Antibiotic found to protect hearing in mice

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A type of antibiotic that can cause hearing loss in people has been found to paradoxically protect the ears when given in extended low doses in very young mice.

The surprise finding came from researchers at Washington University School of Medicine in St. Louis who looked to see if loud noise and the antibiotic kanamycin together would produce a bigger hearing loss than either factor by itself. The results will appear in an upcoming issue of the *Journal of the Association for Research in Otolaryngology* and are now available online.

"The protective effect of this type of antibiotic is a previously unknown phenomenon that now leads to at least a dozen important questions about what mechanisms cause hearing loss and what mechanisms could be protective," says senior author William W. Clark, Ph.D., professor of otolaryngology and director of the Program in Audiology and Communication Sciences, a division of CID at Washington University School of Medicine.

The research project arose out of concern for premature infants being airlifted to St. Louis Children's Hospital from remote locations across the bi-state area. Mary Jude Weathers, a flight nurse who supervised the transport of these infants wondered whether the babies were being exposed to potentially damaging amounts of noise from the helicopters. She approached Clark, who was worried about hearing loss in these newborns for a different reason: they were being given the drug gentamicin, which is closely related to kanamycin.

Gentamicin is one of a group of antibiotics used to help treat and prevent a variety of bacterial infections. Unfortunately these antibiotics can produce severe hearing loss in some circumstances. But premature infants need something to protect their compromised immune systems during air transport. Babies get gentamicin because it can protect against a wide range of infectious bacteria, and it is the mildest antibiotic in its class.

"There was good evidence from laboratory studies in animals that gentamicin and noise had a synergistic interaction, and that the drug would amplify potential noise damage," Clark says. "So it seemed logical to assume that people on gentamicin would be more susceptible to noise induced hearing loss, and we were especially concerned for these infants."

Because these babies were so fragile, Clark turned to researchers who worked with mice to answer this question. Both humans and mice are particularly vulnerable to noise- and drug-induced hearing loss at young ages. Sound levels measured by Clark and Weathers showed that the infants were exposed to almost 100 decibels for a period of 12 minutes before takeoff, similar to a lawn mower or chain saw. These levels could be especially damaging to premature babies.

"The laboratory mouse is a well-established model for human hearing," says coauthor Kevin K. Ohlemiller, Ph.D., research associate professor of otolaryngology. "They possess similar inner ear anatomy and physiology and similar patterns of age-related, noise-induced and drug-related hearing loss."

Ohlemiller worked with Elizabeth A. Fernandez, then a doctoral student in the Program in Audiology and Communication Sciences, to see if loud noise and a low dose of kanamycin would exacerbate each other's effects. Because the first month of life is when mice are most vulnerable

to noise and drugs that damage hearing, 20- to 30-day old mice were injected with either kanamycin or saline solution twice a day for 11 days. They were then exposed to 110 decibels of noise for 30 seconds.

Two surprising findings arose. First, this particular strain of mice was very sensitive to noise-induced hearing loss. Significant loss of some sensory cells in the ear resulted in permanent hearing damage, even over the short time span. Second, a regular, low dose of kanamycin completely protected the mice against this sensory cell damage and hearing loss. The protective effect of repeated doses persists for at least two days after the last injection, the scientists noted.

Researchers plan to use these findings in a number of different ways. They can map the genes in this strain of mice to determine what makes them so noise-sensitive and possibly figure out how kanamycin protects sensory cells in the ear. In addition, the findings open up new possibilities for clinical research. Learning how kanamycin protects the ear's sensory cells could help scientists develop drugs with similar effects. Medications that protect the ears from damaging noise levels could benefit a wide range of groups, from soldiers to airline workers to premature babies.

"This very dramatically points out the benefits of having basic scientists who can take a clinical problem and find a result opposite of what we expected," Clark says. "These results not only energize laboratory scientists and begin new lines of research, but they also have implications for clinical practice. This has been an amazing sequence of events, to start a project in a helicopter and end up under a microscope."

More information: Fernandez EA, Ohlemiller KK, Gagnon PM, Clark WW. Protection against noise-induced hearing loss in young CBA/J mice by low-dose kanamycin. Journal of the Association for Research in Otolaryngology. Jan. 22, 2010

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