8000 Hz, by the time audiologists detect new/additional hearing loss, hearing loss will have already affected those frequencies necessary for speech.

How good is high-frequency testing? When researchers compared testing high frequencies versus testing conventional frequencies, one study revealed that 52% of hearing losses were first detected in the high-frequency range only. That study revealed that more than half the people with drug-induced hearing loss have hearing loss that was **not** detected by conventional means. If only high-frequency hearing testing had been done, 67% of all the ears demonstrating initial hearing loss due to ototoxicity would have been found.⁷

Another study revealed that only 13.5% of the people (ears) studied had initial drug-related hearing loss in the conventional frequencies. An additional 24% had initial detectable hearing loss in the conventional frequencies as well as the high frequencies. Thus, a whopping 62.5% of drug-induced hearing loss likely goes undetected because it initially **only** occurs in the traditionally not-tested high frequencies!⁸ If only the high frequencies had been tested, 86% of all cases of drug-induced hearing loss would have been detected.

The Five-frequency Hearing Testing Process

Testing all frequencies between 125 Hz and 20,000 Hz is time consuming and of course, adds additional expense to the evaluation. Fortunately, researchers have recently discovered a five-frequency slope that is very sensitive to the ravages of ototoxic drugs. The beauty of this five-frequency slope testing is that it is highly sensitive to **initial** ototoxic hearing loss.

This five-frequency range varies depending on each person's pre-existing hearing loss and thus is unique to each person. These five frequencies are generally separated by 1/6 octave.

For example, a person with pre-existing hearing loss might have a five-frequency slope consisting of 8, 9, 10, 11.2 and 12.5 kHz.⁹ Since each person's hearing loss is unique, the testing process is tailored for each person and this can be easily and accurately accomplished.

Using an audiometer calibrated to accurately test up to 20,000 Hz, determine the highest frequency your patient can hear. (Note: the hearing loss at this frequency must be 100 dB or less.) Second, test this frequency and the next four lower consecutive audiometric test frequencies. This becomes the individual patient's five-frequency slope range.⁶

Depending on the patient's particular hearing loss, this five-frequency

slope may all lie within the extended high-frequency range, it may straddle the 8,000 Hz boundary, or it may reside completely within the conventional frequencies.

Just how effective is this five-frequency slope in detecting hearing loss from ototoxic drugs? The results may surprise you!

In one study of the ototoxic effects of **Cisplatin**, if only the five frequencies in the five-frequency slope had been tested, 93% of the people with ototoxic drug-induced hearing loss would have been detected.⁶ This is in sharp contrast to the 39% detected in this same study using only the conventional frequencies.

Other studies have yielded similar results. For example, another study reported that if only the five-frequency slope values were tested, hearing loss due to AMINOGLYCOSIDE antibiotics would be detected 84% of the time, and for **Cisplatin**, the results would be 94%.⁹ Another study revealed that initial hearing loss would have been detected in 89% of the people with hearing loss if only the five-frequency slope had been tested. Testing only conventional frequencies caught just 37%.⁸

Based on results such as these, the routine use of high-frequency audiometry is not just "nice," it is essential.¹⁵

For hospital in-patients who must undergo drug therapy with ototoxic drugs, having complete audiometric testing can be a problem, especially if they are unconscious, semi-conscious or very sick. In such cases, using a conventional audiometer and test protocols is difficult, if not impossible. In these situations, auditory brainstem response (ABR) techniques modified to work in the higher frequencies can be effective tools. In one such study, high-frequency tone-burst-evoked ABRs identified 93% of the initial changes in hearing loss.⁷

The five-frequency slope protocol is fast and efficient and has been proven effective in providing early warning of hearing loss.

I recommend that the five-frequency slope protocol become the accepted standard practice in audiometric testing to help patients save precious hearing that otherwise might be lost to the ravages of ototoxic drugs.

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The information in this paper was taken from the second edition of the book ***Ototoxic Drugs Exposed*** by the same author. To learn more about ototoxicity in general, or to learn the specific ototoxic side effects of the 743 ototoxic drugs, 30 herbs and 148 chemicals mentioned in this book, get your own copy of ***Ototoxic Drugs Exposed***.

If you would like to join an information and support E-mail list for people who have damaged their ears from taking ototoxic drugs, type your E-mail address in the box and click on the Yahoo Groups button. (You can unsubscribe at any time.)

Subscribe to the Ototoxic-Drug list



Notes

In this paper, drug classes are in full capitals (LOOP DIURETICS), generic drug names and ototoxic chemicals are in bold (**Enalapril, toluene**) with generic drug names being capitalized and chemical names all in lower case.

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"The wages of sin is death, but the gift of God is eternal life [which also includes perfect hearing] through Jesus Christ our Lord." [Romans 6:23]

"But know this, in the last days perilous times will come" [2 Timothy 3:1]. "For there will be famines, pestilences, and [severe] earthquakes in various places" [Matthew 24:7], "distress of nations, the sea and the waves roaring"—tsunamis, hurricanes—Luke 21:25, but this is good news if you have put your trust in the Lord Jesus Christ, for "when these things begin to happen, lift up your heads [and rejoice] because your redemption draws near" [Luke 21:28].

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