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Noise-Induced Hearing Loss, Cell Death, and More: Interview with Donald Henderson, PhD

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Douglas L. Beck, AuD, Web content editor, interviews Dr. Henderson on a variety of topics relating to pharmacological solutions and interventions regarding noise exposure and noise-induced hearing loss.

Academy: Good Morning, Don. Thanks for your time today.

Henderson: Hi, Doug. My pleasure. It's always nice to chat with a UB alum.

Academy: Don, you've done some extraordinary work regarding pharmacologic mechanisms as they relate to hearing protection and noise-induced hearing loss. How did you get involved?

Henderson: This area is relatively new, and I became interested in protecting the ear from noise-induced hearing loss because of a number of basic science findings. For example, we have recently learned that high-level noise exposure creates a level of oxidative stress within the cells of the cochlea.

Academy: And in this context, oxidative stress refers to the situation in which the cochlea is generating large numbers of free radicals?

Henderson: Exactly, and these are greater numbers of free radicals than can be neutralized via the natural protective action of cochlear antioxidants. I should mention that antioxidants are found in all tissues of the human body. Free radicals are oxygen or nitrogen molecules with un-paired, or free electrons. And simply, these molecules attack the nucleus or the mitochondria or the cell membranes of surrounding, and the cochlear damage leads to the resultant noise-induced hearing loss. In fact, the primary site from which the free radicals emerge are the mitochondria of the outer hair cells. We think this is true because the outer hair cells consume a lot of energy.

Academy: I believe you mean the outer hair cells consume a lot of energy in their role as the cochlear amplifier?

Henderson: Yes, that's correct. The outer hair cells use a lot of energy and a lot of oxygen.

Academy: And so even though noise-induced hearing loss looks like a "mechanical event," it may actually be a chemical event or perhaps a chemical event that results from an initial mechanical insult?

Henderson: Exactly. And if this is true, then we think there is an excellent likelihood that we can intervene in the process through chemical measures.

Academy: And just to be clear…some pharmacological solutions have been shown to work in animals, and some of the proposed solutions are available in pharmacies and health food stores, but there have not yet been large-scale randomized tests of humans to prove that pharmacological

intervention and preventative measures work in humans.

And therefore, I want to be sure to say that in no way are you suggesting that chemical and pharmaceutical solutions and alternatives are to be used instead of normal hearing protection protocols, but indeed, the probable outcome of the research is that pharmacological agents may be advisable in addition to standard and historic hearing protection protocols.

Henderson: Yes, that's the direction we're going.

Academy: Okay, and so as the outer hair cells are damaged by a mechanical process, such as loud noise exposure, and the mitochondria give off free radicals that is a chemical process, the cells start to die off.

Henderson: Yes, and there are two cell death processes: necrosis and apoptosis. This is very important because apoptosis is a highly regulated event within a cell. The cell gets a trigger that indicates time is up, time to die, the proteins begin to break down, and the cell implodes. The components are carried off via the waste disposal system of the cochlea. However, maybe we can alter the outcome and prevent the cell death by blocking the trigger for apoptosis.

Academy: And then, what's the best relative description of necrosis?

Henderson: I think of necrosis more as passive cell death. The cell membrane is damaged and as calcium moves in and water moves in, the cellular contents slip out. The cell gets larger and finally ruptures and the cell contents can actually pollute the local area, and that local pollution can further damage neighboring cells with the reaction of trace amount of iron and oxygen radicals creating hydroxyl radicals, which are very toxic.

Academy: Okay. And there are two broad classifications of drugs being developed to be used in these endeavors, right?

Henderson: Yes. There are drugs that act as boosters to the normal antioxidant defense system of the cochlea, and there are drugs that prevent apoptosis. The larger category at this time is the antioxidant drugs, such as N-acetyl-L-cysteine ("L-NAC"), D-methionine and both promote glutathione (also called GSH). GSH is a naturally occurring antioxidant, and it protects cells from free radical damage, and so these drugs promote glutathione synthesis. However, it's difficult to give GSH orally because much of their activity is absorbed in the stomach and intestines, and so very little makes it to the target organ. So, one goal is to make the building blocks of glutathione more easily accessible and available for the cells to prevent free radicals from damaging cells and to prevent the apoptosis trigger.

Academy: And if I recall, the U.S. Navy was looking at L-NAC years ago?

Henderson: Yes. That's right. But the study was not as well controlled as would have liked.

Academy: Yes, well, of course one cannot take a group of humans, expose some to this, some to that, and then compare and see where less damage was done!

Henderson: Exactly. And the experiments made some assumptions about all subjects receiving equivalent noise exposures, but in the end, it was very hard to sort out. Some of the Navy personnel wore hearing protection (which was a reasonable idea!) and some didn't, and so it's very difficult to make a control and experimental group and to really document the outcomes.

Academy: And so maybe the only way is a shotgun style study, looking at very large groups and long-term trends over decades?

Henderson: Right, or maybe study musicians who experience TTS in their day-to-day music routines. Or maybe we would study people in noisy industrial situations. One might assume if we prevent some musicians or workers from experiencing TTS, we can safely assume they won't be

developing PTS. And so there are a number of studies that can be done that may allow us to draw some fairly solid conclusions, but variability is difficult to overcome, and safety is of paramount concern.

Academy: But regarding animal studies, we can make some very strong statements.

Henderson: Exactly. There is no question that in animal studies, these drugs prevent noise-induced hearing loss. But again, in animal lab situations, we control everything; we test their hearing and we know the results, we know exactly the sounds they're exposed to in loudness and duration, we know the strength of the drugs administered, and we can measure the outcome.

Academy: So it appears the science is very solid, but the human applicability is as of yet to be defined.

Henderson: Yes. But to me, there really is no doubt. These approaches work for animals, and the animals used have auditory system and biochemistry similar to humans. I'm confident with more experiments in humans, that it'll be clear that the pharmacological contribution is worthwhile, beneficial, and protective.

Academy: Don, have you had personal human experience with these drugs?

Henderson: Well, I have a friend who is a music professor and conductor. She was having difficulty with TTS, tinnitus, and hyperacusis after practicing with an orchestra in a very reverberant room. I suggested she might try a combination of L-NAC and acetyl-L-carnitine (ALCAR), nutraceuticals we have studies with chinchillas. She purchased them from a health food store and after two weeks, she was relieved of her symptoms. Of course that's not to say that would happen for anyone else, but it worked for her, and so to me, that's very encouraging.

Academy: Amazing. And so far we've actually only addressed free radicals and antioxidants, but there's also a lot being done with regard to Src inhibitors and blocking apoptosis when cells physically lose their connections with neighboring cells.

Henderson: Exactly, and drugs that block apoptosis are very promising with regard to preventing noise-induced hearing loss. But we can chat about that another time.

Academy: Don, this is fascinating. Thanks so much for your time and knowledge.

Henderson: My pleasure, Doug.

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