

Medications That Can Cause Deafness

We don't know yet exactly how these ototoxic drugs work. We know that there is one particular target: the outer hair cells of the inner ear.

Many commonly prescribed medications that are extremely effective at controlling a targeted disease, or alleviating symptoms such as chronic pain, can also destroy a patient's ability to hear. Because of this negative side effect, these drugs are said to be ototoxic. Unfortunately, many ototoxic drugs are among the best available to prevent deadly infections or fight serious illnesses, and in many instances equally effective alternative treatments have not been developed.

Ototoxic drugs include aminoglycoside antibiotics that are used against tuberculosis, diuretics to fight congestive heart failure, platinum-based chemotherapeutic agents for cancer, certain non-steroidal anti-inflammatory drugs, anti-malarial medications, and prescription painkillers that combine hydrocodone and acetaminophen such as Vicodin®. Hydrocodone is a synthetic opiate, almost equal to morphine in pain relief. Acetaminophen is a mild analgesic sold over the counter as Tylenol®. Long-term use of natural opiates, such as morphine and codeine, does not cause hearing loss.

Hydrocodone-containing painkillers (Vicodin®, Lortab®, and

Lorcet®) are the most commonly prescribed opiates in the U.S. In 2006, more than 70 million prescriptions were written for Vicodin®. Prescriptions written for narcotic analgesics make them widely available in the population. Drugs like Vicodin® are subject to abuse and are especially dangerous in light of a tendency toward tolerance, dependency and addiction. Levels of consumption frequently exceed the prescribed amount. The usual adult dosage is one or two tablets every four to six hours. According to the Federal Drug Administration, the total daily dosage should not exceed eight tablets. Patients or users addicted to these painkillers often consume in excess of 30 tablets daily.

Studies reporting on drug abuse among teenagers indicate that due to their morphine-like high and widespread availability in the home, painkillers are the drug of choice

for that age group. Many parents are unaware of the extent of teen prescription drug abuse, or of the consequence of potential hearing loss.

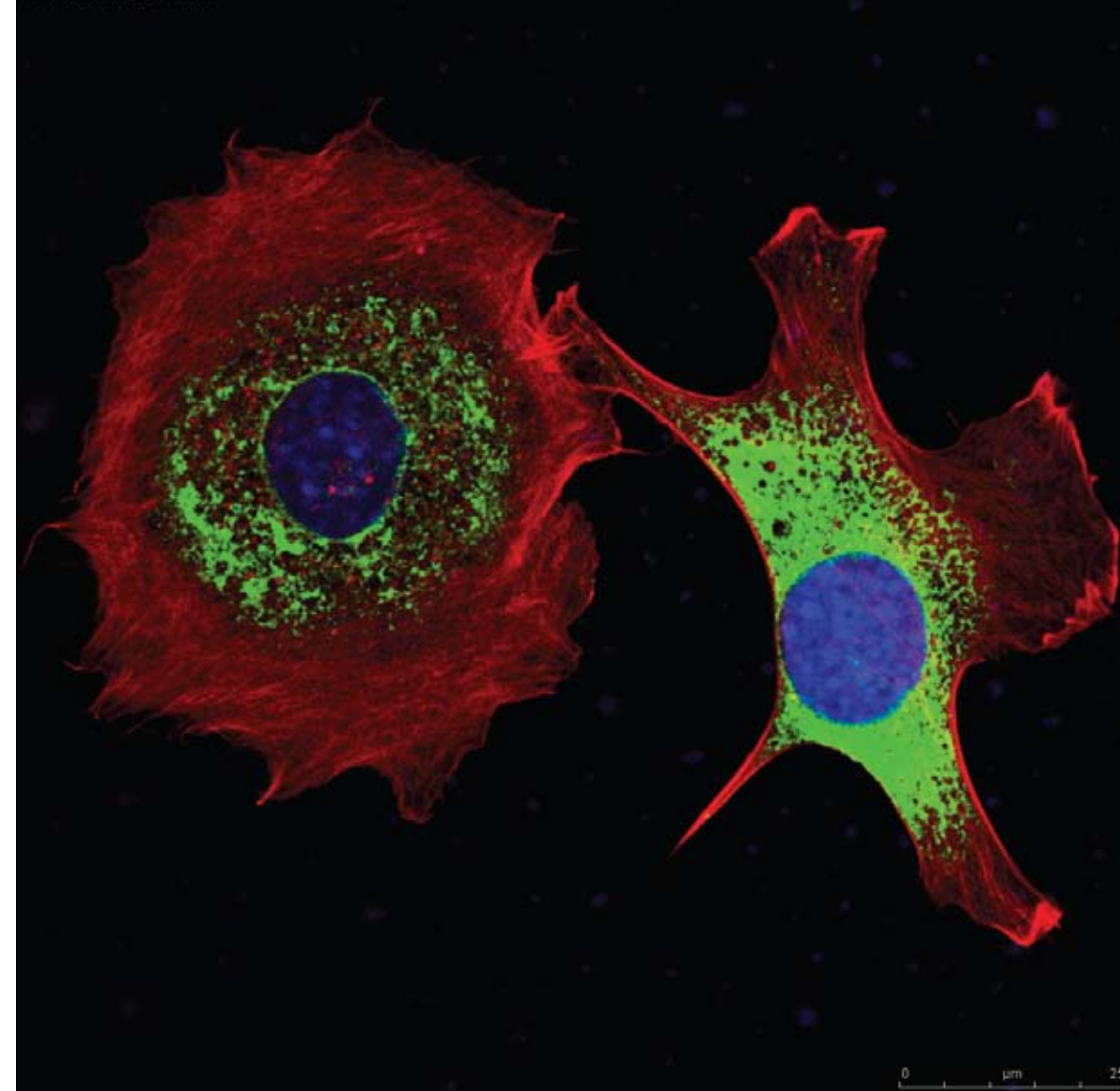
How do ototoxic agents cause deafness?

"My associates and I had made the clinical observation of rapidly progressive hearing loss in patients using significantly more than the prescribed dose of Vicodin®," said William M. Luxford, MD, House Clinic. "We could not explain why the loss was occurring, so I approached Federico Kalinec, Ph.D., scientist at the House Ear Institute, to help determine the cause of the hearing loss and possible preventative measures," Luxford continued.

"We don't know yet exactly how these ototoxic drugs work. We know that there is one particular target: The outer hair cells of the inner ear," Kalinec stated. "One of the

"How does the ototoxic drug activate a signaling mechanism inside the auditory cell that induces cell death?"

FEDERICO KALINEC, PHD



Confocal micrograph showing activation of the protein GRP78 (green) in the endoplasmic reticulum of the HEI-OC1 cells exposed to L-carnitine.

mysteries is why ototoxic drugs target only these cells and no other cells in the organ of Corti. This is part of our research: how does the ototoxic drug activate a signaling mechanism inside the auditory cell that induces cell death," he continued. Results from the study suggest that acetaminophen is the primary ototoxic agent; however, hydrocodone seems to work synergistically in the combination. A genetic trigger linked to stress may also play a part in the destruction of auditory cells. Doctors Luxford and Kalinec, along with Gilda Kalinec and Joshua G. Yorgason, are collaborating on the study of the cell and molecular bases of acetaminophen/hydrocodone ototoxicity.

For reasons unknown and still under investigation, the most common

animal models used for biological research, mice and rats, are resistant to some ototoxic drugs. These and other limitations associated with animal studies have led to the development of an auditory cell line, termed House Ear Institute Organ of Corti 1 (HEI-OC1) which excels as an in vitro system to investigate ototoxicity. Working with this cell line facilitates high throughput screening technology at the planning, execution and evaluation stages of experiments, increasing productivity while lowering costs. This cell line is available without cost to all investigators and currently is being used in dozens of laboratories in the U.S. and other countries.

Working with his team, Kalinec also evaluates chemical compounds, seeking one with the ability to protect

sensory cells against ototoxic attack. "To date we don't have any substance proved or approved that really protects against ototoxic drugs; however, there are several promising substances. In fact, in our lab we are working with one natural micronutrient, L-carnitine, which is actually able to significantly protect against the ototoxicity of gentamicin, one of the aminoglycoside antibiotics. We are currently examining the molecular mechanism active in L-carnitine and also working to prove that this is absolutely safe for



Woman Loses Hearing to Prescription Pain Killers

Eight years ago, Shannon Menosky was trying to carry furniture down the stairs when she slipped and fell, injuring her back. The herniated disk that resulted caused severe pain that wouldn't go away. She went to an orthopedic specialist who gave her cortisone shots and prescribed strong pain-relieving medications, including Vicodin®. She took these medications for over a year, trying to ease the pain. A normal dose is four pills in 24 hours. As her pain continued the dosage increased, until ultimately she was taking as many as 50 to 60 pills per day.

"Finally I became so ill that I had to go to the emergency room. The doctor there told me that I was having withdrawals from Vicodin®," Shannon stated. "I tried to stop, but because of the pain it became a vicious circle. I tried to go through rehab a couple of times, but each time I went there I had a terrible reaction: My body became completely swollen and I couldn't breathe, so I would end up in the hospital," she added.

In all, Shannon was taking medication for about five years before she lost her hearing. "That happened very suddenly," she indicated. "I noticed for a few weeks that my hearing wasn't as good as it should be. My kids would have to say 'Mom! Mom!!' to get my

attention. But I was swimming a lot at the time, so I thought maybe I just had water in my ears. I went to the doctor and he said, 'There is nothing in your ears,' and within two weeks I was completely deaf," Shannon said.

"I was referred to the House Clinic and, I'll never forget, the doctor had to write notes to communicate with me because I could not hear. He asked me if I was taking Vicodin®, and when I admitted that I was, and how much, he said that was why I was deaf now. I was crying, but he added that the good news was, 'we can fix it'. When I saw Dr. Friedman again, he told me that before I could have a cochlear implant I would need to get off Vicodin®," she stated.

"I had tried before, and I was so depressed because of not being able to hear. That's what I wish a lot of people would understand. I think that not being able to hear made my addiction to Vicodin® even worse. I cut myself off from the world. I couldn't hear my children any longer. I was afraid to go out because I wouldn't know what anyone was saying. So for two years I stayed in the house and didn't get help, didn't do anything. Then my father died, and right after that I just did it the hard way. And I haven't taken anything since," Shannon said.

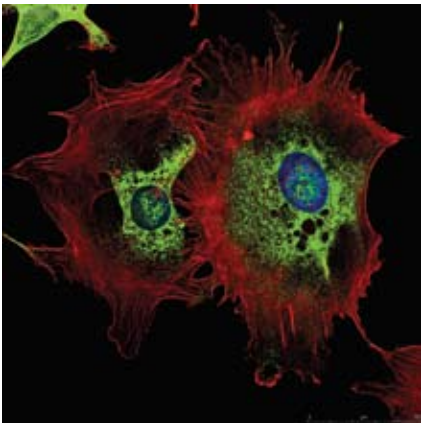
"After I had surgery for the cochlear implant they told me not to get my

hopes up, but when they first turned on the implant – I could hear! Voices sounded a little cartoon-y at first. It took a while to be able to distinguish between different voices. But when they tested my hearing we were all surprised at how well I tested. My hearing is really good now," Shannon continued.

"My life will never be the same as it was before. I used to work as a veterinary assistant and part-time as a waitress. My back is better now, but they've told me that I can't go back to work. Although I can hear well enough to use the phone, I still have a problem hearing in crowded places like a restaurant, where many people are talking," she said. "I want everyone to be aware that certain drugs can cause you to lose your hearing," Shannon added. ❖

"If my story helps one person avoid the problems I've had, I'm happy to tell it."

– SHANNON MENOSKY



Confocal micrograph showing activation of the protein GRP78 (green) in the endoplasmic reticulum of the HEI-OC1 cells exposed to L-carnitine plus acetaminophen.

humans," Kalinec said.

"If we are able to discover one safe and effective agent capable of preventing the negative side effects of aminoglycoside antibiotics, that would be a huge advance, not only for our research but for the treatment of different diseases. You have, for instance, a serious disease like tuberculosis. Around the world it is one of the most critical health

problems. Many drugs most recommended for treatment of this disease are ototoxic. The negative side effects make it very difficult for doctors to use the drug in the best way, at the right doses, against tuberculosis. So by finding a way to prevent ototoxic hearing loss, we would also be effectively increasing the efficacy of treatment for critical diseases," Kalinec added. ❖

If we are able to discover one safe and effective agent capable of preventing the negative side effects of aminoglycoside antibiotics, that would be a huge advance.