Dr. Jason Barnes:

Hey there. Welcome to another episode of ENT in a Nutshell. My name's Jason Barnes, and today we are joined by Dr. Brendan O'Connell neurotologist and skull base surgeon and Dr. Pat Roush an audiologist and former director of a tertiary peds audiology center. And we will be discussing pediatric sensorineural hearing loss. Dr. Roush, Dr. O'Connell, thanks so much for being here.

Dr. Patricia Roush:

Thanks for having us.

Dr. Brendan O'Connell:

Yeah. Thanks for having us.

Dr. Jason Barnes:

Pediatric sensorineural hearing loss is kind of a big topic. So I'm excited to talk about it today. Upfront, I will say we're not going to be talking about conductive hearing loss, which is common, but not necessarily relevant or as relevant in this conversation. So to start, Dr. Roush, could you tell us a little bit about the epidemiology of pediatric sensorineural hearing loss?

Dr. Patricia Roush:

Sure. Pediatric hearing loss is actually quite common. It affects one to two newborns per 1000 births. And one of the things that's important to remember is that there are varying degrees of hearing loss. And although one to two infants are born with hearing loss, many will have hearing loss as they get older. So there are things that impact the ear as children age, and we do see a greater prevalence as children move through the school years.

It's one of the most common sensory deficits in developed countries, and it's three times more common than Down syndrome and six times more common than spina bifida. So for children with severe to profound hearing loss, the lifetime cost of hearing loss is staggering, greater than a million dollars, when you think about special education and interventions that are needed. In the past, the average age of detection was between 12 to 18 months, sometimes even as late as two years. But with the advent of newborn hearing screening in the last 20 years, the average age of detection is now younger than six months.

Dr. Jason Barnes:

And Dr. O'Connell, when you see these patients in clinic, what are some of the questions you ask the parents regarding getting a full history on these kids?

Dr. Brendan O'Connell:

For pediatric hearing loss, we have to put on a hat in which the history taking examination and comprehensive care starts with a focus on prenatal history then obviously the neonatal and postnatal cause. So we're thinking about prenatal issues. You're going to think about maternal infections, other exposures, drug exposures from a maternal standpoint. Really around the time of birth, I'm going to think about term, so premature, on term, birth weight, time spent in an intensive care unit, time spent on a ventilator, issues such as hyperbilirubinemia, infection.

And then with respect to postnatal cause, again, infection comes up and any medications that potentially could be ototoxic. I think if we are focusing on congenital hearing loss, obviously the

diagnosis is going to potentially be made or suggested with a newborn hearing screen and then followed up with audiometric testing, which we'll get to later. But it's a bit different if it's a late diagnosis.

So in those situations, actually age of onset, how the hearing loss was diagnosed, was it a school screen? Was it parental suspicion? Was it diagnosed by the pediatrician? So those are important concepts when you're not dealing with the congenitally referred failed-newborn-screen child. I think it's really important to have a multi-disciplinary team taking care of these patients. So I always will ask families, has anything happened since the last visit? Are there any associated conditions that have been diagnosed by other providers?

Has your pediatrician noticed anything different than last visit? Because these things evolve. I mean, a lot of times at the first visit, if you're seeing a kid that failed their screen and you're seeing them for their two or their three-month natural sleep ABR, a lot of issues may not yet have manifested. It can be hard to identify certain features. They may not have tone issues, they may not have motor delays yet, or speech delays, obviously.

So continuing to revisit the idea of are there any new associated medical conditions that have been diagnosed by any provider, is something that I would just continue to harp on at every visit that you see these children back at. And then family history, it's fairly intuitive there. So asking about first and second and even third degree relatives.

Dr. Jason Barnes:

And can you tell us, Dr. O'Connell, a little bit of what you're looking for on physical exam when you evaluate these kids?

Dr. Brendan O'Connell:

Yeah. It's a complete exam again. I mean, it's a 10-system exam. And there are things that you focus on. Obviously the ear is going to be a focus of attention for any patient with hearing loss. But looking for other stigmata of various syndromes, I certainly take a close look at the neck and the periauricular region looking for any pits or tags, external ear malformations, deformities.

A lot of this can, again, can be challenging in a two or three-month-old infant, particularly one that was premature and a small. I think, doing the best you can and continuing to repeat that over time to ensure that you're not missing anything, it is a feature that would suggest the potential etiology is important. It can be hard to get a good look or at the soft palate or the palate even in some of these young babies. And taking a good feel there, just continuing to revisit a comprehensive exam at all time points is critical.

Dr. Jason Barnes:

And Dr. Roush, Dr. O'Connell mentioned the newborn hearing screen, which is where some of these kids are first identified with hearing loss. Can you tell us a little bit more about how the newborn hearing screen works and what it entails?

Dr. Patricia Roush:

Sure. There are essentially two types of screening. One is based on auditory brainstem response, the other is based on otoacoustic emissions. I would say the majority of nurseries in the United States are using an auditory-based response measure, but not all. And it is important to know which procedure was used because the auditory brainstem response screen is really evaluating the hearing from the

outer ear to the lower brainstem, whereas as you know, the otoacoustic emissions screen is really just looking at outer hair cell function.

It's important to consider that particularly when we're thinking about which population we're screening. If we're in a well-baby nursery, the Joint Committee on Infant Hearing, which is an organization that has been in existence for decades now in the United States, recently came out with new guidelines in regard to newborn screening and management.

And they did say that either method could be used in a well-baby nursery, but still because of the higher likelihood of conditions like auditory neuropathy, which we'll talk about a little bit later, in the intensive care nursery, they continue to advocate for an auditory brainstem response screen in the intensive care nursery. For most infants, they'll have a screen in the hospital and generally that's done as close to discharge as possible.

But with many infants being discharged within 24 hours, sometimes they're quite young at the time of that first screen. So they'll often, depending on the state protocol, will return for a second screen as an outpatient. And that should be done within the first month of life.

Dr. Jason Barnes:

And before we move on to pathophysiology, we're going to be weaving through talking about unilateral versus bilateral hearing loss. Dr. Roush, can you give us a brief understanding of how our evaluation changes if this is unilateral versus bilateral?

Dr. Patricia Roush:

Sure. If an infant fails a newborn screen, whether it's unilateral or bilateral, at the point of the rescreen, we would still want to rescreen both ears. Because there are conditions that have progressive onset and can initially begin with a unilateral hearing loss and quickly change to bilateral. So at the rescreen we would rescreen both ears, and certainly at the diagnostic evaluation for hearing we would be doing a comprehensive hearing assessment of each ear.

I think that in terms of our medical workup and our imaging and that kind of thing, we may make different decisions based on whether the presenting hearing loss is unilateral or bilateral. But both are important, both affect the child and their long-term outcomes, so we would certainly want to know in a complete way, the status of the hearing for each ear.

Dr. Jason Barnes:

So now moving on to pathophysiology, this is usually separated into congenital versus acquired hearing loss. To start Dr. O'Connell, can you talk to us about some of the congenital causes of hearing loss and how this is usually broken down?

Dr. Brendan O'Connell:

A large subset of congenital loss will be due to genetic or hereditary causes. Essentially there's a gene mutation that's responsible for the hearing loss. That number's going to be somewhere between 50% and 70%, and that number is changing all the time because we're identifying more and more genes, incredibly heterogeneous group of genes that are responsible for congenital hearing loss. The other remaining 30%, 40%, 50%, whatever it is, is going to be non-genetic or environmental.

Of those genetic causes, the majority are going to be non-syndromic with the minority being syndromic. So of those 50%, let's say 40% of them will be non-syndromic and 10% will be syndromic, which essentially implies that there is another feature. Right? Something else that can be appreciated on

exam or on imaging or on diagnostics other than the hearing loss. Of the non-syndromic cases, the majority are going to be autosomal recessive, and the largest subset of that group are going to be connexin-related hearing losses.

So connexin 26, gap junction protein involved in potassium transport in the inner ear is going to make up the majority of those autosomal recessive non-syndromic hearing losses. And that's a huge overall proportion of what we see on a day-to-day basis. So, that's one that I think very much is high-yield in terms of thinking about testing that can yield an etiology. I don't think this talk is necessarily geared towards going through the specifics of the different syndromes and features of the different syndromes.

Essentially, you can rule out syndromic hearing loss largely with physical exam and family history. Again, they're going to be other features that are going to present themselves, and in these situations, it's critically important to have a multidisciplinary team. I think that if a syndrome is suspected, directed testing and directed evaluation to that syndrome obviously has value. Whereas if you're in the category of more sort of the isolated hearing loss of suspicion of it being non-syndromic, there is certainly a role for considering genetics to evaluate for potential genetic causes and rule out what could be non-syndromic hearing loss mimics.

Which to me the main one that stands out there is something like Ushers where early on it may look like it's just hearing loss, but we know that Ushers has other implications, vision and balance, and that would be something that wouldn't be detected until later in life, if you did not have a genetic screen that ruled that out. Switching gears a bit away from that genetics bin into the environmental bin. I know we touched on CMV. And again, that's going to be the primary cause in that group, and like connexin something that we have to think about in all these children in which the etiology remains unknown.

We have the ability here in North Carolina to test for both connexin and CMV on what we call a Guthrie card, which is blood obtained from the heel stick within the first few days of life. And as you know, the challenge with diagnosing CMV is that once you get outside of that first two or three-week window, you can't confidently make the diagnosis of congenital CMV. So in our practice, in a child without other features and hearing loss is identified early in life, I think the yield of targeted testing for both connexin and CMV is very high and something that we advocate for, and we fortunately have the ability to do by sending this Guthrie card.

The other large bin of hearing loss that we as a center advocate for exploring in every child diagnosed with hearing loss is inner ear malformation. So, perhaps 20% or 30% of congenital loss will be associated with some form of inner ear malformation. So we do get and recommend imaging in children. And what study that is is up for debate, and the timing of that is up for debate as well. But we generally will start with an MRI scan as it avoids ionizing radiation, and there's this very good detail in general on cochlear vestibular malformations, and the status of the hearing nerve, and also a picture of the entire brain.

And then we will follow that up potentially with a CT scan if there are features that we want to further explore, potentially borderline even, CT can be better at evaluating cochlear aperture looking to see if there's any sign of a nerve, if MRI suggests cochlear nerve deficiency, any channel in which the nerve can pass through into the base of the cochlear modiolus. And obviously looking for ossification, CT would be more sensitive than MRI. But we may touch on this a bit later, but that's generally how I would group things and how I think about workup of the congenital loss.

Dr. Patricia Roush:

If I could just add, I'd just like to make the point that I think it's also important, whether we're an audiologist or an otolaryngologist to make sure that we're asking families what do they think about how their child hears, particularly when we're evaluating an older child. Parents in many cases have a pretty good suspicion when their child has hearing loss. And so if we ask and listen to their explanation, that can also be very helpful in including in our workup.

Dr. Jason Barnes:

And next Dr. Roush, do you mind telling us about the acquired types of hearing loss?

Dr. Patricia Roush:

Sure. The most common acquired type hearing loss is of course, when an infant is born prematurely. And a lot of the effects of prematurity, the treatments that are given to sustain their life can have a negative effect on the ear. Some of the medications they receive, episodes of lack of oxygen following birth and so forth. As Dr. O'Connell mentioned, hyperbilirubinemia can play a role in hearing loss, both in typical sensorineural hearing loss, and also in auditory neuropathy-type hearing loss.

Infants who have any type of cancer are often treated with drugs such as cisplatin that can have a negative impact on hearing. So audiologists play a big role in monitoring hearing for children who are receiving chemotherapy. Of course, things like noise, not uncommon around the 4th of July for us to evaluate a child who's been too close to a firecracker, head trauma. Certainly there can be other impacts like that, that can negatively affect hearing. Meningitis is something that we'll ask Dr. O'Connell to comment on, but certainly every year we see numerous children in our clinics that are having impacts on their hearing related to meningitis.

And the key there is to educate our related professionals of the importance of getting a full hearing evaluation when a child has had meningitis. Because time is of the essence. We know that meningitis can cause ossification of the cochlea in a fairly short time span. So one of the important messages we want to get out to other healthcare providers that are going to be caring for infants and children who acquire meningitis is the importance of referral to audiology and ENT so that we can evaluate their hearing in sufficient time to act in the way of cochlear implantation, if that's necessary.

Dr. Jason Barnes:

And I wanted to talk about a couple of more kind of specific aspects of the pathophysiology of some of these hearing losses. Dr. O'Connell, you mentioned enlarged vestibular aqueduct. Could you touch on that in a little more depth?

Dr. Brendan O'Connell:

Sure. That's one that will readily be picked up by imaging. You can see it on MRI and CT. Perhaps CT is a bit better, but I think if it's an obvious EVA, you will see it on a heavily-weighted fine cut T2 sequence, a CISS or a FIESTA sequence.

You'll see an enlarged sac and an enlarged duct. Interestingly, if it's very big, it can oftentimes look like the sigmoid sinus, but it's actually just a very large sac. The diagnosis on CT has been described before in two different ways. One being if the diameter of the duct is greater than 1.5 millimeters or larger than the diameter of the posterior semicircular canal, if we see bilateral EVA, we have to have suspicion for underlying Pendred syndrome, which is a mutation in SLC26A4. And that's associated with an enlarged thyroid, which doesn't manifest until later in life.

Another imaging finding that's oftentimes associated with EVA is incomplete partition type II, oftentimes also referred to as a Mondini malformation. And this is where we will see sort of a cystic cochlear apex. There's not a full two and a half turns. You lose a little bit of that definition of the modiolus in the apex. And you can appreciate that both on CT and MRI. EVA in general can be progressive. You can have unilateral or bilateral EVA. As I mentioned before, bilateral EVA has association with Pendred. I don't know how strong this data is honestly, but there's anecdotal evidence and certainly stories that we've all seen patients that we've all taken care of where there has been hearing loss that's been precipitated by head trauma.

Now, does that happen in every case of EVA? No. But can it happen? Yes. And it's always a question that families ask. "Oh. What do I need to do if my child has a diagnosis of EVA? What can they or can't they do?" And that's a very hard question to answer. A lot of times I think you got to... I largely defer that decision to them. I think if it were my child, I would avoid very high-risk activities. Things like football. I don't think I'd let my kid play football if they had EVA.

But outside of that, I think they have to live their life. And I would let my child engage in most other activities as long as I didn't feel like that specific activity put them at greatly increased risk for head trauma.

Dr. Jason Barnes:

And Dr. Roush, we'll talk about this a bit more in the workup section, but can you tell us a little bit about auditory neuropathy spectrum disorder?

Dr. Patricia Roush:

Sure. Auditory neuropathy spectrum disorder is something that has to be diagnosed with an auditory brainstem response evaluation. There are specific protocols that allow us to look for auditory neuropathy, but any audiologist who is evaluating a child following a failed newborn screening should be doing, having their protocols set up so that they can look for that. And basically the findings are an absent auditory brainstem response with evidence of outer hair cell function. And that evidence about a hair cell function can either be present otoacoustic emissions when an auditory brainstem response is absent or seeing the presence of the cochlear microphonic, which is an electrophysiologic response that occurs before the Wave I in the ABR.

And so if we see a cochlear microphonic with no subsequent neural waves in the ABR, then either of those conditions qualifies for a diagnosis of auditory neuropathy. It affects about 10% of children with permanent hearing loss. There are now numerous studies over the last 20 years looking at this population of infants and children in particular, as we're talking about pediatric population today who have this condition. And for most audiologist, and ENTs the infants who have auditory neuropathy will be coming out of the intensive care nursery.

About 50% or so of children who have the condition will have it related to either a lack of oxygen, a period of anoxia, hyperbilirubinemia or other impacts from treatment in the newborn intensive care nursery. In the other cases of auditory neuropathy, there can be a variety of conditions, some that are genetic. A common one that we might see among genetic causes of auditory neuropathy is due to otoferlin mutation. And that's something that we can send out for and find out whether there is an otoferlin mutation.

So if the infant is presenting with auditory neuropathy and coming from the well-baby nursery, that would be high on our list of suspicions. But it's also important to remember that a subset of infants who present with auditory neuropathy could have other neurologic conditions such as Charcot-Marie-

Tooth disorder, Friedreich's ataxia, Gaucher disease. And some of these conditions will affect infants and not be noticeable, as Dr. O'Connell was saying, because we're seeing the infant at a very young age.

So this is where genetics can come in. If there's not another explanation, if the infant wasn't an early premature baby, then certainly we would want to make sure that we're exploring other possible reasons for them to have auditory neuropathy. One of the challenges with auditory neuropathy is that really when infants are diagnosed, we know very little about their functional hearing, other than the fact that they have an electrophysiologic test that points in this direction.

And it's only through later behavioral testing when the infant's at least six months of age, that we can begin to sort out whether this is an infant that could have fairly normal thresholds for hearing or whether they have a profound hearing loss and could, for example, require cochlear implantation. We even see some infants who have the auditory neuropathy pattern. In fact, it's not that uncommon for infants who have the auditory neuropathy pattern to have absent or deficient cochlear nerves. And this is where looking to MRI will help us out.

And then as the infant gets older, we'll do behavioral testing to, as I said, figure out their functional hearing status. If they have thresholds that are in a range that we would typically provide hearing aids, then we would initially start with amplification to see whether they benefit. Some infants will benefit. Some children will benefit from hearing aids with auditory neuropathy. Some will require a cochlear implantation even with relatively good hearing thresholds because the quality of the sound that they receive is poor.

It's also important to remember that a small set of children who present with the auditory neuropathy pattern will have normal hearing thresholds, and in fact, go on to develop speech and language in an appropriate way without any intervention. They'll be monitored carefully, but they may not need hearing aids or cochlear implants. So it's a heterogeneous disorder and we certainly need to use all the tools in our toolbox to sort it out.

Dr. Jason Barnes:

So we've talked about the presentation and some of the causes of hearing loss in kids. And I next wanted to ask you Dr. Roush a little bit about the natural history. How do you counsel parents and families on the ramifications of untreated hearing loss in kids?

Dr. Patricia Roush:

There are a wide range of hearing loss. And so children who have milder degrees of hearing loss will continue to respond to sound. And it's important to help families to understand that even relatively mild degrees of hearing loss can have a significant impact on their learning, their cognitive development, their socialization, and their educational performance. In some cases, families understand that. In other cases, we need to demonstrate it.

And there are ways that audiologists have to demonstrate what the child can and cannot hear in the sound booth. And for families who are having difficulty accepting the diagnosis, I think when we show them by demonstrating through the loud speakers with their child sitting in the room and the family sitting in the room with them, I think that that goes a long way toward helping them to understand so that they'll take the measures that will allow their child to be successful.

Dr. Jason Barnes:

So moving on to the workup part of this podcast, I wanted to talk about audiologic evaluation and imaging studies, as well as some other things. Dr. Roush, can you tell us about the different options for audiologic evaluation for these kids?

Dr. Patricia Roush:

Sure. Professional organizations such as the American Academy of Audiology and the American Speech and Hearing Association have defined protocols that have been peer reviewed and so forth. For the young infant, we've touched on newborn hearing screening. We mentioned that there are two types of newborn screening, otoacoustic emissions and ABR-based. But those are just screenings. They don't allow us to know the degree of hearing loss.

And so we move quickly from the screening process, which really should end at one month of age. And I, especially in this forum, I'd like to just emphasize the point that the screening process should end by one month of age. Once an infant has had their screen in the hospital and perhaps their second level screen as an outpatient within the first month of life, at that point, if they go to an ENT office in their local community, they shouldn't be screened again.

They really should be referred to a center, whether that's that office, or if that office doesn't have the capability, they should be referred to a center where they can get a comprehensive auditory brainstem response evaluation. Another tool that we have now is auditory steady state response. So either of those will allow us to use frequency-specific tone burst to define what the child's estimated hearing thresholds are for each ear. So we're going to use these if... For example, if we're using ABR, we're going to look at four frequencies 500, 1000, 2000 and 4000 for each ear.

We can test by air conduction and bone conduction. We're going to use our tympanometry to make sure that there's not middle ear problems that are overlaid on top of any underlying sensory neural hearing loss. And otoacoustic emissions will play a role in addition to a tool for screening, they also play a role in our diagnostic assessment as crosscheck. For example, if an infant came in and had no response on an ABR normal tympanometry, but present otoacoustic emissions, then we will suspect that this is an infant that has auditory neuropathy.

So we use a comprehensive battery. We test each ear, we do air conduction, bone conduction, tympanometry and otoacoustic emissions. But it does require expertise. That requires someone that has the experience, someone that's doing it routinely. And unfortunately families can get misinformation if they go to a place that doesn't routinely see infants. Like anything else that we do professionally, if we have a high volume of patients, and if we're doing this on a routine basis, we get better at it. And so when a center sees a child and suspects hearing loss, but if they don't have the tools or the expertise, my main message would be to refer to a center that does so that they can have a comprehensive evaluation.

Once we do the ABR, we can intervene right away with amplification. In our center, it's not at all uncommon for infants to have their diagnostic ABR at six or eight weeks of age. And then immediately, if the family's ready to move on to the fitting of amplification by the time they're... just a couple of weeks after diagnosis, once we get all of the technology into the center. From there, we're going to continue to see the infant, monitor for middle ear status, work with the family, we're going to enroll in early intervention.

And then when the infant gets to be between six and seven months of age, we're going to go ahead and put them in a sound booth. And we can test again with individual ears. We can either use their ear-molds from their hearing aids to attach to our insert earphone transducers. If the infant won't tolerate that, we can certainly test through loudspeakers, what we call sound field testing. But our goal really at that point is to determine, has there been any change since the initial ABR?

And we know that probably 20% or 30% of children will have progressive hearing loss. So it's important that we take another point in time to monitor their hearing. So at six to seven months of age, we'll look, is this still a stable hearing loss, or has it changed? If it's changed, we're going to make changes in their technology. We may adjust their hearing aids based on those new changes.

And then we'll monitor them. The young infant we'll monitor every three months until they're about three years of age. And then at that point, we may see them every six months. And during those visits we're taking new ear impressions, assessing whether hearing aids are adequate or whether they need to be referred to our cochlear implant team for consideration of a cochlear implant.

Dr. Jason Barnes:

And Dr. O'Connell, imaging plays a role in the situation as well. Can you tell us when you decide to pursue MRI or CT scan in these kids?

Dr. Brendan O'Connell:

We as a center recommend imaging in, like I said earlier, just about every child with hearing loss because the diagnostic yield is high. And we typically are going to start with an MRI scan. So there's pluses and minuses to both MRI and CT. We generally start with a non-contrasted MRI with a heavily weighted T2 fine cut sequences through the inner ear and the IAC. And really that gives us just about all the information we need to evaluate for cochleovestibular malformations. And also added benefit over a CT scan, it shows us the entire brain, and it tells us what's happening at the level of the eighth nerve, neither of which a CT scan can do.

Another advantage of MRI is that it avoids ionizing radiation. There's a lot in both medical literature and lay press these days about the adverse effects and long-term cancer risks of radiation early in life. So an MRI avoids that, obviates that risk. An obvious downside sort of juxtaposed with the radiation risk is the fact that the MRI is going to require sedation.

It's a long test and the child's going to likely... or is going to need to be sedated for the MRI. Now a CT scan, depending on the age of the child may or may not require sedation. In my experience, usually, any child under five is going to require sedation for the CT, but a very mature five or six-year-old perhaps could undergo a CT scan, CT temporal bone, without sedation. So, that's just a point that's worth considering.

But again, given the advantages of MRI, the fact that a lot of times, I mean, not every time, but a lot of times there's other things we're thinking about and other things we may need to do that we can always add on to a sedation, whether that be an exam under anesthesia of the ears with potential need for tubes, repeat ABR.

A lot of times we'll consolidate those into one event, one sedation, and accomplish those goals in one sitting. I think it's worth, just in the context of the need for repeat ABR mentioning... or sedated ABR. Dr. Roush's discussion of ABR was fantastic. One thing that I'll mention is that there is a difference between natural sleep ABR and sedated ABR. And it all depends on the age of the child, obviously maturity of the child too.

We can generally... And correct me if I'm wrong Dr. Roush, do a sleep ABR, meaning avoid sedation and get most of what we need in children less than three months of age, sometimes less than four months of age. So that highlights that importance of early referral for that diagnostic ABR. Once a child gets much above four months, it's much harder for them to perform that natural state sleep for that natural sleep ABR, and then they almost require sedation for their ABR.

And that just ties in with that role of imaging. So there's certainly kids that we see, not ideally, but we see that perhaps are referred a little bit late that we just can't get the information from this natural sleep ABR and needs sedation anyways for their diagnostics. And we'll add MRI onto that.

Dr. Jason Barnes:

And talking a little bit more about the workup, Dr. O'Connell, can you tell us how you approach the difference between unilateral and bilateral hearing and how that affects obtaining infectious workups or genetic workups?

Dr. Brendan O'Connell:

Yeah. In terms of genetic causes of unilateral hearing loss, I mean, they're going to be few and far between... I think Waardenburg is one that would come to mind as something that could be associated with a unilateral loss. For me, I mean the number one thing in terms of identifying the etiology of unilateral loss is going to be imaging. You're going to want to, if it's a profound loss rule out cochlear nerve deficiency.

If it's anything in between rule out an inner ear malformation. And certainly I think EVA IP2 would go high on the list of being probably the most likely cause in that scenario. I'm probably less inclined to strongly encourage parents and families to pursue genetic evaluation in cases of unilateral loss, thinking less about infectious causes, other systemic or multifocal syndromic causes for sure are going to be less common.

So I think again, imaging would be the initial step for me in cases of unilateral with... but still keeping in mind other causes. And it all comes back to I think the... Identifying an etiology is crucial and should always be our goal. So I think we always need to start with what we think is going to be the highest yield diagnostic intervention, and then go from there.

And if we're left without answers, certainly in situations in which there's other findings that are concerning, then I have a very low threshold to at any point for any child refer to people that honestly, I think are a lot smarter than me like a really good geneticist. But upfront I would start with imaging and rule out our losses.

Dr. Jason Barnes:

And Dr. O'Connell another question that I feel like is often asked in clinic is when should a child obtain an EKG or ophthalmologic evaluation? How do you counsel parents on that? And when do you refer to these other subspecialties?

Dr. Brendan O'Connell:

Sure. Good question. So I'll start with EKG. As part of the history taking, I don't think I mentioned it before, but I always ask about... if it's a very young child, I ask about is there a family history of members with recurrent syncopal episodes or seizures or early sudden cardiac death? And if the answer to that is yes. Then I absolutely will get an EKG on the child.

If the answer to that is no, I think it's a bit controversial. Now, we used to get EKGs on every child that came through. And what we found, I don't know that it's actually published data, but what we found was that we were identifying a lot of sort of EKG variants of unknown clinical significance with many referrals to cardiology that ultimately didn't lead to anything meaningful. And that led to a change in practice pattern here where we stopped routinely ordering EKGs and did it in a more directed fashion like I talked about before for situations in which there was a strong family history.

Now with that obviously comes a little bit of risk of missing something that's potentially life-threatening. And that's why I think it's important to continue to revisit questions like this at subsequent follow-ups. "Have you, since last visit, had any episodes of concern for syncope or seizures?" And if that ever becomes yes, then again, we'll then move towards the direction of EKG. I think some of that's obviated for the child that ever goes for comprehensive genetic testing. So another benefit of considering a genetics referral is that this could potentially be detected via genetics test without the need to get an EKG and go down a rabbit hole of workup where you're no longer actually looking for Jervell Lange but you're chasing sort of changes of unknown clinical significance on an EKG when you've seen them for hearing loss.

So, that's my perspective on EKG. In regards to ophthalmology, I do encourage all families to at some point seek an ophthalmologic evaluation. The primary reason for that is both vision and hearing our senses. And I think if one senses at all down, we want to ensure that the others are perfect. And a lot of times that may just be the fact that the child gets fit with glasses not that a finding is discovered that then leads to a syndrome that associates hearing and vision.

But there are certainly situations in which there can be associations between hearing and vision. And that's yet another way that I think you can evaluate those. And back on the topic of genetics, people that are strong proponents of genetic... companies for genetic testing will say, "Well, we could eliminate some of those referrals and be more cost-effective if we just test comprehensively for all genetic defects."

So it's an evolving field. And I think one of the issues with it is that genetic hearing loss is so complex. It's so heterogeneous that there's new genes being added all the time and our understanding of those is changing. And I think the next five to 10 years will be very interesting in terms of what we learn and discover in that regard.

Dr. Jason Barnes:

And Dr. Roush, another part of the workup sometimes includes genetic testing. Can you elaborate a bit more on when you might encourage families to pursue a more in-depth genetic testing and what that looks like?

Dr. Patricia Roush:

Sure. Again, I think it's important... Our history with the family is very important, what they tell us and certainly what the child's diagnosis is. For the child who comes in with typical sensorineural hearing loss, if we have information from the Guthrie card that tells us that CMV is negative, and if the connexin 26 test is also negative, and imaging does not have any benefit for that child in terms of determining etiology, referral for a more comprehensive panel is something that we should certainly offer to families.

In some cases, cost is a barrier to families. But we're finding that insurance is covering in a lot of cases. And for many families the cause is very important. So of course it all depends on what the family wants to do. Some families want to pursue genetic testing, others don't. But we now have panels that are available, that where we can send out for a comprehensive panel that will look for hundreds of different genes that could be the explanation for the child's hearing loss. Particularly going back to the child with auditory neuropathy, there's work now to...

While some of the genes for auditory neuropathy will be included in a comprehensive hearing loss panel, there are efforts in genetics centers to come up with panels that are specific to auditory neuropathy. So depending on what we know about the infant, their hearing loss, their family history, the otolaryngologist can request more comprehensive panels to be done. And I do think that in our

experience that has been very helpful. We recently had a child with... presented with auditory neuropathy and no other presentation at birth, who over the course of the first few months of life began to present with neurologic problems and signs.

And it was only through a comprehensive genetics panel that we were able to learn that the child in fact had a very serious progressive neurologic disease. So genetics can certainly play an important role in the management of the child with hearing loss.

Dr. Jason Barnes:

Finally, I wanted to move on to treatment. And we are going to have an episode on pediatric cochlear implantation. But could you tell us, Dr. O'Connell, a little bit about the treatment options for pediatric sensory neural hearing loss and how you consider when to trial these or pursue these?

Dr. Brendan O'Connell:

Yeah. The treatment options are in my mind going to be two-fold. I mean, they're going to be hearing aids or cochlear implants at this point. And there's very clear cut scenarios in which one is better than the other, then there's some areas where it's fairly gray. I think for the child... And I think there is a nice article that Dr. Roush was an author on before my time here that went through sort of your infant with the no-response ABR and how often that child ended up being a candidate for a cochlear implant.

And just about every child that has no-response ABR at our center went on to receive a cochlear implant. And the only reason those that didn't receive a cochlear implant were for issues not related to their actual hearing levels. They were candidates for cochlear implants.

So your child with severe to profound loss, certainly those with no-response ABR, we're already thinking along the lines of a cochlear implant and given that there's increasing evidence that it's time-sensitive, the sooner you can do it, the better. We're almost gearing that first year towards the idea of getting an implant in before 12 months of age for that no-response ABR child. For your mild moderate loss, I mean, obviously that's going to be more you're hearing aid candidate.

And then that moderately severe to severe loss, that's tricky. In an adult, what we rely on in those scenarios is speech understanding, word recognition, sentence recognition, and quiet and a noise to help make that determination of how meaningful and clear the auditory input is in the face of a moderately severe loss. In children, it's much more complicated. You oftentimes just have the thresholds, you can't get speech recognition data until a child is older.

In a normally developing child, I mean, maybe that age is three. Dr. Roush may have a comment there. And we're starting to focus a bit more on trying to get aided speech understanding in children that are capable of performing that test. But for the younger kid, that's again where the multidisciplinary team is absolutely critical. And people with experience from the speech-language pathology standpoint and with AVT training and experience with cochlear implants really help us make the determination of are the hearing aids providing adequate benefit or not.

And oftentimes that decision as to whether or not to continue with the hearing aid or move towards an implant is predicated on that, both audiology and speech language evaluation.

Dr. Jason Barnes:

Dr. Roush I'm getting ready to move on to our summary here. But I was hoping before I summarize our episode, you could kind of give us a summary of what the first year or so looks like in terms of workup and hearing tests for kids who are diagnosed with hearing loss at an early age.

Dr. Patricia Roush:

Sure. I think that the first year following diagnosis is a really eventful year. I think you could say it's challenging. I think families need a lot of support. I think some of the things that are key are making sure that our screening protocols for our States are good and intact and that they have good quality assurance measures, so that infants get through that screening process in an efficient way. As Dr. O'Connell was saying, it's really critical that a center like ours that has the comprehensive services receives the infants following a failed newborn screening, if they're going to come to us for their diagnostic ABR well prior to three months of age. So the sooner we get the referral, the quicker we can act on it.

In our center, we do several diagnostic ABRs every week. We will hopefully get the infant at that point for a natural sleep ABR. We allow sufficient time during that appointment so that we can not only do a comprehensive ABR, OAEs, tympanometry, but we want to allow enough time to counsel the family, because this is our opportunity to make sure that they understand the impact of this hearing loss on their infant, so that they can take the appropriate measures. And I think counseling them appropriately and giving them time to ask questions goes a long way to establishing a relationship that we're going to have with this family for, in some cases, many, many years to come.

So after the diagnostic ABR, and in some cases on that same day ear impressions, they'll see the physician who will do this comprehensive workup that we've been talking about this morning. Any testing that's needed in our center, we, as Dr. O'Connell said, we have a good workup that allows us to start with this Guthrie card, the blood spot from the newborn screening. And that right away will give us some indication of whether they have the most common genetic hearing loss connexin or whether CMV was detected from the blood spot at birth.

I will point out just to say that, that test, although if it's positive, it's useful, if it's negative it does not mean that the infant doesn't have congenital CMV. And there are a lot of efforts across the United States to come up with better testing of the newborn for CMV. But certainly in our center having access to that has yielded the diagnosis in many cases. So between looking for connexin, CMV, and then our imaging, in many cases, we have the etiology by just looking at those three things. If not, as Dr. O'Connell said, we'll go onto more comprehensive evaluation.

From there the child, and their family will return for hearing aid fitting in many cases. The branch points are different. If it's a profound hearing loss then they're going to be moving forward relatively quickly so that we can give them access to sound at a young age. And our goal is to have that done even by nine months of age, if we have all of the information we need. If we have diagnostic ABR or ASSR to indicate that the child has a severe or profound hearing loss, if we have behavioral confirmation of that profound hearing loss then we can move, if the family is interested, toward cochlear implantation and the appropriate rehabilitation for that track.

On the other hand, if it's a child with a mild or moderate hearing loss and they get their hearing aids at two or three months of age, they're going to need to have frequent visits to have ear-molds made because the ear grows rapidly in the first year of life. So there'll be many visits, sometimes as many as six sets of ear-molds even in the first year of life. So they need to work with a center that's has the capability to provide these services in an efficient manner.

And then behavioral hearing testing is a big component. We haven't spent much time on that today. But really behavioral testing is the gold standard. The ABR certainly gives us a good estimate of thresholds, but the true gold standard for how an infant hears is how do they respond to sound? And so for the very young infant, that's a procedure called visual reinforcement audiometry that most infants are able to do by six or seven months of age if they're typically developing. If they have other conditions that affect their motor development or cognitive development, that may be harder to do. It may be

more difficult, and they may need to be a bit older and require more frequent testing to get the thresholds that we need.

Once we have our initial behavioral test, as I mentioned earlier, we want to monitor over time. And so that first year the family does need to come back to the center for a variety of visits. And simultaneously as we're doing medical workup, audiologic workup, they're connecting with their State's early intervention program, getting the referrals they need. And hopefully in addition to that, we've connected them with other families so that they can have the support they need as they go through this challenging time for them. We have a number of organizations in our state that provide parent support.

And I think that makes a huge difference in a family's ability to cope with this new diagnosis and also learn from other families that have gone before them. So that's also a big part of what we do, is we connect families to other families and the intervention that they need to have the best outcome for their child.

Dr. Jason Barnes:

Well, Dr. Roush, Dr. O'Connell, this has been a great discussion about pediatric sensory neural hearing loss. And I just want to say, thank you. And I'll now move into our discussion. To start, pediatric sensory neural hearing loss occurs in about one to two children per 1000 children. An initial evaluation should include a thorough history, including asking questions about perinatal infections, ICU stay, prematurity, and other questions surrounding that topic. Family history should also be obtained to understand the hereditary risk of hearing loss.

50% of pediatric hearing loss or up to 50% can be hereditary. And two thirds of this is non-syndromic, the majority of which are caused by a defect in the GJB2 gene, which codes for that connexin 26 protein. Some of the common syndromic entities include Pendred, Jervell Lange-Nielsen, Waardenburg, branchiootorenal, Alport, and Usher syndromes. And some acquired causes include meningitis, CMV, noise exposure, and trauma. Workup includes audiologic evaluation in the form of OAE, ABR, and then eventually behavioral audiometry.

And treatment of course begins with habilitation but also can include hearing aids or potentially lead to cochlear implantation depending on the severity of hearing loss. Dr. O'Connell, Dr. Roush, thanks so much. Is there anything else you'd like to add?

Dr. Patricia Roush:

No. We appreciate very much you're taking the time to address this important topic. Thank you for having us.

Dr. Brendan O'Connell:

Yeah. Thanks very much for the invitation.

Dr. Jason Barnes:

Thank you. I'll now move on to the question asking portion of our time together. As a reminder, I'll ask a question, pause for a few seconds, to give you a chance to think about the answers and then give the answer. So the first question is, what is the breakdown of syndromic versus non-syndromic children affected by hearing loss?

So, as we mentioned before, up to 50% of pediatric hearing loss can be hereditary. Two thirds of these are non-syndromic, one-third of which are syndromic. And about 75% of the syndromic cases are

caused by an autosomal dominant cause. For our next question, what is the most common non-syndromic cause of pediatric sensory neural hearing loss?

The most common cause of genetic non-syndromic hearing loss is the GJB2 mutation, which codes for the connexin 26 protein. For our next question, in obtaining CT and MRI imaging studies for children with sensory neural hearing loss, what are we looking for in these different imaging studies?

So on CT scan, you can look for things like cochlear hypoplasia, enlarge vestibular aqueducts, trauma, IAC stenosis, possible cochlear nerve hypoplasia and semicircular canal dysplasia. And on the MRI, we want a heavily-weighted T2 image, such as a CISS or a FIESTA. And this is really good for evaluating the nerve specifically, but as Dr. O'Connell mentioned, you can get a good idea of all of the previously mentioned structures as well.

And finally, as a bonus question, we didn't specifically cover all of the syndromes in this talk, but what are some common characteristics of the following syndromic etiologies of hearing loss? To include Pendred syndrome, branchiootorenal, Waardenburg and Jervell Lange-Nielsen. So for Pendred syndrome the main buzzword that goes along with that is that it's associated with an enlarged thyroid or goiter.

For branchiootorenal, on physical exam you would see preauricular pits or tags. For Waardenburg syndrome, this is the one that's associated with a white forelock or a heterochromatic iris. And for Jervell Lange-Nielsen, this is consistent with the history of syncope or a history of seizure. That's it for today. Thanks so much for listening and we'll see you next time.