REVOLUTIONIZING CHILDHOOD HEARING LOSS TREATMENT WITH GENETIC THERAPY

Dr. Caraway:

Lately, there's been a lot of conversation in the hearing healthcare industry about genetic therapies to treat hearing loss in infants and young children, but what does this mean for you as a parent of a child with hearing loss today? Let's talk about what this research means, and what you need to know.

Hi, I'm Dr. Teresa Caraway with Hearing First, we're here to help and support families just like yours who have a child with hearing loss.

Because this information on genetic therapies is so new, we all have more questions than answers. So to shed more light on this exciting topic, I'd like to introduce you to Dr. Jace Wolf. He's a pediatric audiologist with over 25 years of experience working with babies and young children who are deaf or hard of hearing.

Dr. Wolfe:

Hi, I'm Dr. Jace Wolfe.

In early 2024, two peer reviewed medical journal articles described two different genetic therapy studies that were conducted in China. Each of these studies included children with a unique type of deafness caused by a mutation in a gene called the Otoferlin gene. Many of the children in these studies had a considerable improvement in their hearing function after receiving genetic therapy for their Otoferlin gene mutation. In some cases, these children went from being completely deaf to hearing loss in the mild to moderate range. Even more exciting, some of these children developed the ability to understand speech in the treated ear. Another report in the New York Times described a similar Otoferlin genetic therapy study being conducted as a clinical trial at multiple centers in the United States under the watch of the U.S. Food and Drug Administration or FDA.

These reports of genetic therapies for childhood hearing loss are very exciting, but they also raise a lot of questions for families of infants and children with hearing loss, and the hearing healthcare professionals who serve them.

In this video, I would like to discuss some of the most common questions I have heard on this new and exciting development.

First, I have heard many people ask what is an Otoferlin mutation?

To answer that, let's first talk a little bit about how the ear works. As you might know, sound travels down the ear canal and is captured by the eardrum which sits at the end of the ear canal. The sound causes the eardrum to vibrate, and those sound vibrations are carried to the inner ear, which is also known as the cochlea. When the sound vibrations travel through the cochlea, the sound stimulates tiny receptors called hair cells. The job of the hair cells is to convert the sound vibrations to a signal that stimulates the hearing nerve to then be carried to the brain.

An Otoferlin mutation causes a disruption in the gene that creates a protein that's necessary for the hair cells to be able to deliver the audio message to the hearing nerve. Without the Otoferlin protein, the audio message could not be transmitted from the hair cells to the hearing nerve. In most cases, this results in profound deafness that is known clinically as a special type of hearing loss called an auditory neuropathy hearing disorder.

Otoferlin gene mutations are responsible for about one to 2% of genetic hearing losses present at birth. The good news is that many children with Otoferlin deafness receive cochlear implants, and go on to listen and talk like children with typical hearing.

With that in mind, I have also heard many people ask, what is genetic therapy?

Well, in short, with genetic therapy, normal genes are transplanted into cells to replace the defective or missing genes in order to correct a genetic disorder, condition or disease.

Genetic therapies can work in several ways. For instance, a genetic therapy may replace a disordered gene with a healthy copy of the gene. Also, a genetic therapy may inactivate a gene that is causing a disease or a new gene may be delivered into the body to help treat a disease.

In the case of the Otoferlin gene therapy studies, a healthy copy of the Otoferlin gene is attached to a harmless virus, which is delivered into the inner ear. The gene therapy also contains an agent called a promoter, which is designed to deliver the healthy gene to the exact place in the inner ear that is affected by the gene mutation. The introduction of the healthy gene is then able to correct for the mutated Otoferlin gene and restore, or partially restore auditory function.

The final question I've heard, and maybe the most important one you're thinking is what do these developments in genetic therapies mean for my baby with hearing loss?

And that's a great question. First things first, it's important to remember that the genetic therapy hearing loss studies conducted so far have only included children with Otoferlin mutations. And remember, Otoferlin mutations only cause about one to 2% of hearing losses present at birth. There are more than 150 genes that cause hearing loss, so we still have a long way to go to create genetic therapies for all the other types of genetic childhood hearing loss. The Otoferlin gene mutation has several properties that make it a simpler gene to treat with genetic therapy. Other genes that cause hearing loss are potentially more challenging to treat with genetic therapies, so it'll probably be many years, or even decades before genetic therapies are available for other types of genetic hearing loss.

Even with the Otoferlin genetic therapy, the studies are in the very early stages, and there is still much, much more to learn before the FDA approves this genetic therapy as a safe and effective treatment. In fact, it'll probably be at least several years before the FDA will approve the Otoferlin and genetic therapy

as a clinical treatment. Given the fact that genetic therapies will not be clinically available for many years at the earliest, we cannot afford to wait for genetic therapies when a baby is born with hearing loss today.

We know that children born with hearing loss must have immediate access to clear speech, to learn how to listen and talk. If a child does not have access to clear speech during the first two to three years of life, changes will occur in the areas of the brain that support listening and talking. This means the child will lose the opportunity to develop typical listening and spoken language abilities. The window for listening and spoken language development will most likely close completely if access to sound is not provided by three to five years old.

The most important thing is to ensure the baby's brain has immediate access to clear speech to develop the neural pathways and networks that allow for typical listening and spoken language development. Your pediatric audiologist and hearing healthcare team can help you determine whether your baby will need hearing aids or cochlear implants to provide the brain stimulation they need to reach their full potential in their listening and spoken language skills.

Does that mean there's no role for genetics with your baby? No, in fact, I would strongly encourage you to talk with your hearing healthcare team about getting genetic testing for your baby if you do not already know the cause of their hearing loss. And this knowledge can help you as a parent, and your hearing healthcare team provide the best possible care for your baby.

Dr. Caraway:

That was a lot of information about exciting new research in the field of hearing healthcare. Hearing First has plenty of resources to support you as you teach your child to listen and talk. Wherever you are on this journey and however you may be feeling, you are not alone, Hearing First is here to help you every step of the way. Subscribe to the YouTube channel for new videos with tips and advice, and for more resources and support, visit hearingfirst.org.