

Will Eiserman:

Welcome to Earworm: Dialogues on Hearing Health You Can't Stop Thinking About.

Earworm is brought to you by the National Center for Hearing Assessment and Management at Utah State University known as NCHAM.

My name is Will Eiserman, and I'm the Associate Director of NCHAM and I'm your host today.

When a baby is born in the United States, there is a corset of screening tests to check for a variety of different conditions, which can be treated if found early in life. These include tests for disorders like sickle cell disease, cystic fibrosis, hypothyroidism, PKU, congenital heart disease, and hearing loss.

Of all of the newborn health screenings, hearing loss constitutes 50% of the positive screens and also 50% of the subsequent positive diagnoses resulting from the screenings making hearing screening, the primary condition being screened for at birth.

The Newborn Hearing screening system known as the Early Hearing Detection and Intervention or EDDI System is lauded as one of the most significant public health achievements of the last several decades. Approximately three in a thousand children are identified with a permanent hearing loss as a result of newborn screening. Despite the significance of this programmatic achievement, it's estimated that the number of children with permanent hearing loss actually doubles in a few short years following the newborn period.

Promising methods now exist, fortunately, that would allow us to identify many of these children who will develop a hearing loss subsequent to the newborn period.

During this episode of Earworm, we will discuss how the existing newborn hearing screening protocol could be expanded and potentially identify children who may be among those who could develop hearing loss in the subsequent months or years after the newborn period.

Our guest today is Dr. Elliot Shearer, who is an Assistant Professor of Otolaryngology Head and Neck Surgery at Harvard Medical School. Dr. Shearer is a pediatric otolaryngologist at Boston Children's Hospital where he caress for children with a wide range of ear, nose, and throat disorders. He has a special interest in the surgical management of pediatric ear disorders, including hearing loss. Dr. Shearer is internationally recognized for his work in developing a new genetic testing platform for the diagnosis of hearing loss and has written many research articles and several book chapters on the subject. Dr. Shearer also studies ways to improve newborn hearing screening tests using technologies and ways to improve outcomes for children with cochlear implants.

So, welcome Dr. Sheer.

Dr. Elliot Shearer:

Thanks for having me. Happy to be here.

Will Eiserman:

Dr. Shearer, 98% of children in the United States are now being screened for hearing loss at birth using physiologic measures. That's yielding about three children in a thousand identified as deaf or hard of hearing shortly after being born. That's a huge accomplishment, right?

Dr. Elliot Shearer:

Yeah. The current newborn hearing screening, which is hugely successful at identifying kids with hearing loss, it's a physiologic screen, so what I mean by that is that we screen hearing in the newborns by either what's called an otoacoustic omission, OAE, or an auditory brainstem response, or ABR, and in each of

these screens, a sound is played into the ear of the newborn and then the response from that is measured.

We've known from years of data that newborn hearing screening has been hugely effective at diagnosing children earlier with hearing loss. And all the data that we have shows that that improves overall language outcomes for those children, so the earlier we can diagnose children, the better. And that doesn't matter what form of language or communication that you use, whether it's spoken language or sign language.

As our understanding of hearing and hearing loss has evolved, we know that there's many different types of hearing loss that are not detected by the newborn hearing screen using just a physiologic measure. So an example of that would be an infectious form of hearing loss called congenital cytomegalovirus Infection or congenital CMV Infection that is very often missed by the newborn hearing screen because it can be a more mild hearing loss that may not be picked up, or it could be a hearing loss that occurs outside of the newborn period. So, after a month or two of life. And really the physiologic newborn hearing screen is not designed to detect that type of hearing loss.

There's also some forms of genetic hearing loss that rapidly progress, so the newborn may hear typically, but then after just a couple months, they may have rapidly progressive hearing loss. An example of that is Myo 15A hearing loss.

And so, there's clearly some forms of childhood hearing loss that are not going to be picked up on the current physiologic screen. It wasn't designed to detect these forms of hearing loss. These are more mild forms of hearing loss. These are asymmetric or unilateral one-sided forms of hearing loss, and then rapidly progressive forms of hearing loss.

Will Eiserman:

We're going to have you expand on both C MV and genetic forms of hearing loss, but before we go there, why is detecting a mild or moderate hearing loss or a loss in just one ear, all that important? Some people might think, "If a child can hear fine in one ear, then that may not be such a big concern."

Dr. Elliot Shearer:

Mild to moderate in unilateral and asymmetric hearing loss is very important to identify. There's been many, many studies showing impacts on expressive and receptive language skills in children and outcomes in school, and so we are detecting these children based on... A lot of times it's childhood screening tests in the pediatrician's office, for instance.

I have a lot of kids that have a more mild to moderate hearing loss that we provide a hearing aid to, and it could be the thing that just boosts them to the next level. The biggest impact I think it has on kids when they are given access to a hearing aid and they have a mild to moderate hearing losses is the family tells me that they're working less hard in the classroom. They don't have to try so hard to hear and they're less mentally tired at the end of the day, and it helps them incorporate into the classroom and do better in school overall.

Will Eiserman:

So, despite all of the well-earned credit of the newborn hearing screening protocol that relies on physiologic screening methods, there are children not being identified at birth who could potentially be identified if we expanded the screening protocol.

Dr. Elliot Shearer:

Actually, in one study that I refer to often from Chicago, from Nancy Young's group, they looked at a large cohort of children undergoing cochlear implantation at about two years of age, and 30% of those children actually passed their newborn hearing screen. Those children were more likely to be diagnosed late and implanted later, so it's important that we identify those children in some way, and although the current physiologic screen has been hugely impactful, I do think there are ways that we can improve the newborn hearing screen protocol.

Will Eiserman:

Let's talk about CMV for a minute and the role it plays in the hearing loss of children that might not be immediately detectable at birth.

Dr. Elliot Shearer:

Yeah. CMV is cytomegalovirus, and the difficult part about CMV hearing loss is it's completely variable. First of all, CMV itself can cause a newborn disorder, which is characterized in its most severe form by seizures and skin changes and jaundice and major developmental issues, but all the way on the other end of the spectrum, you can have some children that are born with CMV that have essentially none of those symptoms or none of those features. And then you have some children who have CMV and have hearing loss.

CMV is all around us. It's a very ubiquitous virus and it seems to be that when a baby is in utero as a fetus, there's a reactivation of the virus or infection of the virus in the mom carrying the fetus, and that can lead to inflammation or infection of the inner ear.

CMV hearing loss is much more common than other forms of hearing loss to be unilateral or one-sided, and it's also much more commonly asymmetric, so one side can be severe or profound, and another side can be mild or moderate. It also can be progressive.

But what's really important about CMV hearing loss is there's a treatment available for it now, so if we identify it early, we can use a drug called Valganciclovir to reduce the viral load within the newborn and there's been some very promising studies shown a stabilization or even a reversal of hearing loss in children that are treated early.

Will Eiserman:

So, in order to identify CMV at birth, how is that done?

Dr. Elliot Shearer:

It's typically done through a swab of saliva or from a urine sample. The testing needs to be done within three weeks after birth, and the reason for that is because the virus is so common in the environment that the baby may be exposed by an older sibling, for instance, or just an adult. And so the gold standard is to have the testing done within the first three weeks of life.

Will Eiserman:

To be clear, the risk of CMV impacting hearing ability is that the child contracts CMV from their mother in utero, not after they're born from a sibling or someone else.

Dr. Elliot Shearer:

That's exactly right. You have to have been exposed in utero to have CMV hearing loss, and so that's why we need to screen very soon after birth.

Will Eiserman:

My understanding is that hospitals in about 20 out of 50 states have some type of targeted CMV screening with infants at birth.

Dr. Elliot Shearer:

It's a patchwork across the United States about what different states are doing for screening. Some states now perform what's called Universal CMV screening, so any child who's born is required to have CMV screening. Other states have the approach where if you refer or fail on the newborn hearing screening, then you are required to have CMV screening.

Will Eiserman:

Okay, so one strategy that's available to help increase the identification of children with early childhood hearing loss is to incorporate CMV screening at birth. Approximately 12% of the children who test positive for CMV at birth develop a hearing loss. In the US That's about 3,600 children a year who will have CMV related hearing loss.

Dr. Elliot Shearer:

I and others think that it would be very helpful for identification of children with hearing loss if we have a universal CMV screening protocol in place, and that's just because children with CMV hearing loss are far more likely to actually pass their newborn hearing screen that's done physiologically and then show up later in clinic with a hearing loss and we wish that we had done testing when the child was a newborn.

Will Eiserman:

So, about 40% of early childhood hearing loss can be attributed to CMV. In an earlier Earworm episode, Dr. Shearer, you indicated that another 40% of early childhood hearing loss can be attributed to genetics.

What about adding universal genetic screening to the universal newborn hearing screening protocol?

Dr. Elliot Shearer:

Yeah, the genetic part is the hardest part, and that's because there are so many genes and so many variants that have been shown to be involved in hearing loss.

Will Eiserman:

But things are changing rapidly in the world of genetics.

Dr. Elliot Shearer:

I think things have changed a lot, especially in the past 15 years or so, and it's all come about because of the Human Genome Project and the contribution of our understanding of genetics and genomics to hearing loss.

For a long time, people have known that hearing loss and reduced hearing in individuals as a genetic underpinning. People have known about this for hundreds of years, but really it's very complicated. There's so many genes that are involved in hearing loss that it took new sequencing technologies that

were brought about after the completion of the Human Genome Project in the early two thousands for us to really understand the genetics and genomics of hearing loss.

Our understanding of hearing loss has improved as we understand the underlying biology of what actually is causing hearing loss, because hearing loss is really a symptom of an underlying difference in the auditory system.

There's 124 different non-syndromic hearing loss genes, so just hearing loss alone, and then there's several hundred syndromic forms of hearing loss. The big shift that happened is in the early 2000, we didn't have the technology, and it wasn't until 2008, 2009 that we started having the technology where we could sequence all these genes at the same time. And what we found is it's really important to sequence them all. You can't just pick one or two and sequence it.

Will Eiserman:

Every form of genetic hearing loss is a little bit different.

Dr. Elliot Shearer:

And that's what makes it interesting and more difficult to understand. There's some genetic forms of hearing loss that are rapidly progressive after birth, like Myo 15A and GJB2 are two genes that are well known to have that form of progression, but there's other genes that can cause more subtle or less rapidly progressive hearing loss over time. So SLC 2684 is an example that can be associated with a steady decrease in hearing over time.

And then there's some genes that will have or will present with more of a mild high frequency hearing loss maybe in the teenage years, and then progress over time to a profound hearing loss. The most prominent example of that is TPR SS3. That gene is actually the most common genetic cause of hearing loss in adults who get cochlear implants. So when you look in large cohorts of adults who get cochlear implants, that gene is a progressive hearing loss that takes years to develop.

Will Eiserman:

We don't really know yet, do we? Precisely how many additional identifications of hearing loss would occur if comprehensive genetic testing were added to the newborn screening protocol?

Dr. Elliot Shearer:

Well, some early studies from China have shown that there's a 30 to 40% increased rate of screening positivity by adding genetics to it, but I think it's hard to say. We really don't know how many children, young children, actually have hearing loss because we have never done comprehensive screening. What I mean by that is test physiologically, but also test for CMV and also test for a genetic forms of hearing loss all at the same time.

And there is a big disconnect where you have about three out of a thousand children that fail or refer on the newborn hearing screening, yet when you look at studies of young teenagers, somewhere between one and 200 or one in 500, or some studies say even more, have a permanent hearing loss. And so there's this big gap where we don't actually know what's happening, because we haven't been able to look.

Fortunately, now we actually have the technology to do this. We have the technology now to screen for CMV, and we have the technology now to screen for genetic forms of hearing loss in young children.

Will Eiserman:

What then are the barriers to adding universal comprehensive genetic screening to the physiologic screening that's already occurring?

Dr. Elliot Shearer:

It gets very expensive to screen all of those genes and all of those variants. I would argue that it's really important that we don't use the expense as a roadblock and just say, "Oh, we can never do it."

I was part of the first team that did comprehensive genetic testing for hearing loss back in 2009 and 2010, and at that time, it costs thousands and thousands and thousands of dollars to perform that testing on just one individual. Now, we do that testing routinely. Prices will continue to fall, technology will continue to improve over time, and I think we're at the point now where we should be able to do comprehensive genetic screening on children. We have the technology to do it. We should be able to get the cost down and our ability to interpret it and understand the results has improved greatly in the past 10 years or so.

So, my lab is working on this. Other labs are working on this where we've come up with a way to perform comprehensive screening of all the hearing loss genes from just a dried blood spot or a saliva swab, and you're able to give a yes, no, maybe sort of answer within a matter of hours after birth.

China and Taiwan have instituted genetic screening where they only screen for a certain small subset of genetic variants that cause hearing loss. That really doesn't work in the United States just because we have so many different populations ethnically and racially, that... And there's so many different forms of hearing loss that it would just not be effective. In the US and Canada, we really have to approach this from a more comprehensive direction.

Will Eiserman:

It's getting less expensive, so where are we?

Dr. Elliot Shearer:

Ultimately, all of this comes down to costs. Someone once told me that to be realistically considered to be added to a newborn screen, it needed to be very cheap, so less than \$10 maybe.

But what I do know is that if you look at all of newborn screening, and depending on what state you're in, they take a dried blood spot from a heel stick, they'll test anywhere between 30 and 60 different conditions. Things like cystic fibrosis and hypothyroidism, and all these enzyme deficiencies that I don't know how to pronounce. But when you look at all the data overall, 50% of all the positive findings on all of newborn screening are hearing loss and so hearing loss is really the primary condition that's identified on newborn screening. When you look in the whole country, 50% of the identifications we make on newborn screening is hearing loss.

And so from my perspective, it's hugely important that we work to improve that portion of the current newborn screen. My lab has set a goal of less than a hundred dollars per screen. I think in the grand scheme of healthcare costs, adding a hundred dollars to a screen for every child doesn't really sound like that much if we're able to improve our ability to detect children who have hearing loss earlier, because ultimately, the earlier you detect a child with hearing loss, the better their language outcomes are later in life.

Will Eiserman:

That was Dr. Elliot Shearer.

I'm Will Eiserman from the National Center for Hearing Assessment and Management at Utah State University.

Check out earwormpodcast.org for other episodes of Earworm: Dialogues on Hearing Health You Can't Stop Thinking About.

Earworm is produced at the National Center for Hearing Assessment and Management and NCHAM at Utah State University, USU, and is funded in part by a cooperative agreement from the Maternal and Child Health Bureau, MCHB of the Health Resources and Services Administration, HRSA, at the United States Department of Health and Human Services.

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