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Grand Rounds: Pediatrics, presented in partnership with Nemours Alfred I. duPont Hospital for Children
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- [Christie] At this time, it is my pleasure to introduce our wonderful pediatric clinicians out from the Nemours Alfred duPont Hospital for Children in Wilmington, Delaware. We have Dr. Yell Inverso, Dr. Andy Lau, Dr. William Parkes, Dr. Jenna Pellicori, and also Dr. Michael Hoffman joining us today. At this time, I'm gonna hand the mic over to you, Dr. Jenna Pellicori.

- [Jenna] Thank you for the introduction, Christie. So Michael and I are excited to be here today to present on a case study highlighting one of the less commonly referenced and encountered sound sensitivity disorders known as misophonia. So we hope that everyone really enjoys the discussion today and take something meaningful away from the course content. We're gonna just begin with some learning objectives. Sorry,. I think this may be a little out of order. Here we go. So we're just gonna begin with some learning objectives. Following completion of this course, participants will be able to identify associated behaviors and characteristics consistent with a clinical diagnosis of misophonia, as well as assess clinically significant quantitative findings based upon self assessment measures, and lastly, participants should recognize effective psychological strategies for managing symptomology and improving quality of life outcomes.

Here's just a brief outline of today's presentation, which is going to include just a little overview of misophonia, a case study presented by the audiologist and psychologist perspective, which is hopefully gonna highlight the importance of multidisciplinary collaboration and patient management, and then we'll conclude with a patient update at the end. So the term was coined by Dr. Jastreboff in 2001 and was derived from the Greek root words, miso and phone, which literally translates to "hatred of sound." You may also hear the condition referred to as selective sound sensitivity syndrome or parosmia. So what is misophonia? Misophonia is a decreased sound tolerance disorder, which is really best classified as a neurophysiological and behavioral condition characterized by an immediate adverse, emotional, and physical response to specific repetitive pattern-based sounds, regardless of their loudness. This ultimately

leads to maladaptive behaviors and sympathetic nervous system arousal. So it's simply put, Kumar's 2017 study the brain basis of misophonia did a good job of really highlighting that the brain subconsciously misinterprets specific sounds as tasks toxic or threatening due to abnormal salience assignment. Unfortunately, the condition can lead to several psychosocial implications, like anxiety, depression, social isolation, and reduced quality of life. In regards to terminology, the repetitive stimuli that elicit the adverse response response are commonly referred to as triggers. Triggers are often auditory or visual in nature and are often produced in the context of typical everyday behaviors, meaning that there are often difficult to avoid. Auditory triggers are oftentimes soft, repetitive pattern-based sounds, such as chewing, breathing, pen licking, snuffling, or keyboard typing. And we know from the literature that the misophonic response often varies across individuals in the environment.

So for an example, you may be triggered by your mother's chewing but not your father's chewing. And in fact, one of the mysteries of misophonia is that people with the condition do seem to be more commonly triggered by family members or individuals that they maintain close relationships with. In regards to age of onset, research suggests that the condition most commonly presents in early adolescents. So our case today highlights an 11 year old female, who began displaying difficulties tolerating the sound of pencil tapping two years ago. However, since that time, she experienced increased difficulty tolerating multiple sounds. This included pen tapping, clicking, chewing, lip smacking, and also slurping. The patient was reported to live with her parents and two older siblings, which included a brother and a sister, and she had noted that she was most commonly triggered by family members, especially her mother and brother. The trigger sounds often resulted in feelings of anger, aggravation, and a general sense of unhappiness and she reported becoming agitated to the point of needing to exit the room or the environment. She also frequently responded to trigger sounds with verbal aggression as well. Per parental report, these reactions appeared to be extreme and were not commensurate at all with this situation. And in addition, the reactions, unfortunately, became progressively worse over the years and

have interfered with mealtime at home and at school. And at the time that we thought the patient initially, she was no longer eating meals with her family and would opt to eat alone. In regards to her birth developmental and medical history, they were all really unremarkable. She denied sensory sensitivities with the exception of those soft repetitive sounds, so a referral to occupational therapy wasn't considered to rule out a sensory processing disorder since there were no other reported sensory sensitivities. She also had denied concerns for hyperacusis, but did report occasional non-bothersome tinnitus and her mother had noted some concerns for her hearing as well, noting that she frequently required repetition of verbal information.

And once her mother had brought that up, the patient had also noted that she felt hyper-focused on trigger sounds and felt like she experienced difficulty filtering out sounds from the background, which is a really interesting statement in light of the available research by Schroeder and colleagues from 2014, which supported the potential for basic impairments and auditory processing in auditory attention in patients with misophonia. Okay, so I'll start by saying, we're very fortunate to have Dr. Hoffman assigned to our Audiology Department to provide behavioral health services to our patients with decreased sound tolerance disorders. And as part of our multidisciplinary approach at Nemours, we had decided to implement an anxiety and depression screening for our case history intake. And this was done in order to better establish the need for referral to psychology and also address some of the psychosocial implications that may be interfering with the patient's quality of life. One of the measures that we had implemented with the 7th Edition of the generalized anxiety disorder scale questionnaire, the child or family is basically instructed to rate how often the child has been bothered by seven scale of items over the past two weeks and upon completion, the scores are added together from the four response categories to obtain a total score. We identified a reasonable cutoff point for identifying the need for further evaluation or referral to psychology as a score of 10 or more. And on this measure, our patient obtained a total score of seven. We also administer the 8th Edition of the personal health questionnaire scale to screen for depression severity and the family

again is instructed to rate how often the child's been bothered by the eight scale items over the past two weeks. And upon completion, again, the clinician will add up the scores from the four response categories to obtain a total score. Our patient obtained a total score of 10 on the screening, basically warning a referral to psychology for further evaluation. With that said, we established this referral criteria and score of 10 or more on these screeners. However, we do offer a referral for psychological services to all patients being seen for concerns for decreased sound tolerance disorders. We just placed higher priority and emphasis on referring and counseling on cases where the child meets the cut point score for an item measure. We also have our patients complete a sound sensitivity questionnaire, which was created to basically quickly highlight the patient's chief complaints and guide which assessment and diagnostic measures would be most pertinent for the appointment. It helps to quickly differentiate between auditory conditions like hyperacusis tinnitus, phonophobia, and misophonia.

So part one includes a brief medical history and looks at risk factors and alternative conditions with potential symptom overlap, all of which our patient responded no to. Although we know from her case history, she did report some concerns again for tinnitus and not only that, but she also had reported some concern that she had a maternal aunt who presented similarly with the same auditory complaints and concerns as well. So although they had indicated that no one in the family presented as having to be misophonia, the case history could have possibly suggested otherwise. Part two then provides a glimpse into the primary sound sensitivity concerns. Questions one through five of this section are broken down to address the specific auditory complaints. Our patient had responded yes to questions one, four, and five, which are specific to misophonia and tinnitus. Although, we know from our case history reports, the tinnitus was considered occasional and non-bothersome. And then part three was designed to identify common auditory behaviors and complaints consistent with concerns to auditory processing or listening difficulties, which we, again, included just given the indications of possible central auditory nervous system involvement. Our patient's responses on this section really had supported her case history or reports,

indicating the need for frequent repetition of verbal information. So in order to assess misophonia symptom severity, our patient completed the misophonia assessment questionnaire, developed in 2013 by Marcia Johnson. And this primarily focuses on the emotional and psychosocial impact of the condition. It's composed of 21 questions based upon how often each item applies to the patient and utilizes a rating scale of zero, not at all, to three, almost all of the time. The total score is then calculated by summing all of the points in each column based upon their numerical point value. Our patient scored a subjective severity rating score of 29, placing her in the moderate range on this assessment. We also utilize the Amsterdam Misophonia Scale developed in 2013 by Schroeder and colleagues at the University of Amsterdam. And this measure was used to measure the impact and fixation with trigger sounds.

So it's composed of six questions, which provide insight into a variety of aspects, including time spent preoccupied by misophonia, the impact of the condition on overall functioning, distress levels, consuming thoughts, and avoidance tendencies. The rating scale ranges from zero to four for each question, and to score the assessment, the clinician must sum the total points from all six questions. Our patients were to subjective severity rating score of 13, again, placing her in that moderate severity range. He then proceeded with objective testing and evaluation of that peripheral auditory system to really aid in coming to a formal differential diagnosis. As part of our routine audiologic assessment, we began with otoscopy and tympanometry to assess for outer and middle ear pathology, which were unremarkable. Ipsilateral and contralateral acoustic reflexes were also evaluated to assess the integrity of the stapedial reflex as well as rule out concerns for auditory neuropathy or retrocochlear pathology, and they were deemed present in all conditions from 500 to 4000 hertz bilaterally. In addition, distortion product otoacoustic emissions were evaluated from two to 5000 hertz in order to provide insight into outer hair sound integrity and function and were present in both ears. We then proceeded with conventional audiometric testing to assess hearing sensitivity and while patients with misophonia present with varying hearing acuity, the literature really suggests that the majority of patients

diagnosed with misophonia will have normal peripheral hearing sensitivity at the time of their initial diagnosis. So as you can see, the patient's hearing threshold start within normal limits from 250 to 8000 hertz, including the interactives. Her speech recognition thresholds and pure tone average were congruent, suggesting good reliability, and her discrimination abilities were also noted as excellent bilaterally. These test results allowed us to rule out concerns for recruitment on alternative decreased sound tolerance disorder, given normal peripheral hearing and also the healthy cochlear function. For a sound sensitivity patients, we also attain loudness discomfort levels to further rule out concerns for a comorbid diagnosis of hyperacusis. The patient's LDLs were negative for hyperacusis since the responses were 95 DB or greater at all frequencies with an acceptable dynamic range of 60 DB or more. There's a little comment just next to 8000 hertz and that's just because that was the max output that we were able to test that. In addition, the patient didn't report any subjective complaints consistent with hyperacusis and denied louder level sounds causing any type of pain or discomfort.

Therefore, we were also able to rule out hyperacusis as an alternative co-occurring decreased sound tolerance disorder. We also evaluate ultra high frequencies, which provides additional insight into the integrity and health of the peripheral hearing system. Many clinicians have raised a concern for abnormally good ultra high frequency hearing sensitivity in patients with misophonia, suggesting that the extended high frequencies that appear to possibly be more sensitive than would be expected and typical adolescents for many of these patients. Unfortunately, normative data in the ultra high frequency range is antiquated for the pediatric population. So we need to work on re-establishing these norms in children and also look at this in a more controlled study. In our example, here, the ultra high frequencies appear to be within normal limits. And then at the bottom, you'll also see the BKB-SIN was completed. This is a part of our protocol for patients with concerns for misophonia and we use it to quickly screen for concerns for auditory figure ground deficit's due to evidence in the literature of those possible early auditory processing concerns or involvement and also

oftentimes subjective complaints as well. We know that in a healthy auditory system, our brains attend to relevant auditory information, such as the speech signal of interest, where we automatically and kind of reflexively filter noise to the background. However, in patients with misophonia, they actually appear fixated and hyper-focused on specific sounds in the background, like chewing rather than the noise itself. And in fact, in 2017 Round and Fannie had conducted a large scale study and 74% of the participants with misophonia had commented that they felt hyperfocused on noises that should have otherwise been filtered to the background and 87% noted difficulty with attention. So it's worth noting that our patient scored within normal limits on the BKB-SIN, although she did report some of those auditory complaints.

Okay, and unfortunately, at this time, there's no universally accepted diagnostic criteria or validated objective measures or biomarkers to identify the presence or severity of misophonia, primarily making it a diagnosis of exclusion. Therefore, it was the clinician's professional opinion that the patient was demonstrating behaviors and characteristics consistent with a clinical diagnosis of misophonia. There's also no empirically supported treatments at this time. However, one thing that many providers and researchers agree upon is that misophonia is a complex and poorly understood condition. And for this reason, a multidisciplinary approach or team-based approach is really important into assessment and intervention and is really considered a crucial for management. So we made the following primary recommendations for our patient. We discussed a referral to psychology to address concerns for anxiety, depression, and sound sensitivity, and to work on coping mechanisms and management strategies for addressing psychosocial implications of the condition. It's also worth noting that in 2017, Schroeder and colleagues reported that cognitive behavioral therapy was effective in reducing misophonia symptoms in 48% of patients, who underwent eight biweekly sessions. We also recommended a trial of sound generators to aid in masking out trigger sounds using an open fit to try to preserve speech intelligibility. The patient was fit with resembling squared five devices and the microphones were turned off and narrowband noise stimuli was selected as the primary masker. In addition, the patient

was counseled on using Bluetooth auditory stimuli as well to basically encourage active listening when appropriate. We also discussed several noisy desensitization exercises, including information on misophonia retraining therapy as recommended by Pawel Jastreboff. However, families should be advised that there is a lot of controversy over exposure therapy with misophonia and Dr. Hoffman will talk a little bit further about this in just a moment. And lastly, we provided an array of classroom accommodations, which unfortunately, we don't have time to go over in detail, but I would be more than happy to share our recommendations if you would like to reach out to me privately, but for now I am going to hand off our discussion to Dr. Hoffman.

- [Michael] All right. Hi, everyone. Hopefully, you can hear me well, and thank you so much for that. Wonderful start, Jenna. So before I dive a little bit more into specifics of this case, a few things to point out about misophonia within the context of pediatrics and psychology. So as what's most what's out there from the research is really primarily in adults. What we have in pediatrics is almost exclusively single person case studies. And so there's not a lot of great information out there to guide treatment for misophonia within children and adolescents. As Jenna referenced, there was that study from Schroeder and colleagues that did look at cognitive behavioral therapy and found that to be effective, but it with adults. And it also offered little to no details about what they actually did within the context of cognitive behavioral therapy. It's a pretty big umbrella to sort of say we did CBT with someone without giving specifics around any clear or standardized treatment protocols. So it's an area for the research that we really need more information on, particularly within children and adolescence. The other piece that really lends credence to doing a multidisciplinary approach is that in the literature among adults, at least, there seems to be increased links between misophonia and other mental health diagnoses. Oftentimes, these include things that would occur somewhere along the anxiety spectrum, OCD, OCD-like behaviors, generalized anxiety, and some ADHD. So many times when I am meeting patients from our clinic, they don't have misophonia in and of itself, there's also some sort of comorbid medical or mental health diagnosis that is going on there. And so I will walk

you through a little bit of what the treatment protocol that I developed with patients is, but a lot more research and knowledge is needed to really understand how valuable these things are or what ways we can improve treatment so they can be more effective for all of our patients. Generally speaking for this case study, she was pretty straight forward. She had the diagnosis of misophonia, but no other clear comorbid mental health diagnoses. And so with that, we were focusing primarily on these pillars of psychoeducation, cognitive-behavioral strategies, relaxation training, biofeedback, and in-vivo practice, which we'll walk through now. Here's a model when I am doing psychoeducation with my patients around how I teach them to think of misophonia. So first you have that sound that must occur that is over here. And for that sound to have any sort of impact on us, we have to actually hear it. And once we are hearing a sound in this case in misophonia trigger, there are two avenues or pathways that would happen.

One would be this cognitive response, which is having these thoughts of, "Oh, my God, this is happening again. These sounds are horrible. I can't stand my mom chewing. I might like stab her in the hand with my fork." Sometimes they get kind of violent. And then there's this physiological responses also happening. So this actual activation of the autonomic nervous system that is going on where kids are probably having increased heart rate, more shallow breathing, they're having these physiological stress responses kicking in. And those two things can inform each other and then from that, there's this behavioral reaction. "I have to leave the room. I can no longer eat with my family, eat in a separate room. I need to take a break from a class," all of those things. So when I'm working with my patients, I am teaching them to think about their response to misophonic triggers within this pathway and then saying from the clear audiological perspective, you might use the sound generators, you might use some sort of hearing device, you might use earplugs, headphones, you're leaving the room, doing things to try and interject here in this part of the pathway so we don't hear it as well or we don't hear it at all. Granted we cannot plug our ears forever and forever, and we have to hear some sounds at some point. So using some other strategies can be

really, really helpful. Cognitive behavioral therapy, relaxation strategies, mindfulness to really target that cognitive response and then using biofeedback, which we'll talk more about in a minute to target that physiological response. Ultimately, with the goal of these things having less of an impact on daily functioning, not feeling like, "I have to get out of the room. I have to escape the sound," where being able to be in certain environments that would be more desirable. So when I'm talking about the physiological response, I really love to show this picture. It's a little busy, I'm not gonna walk through everything, but teaching the patients to really think about when they are hearing a misophonic trigger that is queuing this sort of fight or flight response that they're having this stress response that is kicking in. And if we are having this whole sympathetic nervous system response, we really wanna figure out a way to engage our parasympathetic nervous system and get us to combat that.

So if we are going into fight or flight mode, how can we get ourselves back to baseline or homeostasis or what is now getting a rhyming couplet known as rest and digest. So thinking about misophonia in that context and having that understanding of that physiological response in addition to the cognitive response really sets up the idea that, "Hey, these CBT strategies or these coping strategies could actually be helpful. How do I get myself back to baseline as fast as possible?" So are they recognizing their cues? Are they understanding, "Oh, I'm starting to get worked up right now." And once the cues are kicking in, how can we regulate? So more specifically, what do some of these things look like? For cognitive behavioral strategies often we are working around things I thought challenging and thought restructuring. So for our patient in this case study, having the thought that there's no way I could possibly ever sit in that kitchen again, if I do what is just going to be torturous and identifying maybe areas of resilience, ways to challenge those thoughts and say, "You know what, I actually sit in the cafeteria at school every day and even though those sounds don't bother me quite as much, I can do it." Or, "I was just at my friend's house yesterday and had a whole bunch of meal time with them sitting at the table." Many times children will say they are focused on these things, like the sounds are happening and

teaching them to say, we can't control what is happening from other people, the other noises people are making, where a kid in our class, but what things are within our control that we can do and how can we identify that? And addressing those catastrophizing thoughts. "So this is horrible. There's absolutely no way I can do this." Really challenged them to recognize how quickly their thoughts may be escalating to this point of helplessness or hopelessness and feeling like, "You know what, I have skills and I have things I can do." Relaxation training. So within this, teaching things like guided imagery. If you're not familiar with this thinking about it as visualization, but really cueing them to use all of their five senses, progressive muscle relaxation, which is a series of tensing and relaxing different muscles to cue some of that relaxation response, and mindfulness based strategies.

So trying to cue attention to other things in the environment or the present moment. Biofeedback has been one of my favorite areas. It's pretty cool in my opinion. But what we do is we hook patients up to a laptop or a computer. We have some sensors that can detect things like heart rate, respiration, it can detect their body temperature and we can actually in real time see what their physiological response looks like when they're engaging in relaxation techniques. So the major core focus of this is diaphragmatic breathing. And there are lots of games and such as part of the software where they can play and they really work on improving their deep breathing or their diaphragmatic breathing and seeing if they can physiologically induce this common response and have some of those physiological markers start to calm down. With that, I often like to think sometimes about exposure therapy as Dr. Pellicori mentioned, this is a pretty controversial area. If you think of misophonia as being some sort of purely learned behavior, as some other psychologists have posited, then yes, it would make sense to go ahead and immediately try and teach them ways to unlearn this behavior by doing exposure therapy in the same way that we may teach someone to get comfortable being around a dog. But, and it seems the research is leaning more in this way, if there is some sort of clear pathway that is occurring in the ideological system in the brain that indicates some sort of misophonia, then trying to correct that through

behavioral strategies isn't going to work. And so when I have used exposure therapy, I very much make sure to get consent from my patients, but the idea is not to get to just totally habituate to a sound, but rather to say, here's a chance to actually practice using some of these techniques in a controlled environment while I have you hooked up to the biofeedback equipment. And so we can see if I do a trigger sound for them, see them jump up and see that physiological reaction and then have them practice calming down. Some patients have really taken all to it and they really like it and other patients are totally opposed to it and would never let me possibly introduce the sound in the room. So it was really variable in terms of what we see, but thinking about it as a chance to practice the strategies is not as a chance to just get to habituation and totally overcome the silence. And so finally, a patient update. So for this case study, after I did some psychotherapy with her and we had all of the strategies that Dr. Pellicori mentioned, she is doing well in school, has benefited significantly from that. The home environment is still a bit more challenging, but working on that. She has been able to rejoin her family for some meal time. Typical masking stimulus she uses is white noise and she seems to prefer the Resound Relief App. And for her coping strategies that she has found effective are mimicry, which I haven't used with many, but she liked that one. So mimicking the behavior. General avoidance, so leaving the room is still always going to be a preferred one, but also mindfulness and some of the diaphragmatic breathing. Given the time that we have right now, I think we're going to hold off on questions for a little bit, but I'm going to pass it over to Dr. Lau, who will talk about our next case study and we can answer any questions we have at the end.

- [Andy] All right, thank you. So my case is about visceral neuritis and the goal is to give us a quick overview of how to target tests in the clinic setting. And so the patient is a 12 year old female and starting about four days prior to when I saw her, she began experiencing dizziness, characterized spinning sensation, the direction which Kimberly pinpoint can go both ways, clockwise counterclockwise. The episodes can last anywhere from second to minutes and typically triggered by any changes in head and body positions. And she reports that when she slows down, keeping still or closing our

highs tend to help. And when she described that, when she closed her eyes, she still feels emotion, but she reports that closing her eyes help because it diminish it's confusion because she thinks things are spinning too much. And other things that she complained off at the time is feeling nauseous and has vomited because of it and she has experienced some tinnitus in her years as well. She also feels like a transient sensation of veering and falling in multiple directions. And other history otological history, she doesn't have any concerns for decreased hearing. She doesn't feel any pressure or tinnitus prior to this, no pain in her ears, and doesn't really have any history of ear infections. And medical history, she did report having dizziness prior and when she was much younger, she had a seizure episodes and there was at least one EEG, where it showed some abnormal activity on the left side of the brain, but it's only one and it wasn't replicated. And she also has a history of migraines reported. But when sh when she complained of dizziness, there was no headaches associated with the migraines and she didn't feel any headache with this current episodes of dizziness. And so just based on the case history, there were several things that we start narrowing down for differential diagnosis.

The top two of vestibular neuritis and labyrinthitis, the differentiation between hearing loss versus no hearing loss, the suggestion of something that's impacting the left side end organ, which we'll talk about that later on. Vestibular migraines similar because she has a history of migraine, so there may be some transition of that. And then benign paroxysmal vertigo of childhood. So these are the top five preferential diagnosis that we're thinking of. And just before I saw her, she did get to be seen by ENT for a quick bedside eval and no spontaneous nystagmus observed. There was some right-beating nystagmus with some torsional component in both the rightward and leftward gaze, more pronounced when she was looking towards the right, which coincides with Alexander's Law. And for a quick refresher, Alexander Law basically states that nystagmus will be stronger when gazing the direction of the relatively healthier ear. So there's a lot of words here, but just think it's that the relatively healthier ear will cause some stronger beatings as more firing on that side, tonic firing. And other findings that

was done was that through MRI imaging studies, there was a suggestion from a mild enlargement of the left vestibular aqueduct, and so EVA is suggested as well. So we updated our differential to include that. So when I go in to see her, so I kind of observed how she was doing. And just prior to me being there, she had an episode just before. So she was carrying herself pretty stiffly and kinda like walking like young Frankenstein in the movie, if you have ever seen it. The way they carrying herself, she's wouldn't move her neck, but she was very articulate and very cognizant of everything that's happening and she was able to describe all her symptoms and her history succinctly. And so as I looked at it, it kinda reconfirm the history. I took a look in her ears to make sure there was no wax buildup and nothing abnormal. And I did a quick tympanogram to make sure that eardrums are moving nicely. And we didn't have an portable audiometer time, so I did a quick screen to see what's going on to give us an indication potentially, is there any hearing loss that could point to labyrinthitis as a potential diagnosis and the DPOAEs were grossly present from two to 8000 hertz bilaterally.

And so I did a quick, and so based on the vestibular testing, the history, I just try to start thinking, what can we do to target test to patient? So when you look at the system, there's basically several things we want to look at. We look at the VOR system and well, first of all, we'll look at the ears and so we can do a quick audiogram or OAEs or middle ear muscle reflexes to do a quick find how the ears are doing in terms of hearing. There is a whole VOR system that we can target tests pretty quickly targeting the semicircular canals for the six star canals and there's a vHIT for that. And then there is the otolith organs that we can test either using SVV by bedside or VEMPs or the auto set privately odor lift system on the saccule and also the inferior nerve pathway, which is targeted by cVEMPs. So this is rubric I use when I try to figure it out what do I need to test and do a quick diagnosis based on these testing bedside eval here. And this is another quick overview that was from Bernard and the colleagues in 2015 on how they would decide to do vestibular assessments quickly and do some rule outs. So I wanna confirm what the EMT is all basic on Alexander's law, so I did an

oculomotor testing as well and I was able to replicate the nystagmus that was seen. And again, rightward gaze was causing more of the intensity, which suggested there may be some relatively hypotension in the left and we see that when we look at the leftward case as well. And I did a head impulse test, a quick lateral condition. So just testing the lateral canals and as you can see here in the graphs, there are some isolated corrective saccades being seen here over saccades being seen here. But what you see in the next slide over here is in the left side, you see quite a few of that and I can repeat to see if I can get better tracings at the time. I usually do about 12 per side to get a good number of power for the study. And you can see here, there's quite a bit of corrective saccades in the left side translation, which means that when she's turning towards her left, there's not recognition and it's causing some retinal slippage and so her eyes have to correct themselves in order to stay focused on a distant object. In this case, in the bedside evaluation, it was my nose basically behind a mask. And the other thing I test for is using cVEMPS, basically trying to see the saccule component and the inferior portion of the nerve. When you do V-HIT, you're targeting the superior portion of the nerve more and so I'm looking for the inferior component as well. And so in the cVEMP, what happened was I got a really strong and robust response and 95 DP SPL in the right side and then on the left side, there's basically no response at the equipment limit.

And that tells me that there is something going on along that pathway, either the saccule going all the way to the inferior vestibular nerve to the vestibulospinal tract. So, so far everything that we looked at coincides with a little bit of a left-sided neuritis, like possible left EVA suggested. And EVA is a kind of a outlier, well, not outlier, there's just so a lot ways to present itself, but we're not seeing some of the classic signs, which involves hearing loss, but we wanna do a quick diagnosis as well. So on the day of the bedside, these are the recommendations that were made. We do wanna see a PT just to make sure that she's able to walk and a half minimize fall risk. We definitely want to do a thorough audiogram prior to being discharged from the hospital so that we can definitively rule out labyrithitis. And if hearing loss is present, we want to treat it. Based

on the acute status of her symptoms, we are going to start steroid treatment, but if there's hearing loss, the goal is to extend a pair of the steroids so that we can treat it differently. And then if there is no hearing loss and we're primary looking at neuritis, we're probably looking to do the standard treatment and taper off a little bit earlier, so that dosage will be different. And prior to discharge, we did perform a full audiogram on her and basically she has normal hearing in both ears. As you can see from the audiogram, excellent word recognition. There is the one thing that was pretty abnormal was that ipsilateral acoustic reflexes on the left side were tested from five, two, and four and 1000 hertz were all absent, always are present bilaterally. In this case, again, we're looking at the facility nerve being compromised in this case. And so this is just those kinds of findings and OES and little bit apps on the left, but it was questionable. I mean, where it matters, it's pretty much within a normal range. So our updated recommendation is to follow up with a primary care and to ideally return for a panel deployment ENT and audiology to see how she does and then a PT referral. And because of the history of migraine, we definitely want her to go back for Neurology Headache Center to have an evaluation there. And that's basically it. So I'm going to pass the mic along to Dr. Inverso and Dr. Parkes.

- [William] Andy, thank you. Hopefully, everyone can hear me okay. We're gonna transition from the vestibular half of the inner ear to the cochlea and talk about a case of post-meningitis hearing loss in a young infant. Hearing loss is a well-described complication and meningitis it's fortunately, become less frequent over time with the advent of vaccination. Prior to vaccination, the problem was much more common and even post vaccination, it does still occur. The problem is known to arise within the cochlea secondary to the body's inflammatory response. We know that it's in the cochlea because of the consistent absence of otoacoustic emissions. The problem arises very early in the disease process. This has been demonstrated across a number of studies showing that hearing loss, if it happens is going to happen usually within the first 24 to 48 hours of the disease process. So the incidents reported in literature is quite variable. As you see here at five to 30%, and the reason for that variability is that

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the studies are largely retrospective. Some of the reports are prior to vaccination breakthroughs in the 1990s, others are more recent, there's variability in the types of testing done, whether or not they did OEs, only OEs in conjunction with diagnostic APRs, et cetera. And there's often a failure to control for concomitant or otitis media and temporary conducted losses from fluid. One thing that's pretty consistently reported is that the incidents of post-meningitic hearing loss is highest with pneumococcus. So this is srep pneumo, it's a specific form of bacteria. It is one of the bacteria that children are vaccinated against as part of routine immunization, but they go through a series of vaccinations. And so early in life, they have not yet developed the immunity that is required. And furthermore, these vaccines don't cover every single strain of pneumococcus that's out there. So even in pre-vaccinated children infection, although less frequent, can still occur.

So this brings us to our case. This is a little Annalise and we've been given permission by her family to use her name and share this picture taken by mom here that you see. She was born full term. She passed her newborn hearing screen in both years and she was perfectly healthy. Right at the start of the pandemic, she was transferred to our hospital from the community hospital. At that point, she was a little over four months old. She was febrile, quite febrile to 105. She'd already had some febrile seizures, given the climate and the pandemic with these fevers and then diagnosis, she was actually tested for COVID. Unfortunately, that came back negative. Upon arrival here, she had a lumbar puncture and was diagnosed with bacterial meningitis, specifically streptococcus pneumonia, which is the pneumococcus. So based on our institutional protocol, an ABR was completed once she was stabilized medically. This was done on March 26, so about 12 days into her hospital stay here just prior to discharge. I'm gonna then turn things over to Dr. Inverso to discuss that protocol here.

- [Yell] Thanks so much, Dr. Parkes. Yeah so, being part of a large children's hospital, we have to have a very specific clinical pathway so that everyone in the institution is aware if they see a baby with meningitis, what to do next, so that no children fall

through the cracks. So per our pathway, an order was placed by the attending team. Most commonly, these children come in through the PICU, but certainly not always this baby was in the PICU. The order was placed for audio electronic assessment per audiologist or just our general consult order. We always want testing completed once the patient is stable and certainly prior to discharge. And then if the patient does come in from an outside institution, just as soon as possible, our clinical protocol is based on really the only published guidelines for this, which come out of the British Columbia. In 2013, we did make some modifications though after an article posted, sorry, published in 2018. So are the audiologic portion of our testing protocol is really based on age. So our goal is obviously age appropriate measures for ear-specific diagnosis. And a lot of this is very clear to the individuals in this room when I've given this presentation outside of the audiology realm, describing that we want to make sure that we're doing testing that is gonna give us all the different parts. We don't want to just have a way list, for example, that isn't gonna give us all the information that we need.

And so sometimes we need to move into objective measures for these really young kids. And that may mean sedation is necessary. So we want to be working in concert with our colleagues and other departments because if these children are being sedated for something else, we wanna make sure that we're doing these things together. And for these very young children, auditory brainstem response testing is often needed. So this is the decision matrix that we have for our group and ultimately, after testing is done, is hearing loss diagnosed. I'm gonna go through the no first 'cause some of these kids, and I will say it is most common with pneumococcal meningitis or bacterial meningitis more broadly that hearing loss is present, but we do the same protocol, whether it's viral or fungal as well, even though those are less commonly seen. We just have the same protocol across the board so that we make sure that we don't miss anybody. If a child is not diagnosed with hearing loss, our protocol is to reevaluate that child in three months, if the child remains without hearing loss, then they are discharged and evaluated as needed like any other child. If the hearing does happen to change, then obviously, we're going to treat and continue followup. If hearing loss is

diagnosed at that initial assessment, we break it into two categories. So if a child has less than severe hearing loss, a referral made immediately laryngology with a retesting in two weeks. If any change or decrease in hearing is noted, then they would move into the severe to profound track, which I'm about to speak about. If it's stable, we're gonna be retesting every three months to a year and obviously treating the hearing loss as we go and our protocol's to test after that first year, every six months to two years. And again, that is also in alignment with making sure that if we are treating, we would be wanting to test it at least that frequency anyway, to keep up with management. For this particular case, we're falling into severe to profound range and so whenever a child is initially tested and shown to have either a unilateral or bilateral severe to profound sensorineural hearing loss, we're gonna move quickly into an autologic examination, MRI testing, cochlear implant eval, and pretty quick, we're gonna retest just to confirm our findings and we try to do that within a 10 day window. So here's Annelise's ABR. And so even if you don't do ABR regularly, you could probably recognize an ABR that shows profound loss pretty easily.

There was a questionable way five in the left ear at like 95, I believe DB, but for the most part, this is the ABR of a child with a profound hearing loss. I will say that the family was not expecting this. They've received a lot of information over the course of their hospital stay and we're so grateful that Annalise was healthy and going to be discharged that this was quite disruptive for them and quite upsetting. And so the audiologist who went up to the floor that day, luckily had a lot of sensitivity and talked to the family for an extended period of time about these results. As expected OES, there was no measurable outer hair function, relatively normal tympanograms, showing a profound bilateral sensorineural hearing loss for clicking all tumors. So because we were at the beginning of COVID, counseling happens via FaceTime. It was all very, do what you can in this situation that you can as safely, but as kind of quickly as possible, the team really pulled together and worked with the family via distance. I came into the hospital the next day and we pulled our action together around this little girl. So I'm

gonna turn it back over to Dr. Parkes to talk about that decision to move quickly. Dr. Parkes.

- [Williams] Sorry, I just had to reactivate my mic there. So when I hear about this baby, I know that we now have this infant with bilateral profound hearing loss, who is ultimately a cochlear implant candidate. We know that because with the severe to profound degree of loss, the literature tells us after meningitis, this is not going to improve spontaneously. There is no treatment to make it better. There is a role for steroids if given either prior to or with the first dose of antibiotics. But if you recall, this diagnosis was made 12 days into the admission and so steroids aren't going to help here. Now, there are some spotted case reports in the literature of spontaneous improvement for more mild to moderate losses after meningitis, but again, when it's severe to profound, it is permanent. So the big question here is when to move forward with cochlear implantation.

So in a typical pre-lingually deafened infant, we here would aim to implant bilaterally simultaneously at roughly nine months of age. When it's post-meningitic, the answer is that it depends. And what we need to figure out is whether or not there's any concern for relatively rare complication after meningitis, known as labyrinthitis ossificans, we'll call it LO for short because it's a long word. So when I heard about the baby and found out about the diagnosis, my first question was what was the organism? And then when I heard it was strep pneumo, I was immediately a little bit more worried about LO because strep pneumo is the most common organism to cause the problem. So this is an inflammatory process. It's really a cascade of events that I've detailed here. It starts with this inflammatory phase in the inner ear, and this is the body is starting to respond to the infection when the antibiotics are kicking in. Then there's this recovery phase, where you have fibrosis and angiogenesis. This is sort of like scar tissue formation within the inner ear. And then that space in the inner ear that should be filled with fluid, starts to drop bits of bone and can become completely filled with bone, and that's the process of mineralization. So if we look here, this is an animal model. And so they were

looking at durables and they were injecting their CSF space with pneumococcus directly. And then they were looking at their temporal bone sequentially over time. And then this section here through the cochlea, we've a durable, we can see that the ST, that circle, that's a scala tympani. There are three fluid-filled compartments in the inner ear. The scala tympani is one of the three. That's precisely where we want to place a cochlear implant and it's exactly where this process is occurring. So the arrows are highlighting this woven bone that's being deposited in that inner ear space where we want to place the implant and this is three weeks out from the infection. And so this actually can occur quite early. Again, going back to our case, she was already 12 days into her hospital stay here and she'd been at the other hospital for a few days. And so we were worried about this. And this study of animals, 64% of them who were infected with strep pneumo, developed labyrinthitis ossoficans. So though it's rare, it is more common with strep pneumo.

So this is a cat scan showing sort of the end stage effects of ossification. So the white arrows are pointing to the cochlea. There should normally be gray within the cochlea, which is a fluid signal, but it's all white, that's all bone. And so you can't really see the cochlea. I know that it should be there 'cause I understand that anatomy, but it's completely filled with bone. Now, this was a CT taken seven years after an episode of meningitis in a child. I actually don't get a CT right away, we get an MRI, and this is why. So here's an MRI and the arrows are pointing to the cochlea and the vestibule. And just next to the cochlea in the vestibule, you can see a brighter white and that CSF around the cochlear nerve and one of the vestibular nerves. And so the arrows are showing sort of this gray or signal in the inner ear, which should be as white as the CSF. And so this T2 signal loss in the cochlea is indicative of that fibrosis or early inflammatory stage of the process that will ultimately lead to bony formation. And right here, we see a CT in the same child in the same day that is showing this normal gray fluid signal in the cochlea. And so you'd look at that and think it was normal, but I look at the MRI and know that fibrosis is already happening. And so we get an MRI and this is a Annalise's MRI. And so the arrows on both sides are pointing to the cochlea and

the vestibule and then the circle is just highlighting that brighter fluid signal of CSF. And so it's kind of hard to see the cochlea and the vestibule, because it's just darker gray and that's indicative of fibrosis. So we got this MRI the day after the ABR, we repeated an ABR to confirm the results and the results were the same. We were already seeing fibrosis. And so we deemed it necessary to proceed with urgent cochlear implantation. If you wait and allow for further deposition of scar and potentially bone formation, it really changes the approach with cochlear implantation. Full insertions may not be possible, you might have to use modify to raise, you might have to drill out the cochlea and in these cases, your outcomes are likely to be compromised. And so this is the one indication for truly urgent cochlear implantation. And so these are some interoperative pictures here. Top left, we're looking through the facial recess at the promitory here in the round window membrane area down there and there's some gelatinous fibrotic material there. We've opened the round window membrane. We've done a wider opening here. Normally, we would just do a slit-like incision in the round window membrane. To keeps things atraumatic here, we've actually opened the membrane entirely to minimize resistance with the insertion. And we can see inside there's blood clot and blood products consistent with that fibrosis that we noted on the MRI and here the electrode is in. So despite the scar tissue that was already forming, we were able to get full insertions bilaterally and I think that was because of how quickly we were able to get in. So all transition back to Yell to wrap up.

- [Yell] Thank you so much. Yeah, so we're so fortunate that this particular family, part of the reason that they are so open and willing to have us share images of a sweet baby Annalise is because they actually were approached by several media outlets and they, were I think, in 89 States and Canada on the news because she was so very young when she was implanted, but right off the bat at her activation, she really responded and we weren't sure. So for those of you who do cochlear implants, activating young children is always a bit of a challenge. Some of the regular methodology we use it activation isn't always accessible to us and parents watch

these great videos where kids have these huge responses. And Annalise could barely hold up her own head the day of her activation. So we activated her at just under a month. Usually, we do activations a little bit earlier, but we waited that full time just cause she was so young. And we had originally hoped that we would be able to have mom and dad, but dad was on Zoom, on a large Zoom screen, so that Annalise could hear his voice as well because we were obviously under visitor restrictions. So we did some objective measures and then did objective offset mapping for the implant audiologists that might be in the room. And she had great eyebrows. She gave me really great facial expressions. And then mom sent me this video, which I'm going to share with you just a day or two after her activation showing what happens every morning when they put her ears her.

- [Annalise's Mom] Good morning. Good morning. Yeah

- [Annalise's Parents] Annalise .

- [Annalise's Dad] Annalise, hey. Hey.

- [Yell] For a child that young, who doesn't really have full head turn, she has very expressive, expressive eyes and that's really a lot of what we were using in addition to the offset information. And we're gonna make our way back to the presentation. We had kind of our standard followup. You'll notice the headband that she was wearing. Mom may had some custom headbands made because would fit or sit on, on Annalise's little ears. I'm trying to think, well, while the presentation comes up, what else I can tell you about her? So we saw her at activation day and then we saw her a week later and she was doing very well. And we've continued to see her regularly since. This first audiogram that you're looking at was the first time I put her in the booth, which was that a month. And again, when you were implanting a child this young, usually the one month is the child is older. At her one month, she was six months. So head turn was still shaky, but reliable. And so, as you could see, she had

really, really great audibility. And then this next one that I just pulled up was at her three months post activation. So she is staying right around in the range that we like to see for audibility with a cochlear implant. Again, there's a lot that we would love to be doing as far as speech, et cetera, that we're not able to do in the booth. I will tell you as far as plan for Annalise, she is doing virtual auditory verbal therapy. Her parents have a goal of fully mainstreaming her when she gets old enough. She's the youngest of four and so she's got lots of access to a speech and language in the home. She has her appointment. We do implant mediated critical auditory of potentials for our implant patients and especially someone that's young where we need all the help we can get in determining and making sure that we're getting threshold information and her map is exactly right.

So we're gonna be doing those at her six month post activation appointment, which is an October, and it'll be our first time doing a six month post activation appointment a month before a child's first birthday. We will also be monitoring her for other signs of delay secondary to meningitis. One thing that people don't always realize is that there's a lot of literature out there showing that meningitis at a very young age are just classified as under 12 months, can also be predictive of poor neuro behavioral outcomes in children, especially some of the things that we would also look at as outcomes with a cochlear implant, linguistic and executive functions, language that are really developing very rapidly in young infants. And so we need to be monitoring a child like Annalise closely. We know we got her access to sound very early. We know that she's got a great supportive family, who's keeping the implants on and they're doing speech, but we need to make sure that we're not assuming that our job is done when it comes to those executive and linguistic functions because the meningitis itself could have an impact on that development based on the age that she was when she had her illness and this neurologic insult. So that is where I wrap on Annalise. Any questions from the group on this particular case before I move on to the next one? Not seeing any pop up in Q&A, but we are doing well on time. We're also going to have a time at the end with all the presenters, but I do know that Dr. Parkes may have to leave us to

go back to the OR at some point. So I did want to make sure if there were questions specifically for Dr. Parkes related to this particular case or even the vestibular case that Dr. Lau had presented since he was also involved in that one, that this would be a great time to ask them. I know one thing that I, let's see, I see one coming up. Somebody was asking if we would be able to share a resource regarding implant mediated kit testing protocols. Yeah, absolutely. The next presentation that I'm going to give is actually on two cases with auditory neuropathy spectrum disorder. And we're going to be talking a little bit about, our cortical odometer potentials a little bit more, but certainly can try to provide that and speak to the leadership from audiology online on the best way to do that. And let's see, why were distortion product OAEs performed as opposed to TOEs. Claudia, I would love to know if that is, I think based on, this is Dr. Viola that this may as well be for Dr. Lau. Am I correct that this question is for Dr. Lau? Yes, it is. Based on who's asking it and I thought I would know.

- [Andy] At the time I had the high frequency OAEs on me, so I was able to get a full spectrum of that. I was hoping to go target high on that so that's really where I went for the diagnostic.

- [Yell] Great, I know one question from the vestibular talk that I was hoping maybe Dr. Parkes could address briefly, is how you address when your colleagues suggest that there's not balance disorders in children. I know I've met a lot of audiologists in my day that don't really understand the prevalence or why we would have a pediatric balance program.

- [William] My back on here, you can hear me okay. So yeah, I think it's, I mean, a lot of things are tougher in kids than they are in adults in terms of figuring stuff out and doing bedside evaluations, examinations, et cetera. And so it can be tough to tease this stuff out and a lot of dizzy stuff isn't truly vestibular. And so you have to filter through quite a bit to get to the case of that truly are. And so I don't know exactly how to get more buy-in from college, but I think for us, what we do is take a multidisciplinary approach.

Dr. Lau and I are paired together. Things are different nowadays because of the pandemic and all the distancing a lot is being done through telehealth and a lot is fragmented. But prior to the pandemic, we had a truly integrated clinic where we were together. We had physical therapy with us, we had a neurologist with us. And so we would bring the kids through a multidisciplinary evaluation, sometimes a few of us in the room together doing the assessments and wants to streamline things for the family to really dig in and tease out who can help what is the true problem. And so, with Dr. Lau doing his testing, if we saw some objective findings that supported the vestibular problem, I could kind of dig through my differential and try and figure that out, occasionally help. A lot of times it's not peripheral, but at least we've ruled that out because a lot of other providers are gonna blame the inner ear for dizziness. And so families hang on to that. And if we can check off that box as normal that we still haven't identified a solution, we've at least push the families in a different direction where they might be able to find help. And we try to provide some of those other sources of help in our clinic, whether it be through physical therapy or whether it be through neurology if it's more of a migraine variant or occasionally, if it really seems like it's nonorganic, especially if children have other mental health issues, anxiety, depression, et cetera, well, we have our close connection to psychology through Dr. Hoffman as well.

And so there are lots of avenues through which we try to help these children and we do our best to not be dismissive of any of the complaints, recognizing that a lot of these dizzy children who were sent to us may not have peripheral problems, but we can at least sort through it and point them in the right direction. And then the last thing I'll say is though there is a lot of dizzy that's not vestibular, there's plenty of vestibular dysfunction in the population of children that we care for. So the coincidence of vestibular dysfunction in children with hearing loss is quite high. I mean, it's probably somewhere between a 1/3 and 2/3 and you just have to look for it. And so you have to ask the questions, you have to look for functional deficits, you have to do the test when indicated. The implant in kids as part of our protocol, we try and test before and after

to monitor their function, moving through the surgery and afterwards CMV is a population with a high incidence of vestibular dysfunction, et cetera. So being in-tuned to all of that is helpful and if you're not in-tuned to it, you can miss it. But if you're looking for it, then you can identify issues early on and provide support before delays become more obvious and more of a problem. So I don't know that I directly answered your question. I went off on a tangent, but I felt like it was in line with what you're asking.

- [Yell] That was perfect, thank you. There is a question coming through, I believe that's for you. Is there a possibility of the root incurrence of bacterial meningitis? Any literature evidence that would suggest if there's any impact to the electrode array or impact of the electrode?

- [William] Yeah, so that's really good question. I'd worry more if there were an anomalous inner ear. So the route of the infection and the inflammatory process getting into the inner ear in this case is a little bit hypothetical. If you have an anomalous inner ear, there can be direct communications between the CSF spaces and interior fluid compartments. And so in those cases, the risk of recurrent meningitis is certainly higher and real. So I think more often, we might see a child who has recurrent meningitis and then look for an inner ear anomaly as a source. But in this case, she has normal inner ear anatomy. With all of our implants, unless there's an anatomic reason that we can't, we'll insert through the round window and then we will pack sort of fibrofatty tissue or fascia around the electrode at the site of insertion to create some really scar tissue to limit the possibility to ace an infection. So puss in the middle ear, finding its way alongside the electrode into the inner ear and potentially getting to the CSF space pretty quickly within a month or two after surgery, a sheet is gonna form around that implant. And that risk of ascending infection is quite low, but we want to make sure that all children who are implanted are vaccinated up to the point that they should be at their current age. We want to make sure that children who were age two and over are also getting an extra pneumococcal vaccine and that's

Pneumovax. And this is all to sort of mitigate the possibility of meningitis post implantation. And then lastly, we take any ear infections incredibly seriously in all our kids with implants. So there's no watchful waiting, there's close followup with high dose Amoxicillin or Augmentin even. And if there are any worrisome signs like signs of mastoiditis or central signs that could be indicative of meningitis, they're going to be admitted for intravenous antibiotics.

- [Yell] Wonderful, thank you. Okay. I am going to move to the next case, 'cause I don't see any other questions, but we will have some time at the end for additional questions. So these next two cases are being presented as a package and they were prepared by Dr. Shanda Brashears, who unfortunately, can't be with us today. So I'm gonna present them in her place. And there are two cortical auditory evoked potential cases that are also in patients who have ABRs and both patients were diagnosed ultimately with auditory neuropathy spectrum disorder. So it's important to understand, and especially if you're new to corticals, that there are some similarities and some differences between these two electrophysiologic measures. So some of the things that these have in common are that they do not require behavioral responses. So they're both objective. They're both electrophysiologic ways to estimate behavioral hearing levels. They are both acquired through signal averaging. They tend to use very similar equipment. Both are tests of detection, but not processing. A lot of people assume because it's cortical that the corticals are a test of auditory processing, but it's not fully. And then they're both subject to room noise and myogenic noise, okay?

Some of the ways in which these tests are different is that ABR is a far field response whereas CAEP is a near field and larger response. ABR you're gonna use a much faster stimulus rate between 20 and 60 pulses per second whereas for CAEP it's extremely slow, about one per second, depending on your protocol. For ABR, you're gonna be measuring through the lower auditory brainstem whereas CAEP is measuring through the auditory cortex. ABR is mostly mature at birth, which is one of the reasons it's able to be used in infants and as part of a newborn hearing screening program

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whereas corticals really don't fully mature until puberty approximately. A speech stimuli is often the stimuli that's used for corticals whereas an ABR, we're using tone bursts or click type stimulus. Those are just some of the things that are different and similar about these two types of tests. So in this first case, this is a kiddo who ultimately was diagnosed with bilateral ANSD and had a history of high bilirubin. The child was born at 36 weeks gestational age, was treated for hyperbilirubinemia with phototherapy and double blood exchange and had IV IVIG infusion. So this child was diagnosed with ASD upon their initial diagnostic ABR at three weeks of age. So as you can see in the images, if you're not used to doing ABR, there's no real neural response that's able to be measured and repeated, but you do see a cochlear microphonic that is able to be when you alternate polarity. Additionally, this patient did have the more classic representation of auditory neuropathy spectrum disorder, which was present in a normal otoacoustic emissions. I always throw out there. I remember when I was in school, ANSD was originally, well back then it was not considered ANSD and had a different names. But auditory neuropathy back then was defined as present OAE and an absent ABR, whereas we know more now that it is more than just a difference in test results.

When this child had their cortical though, you'll notice, so an ABR can give us a diagnosis of ANSD, but it really can't pinpoint the severity of the impairment. We all have had patients who have ANSD, who perform differently than what the ABR suggests. Often these kids are missed depending on the type of ABR that was done and the parents are like, "But I don't understand, they have head turn, they startle, they do this, they do this, I don't understand how they can have a profound hearing loss." And then maybe later down the line, it's determined that that was a misdiagnosis and they actually have ANSD. The parents of this particular child reported no startling to sounds of any kind early on at a young age. And at five weeks they had the cortical evaluation and it was to dost stimulus and it showed absent responses at 90 DB, normal hearing levels consistent with a severe or severe to profound level of hearing impairment, which at the time did respond nicely with their ABR, showing that not only

was their ABR accurate, but that this is not a child necessarily that is performing differently than their EBR. However, one thing that's interesting is at one year of this, this was a kiddo who we were monitoring very closely. With a child who has a traditional profound hearing loss, they go on the cochlear implant track and we can move them through very, very quickly. We have a slightly different process for children who have ANSD because sometimes maturationally things can change. And so we monitor them a little bit differently in that first year. And so at one year, we were continuing to monitor them and the parent reported inconsistent, but some improved listening behaviors and vocalizations, and the ABR that was repeated showed present, but very delayed responses. Wave V is approximately 3.5 milliseconds delayed from where it should be. And then a present cortical.

So you could see that maturational effect was taking place for this particular patient. This patient had been and was fit with hearing aids as part of their cochlear implant candidacy process and their sound field responses to aided stimuli with the cortical at 90 DB showed performance interestingly that was poor with their hearing aids than without them. And so often when kids aren't able to give us a lot of feedback or information or they're very young, we do aided and unaided corticals as part of our protocol. And so if you look over here, normally you would expect this to be flip-flopped. You would expect that the side that does not have corticals would be the unaided and that this would be our aided, but it's actually the opposite. This is our unaided cortical and our aided cortical is, sorry, I'm just gonna grab my pointer here. So this is our unaided cortical, and this is our aided cortical, which is slightly different than what one might expect. But I did align with the, what the parents were saying, and it highlights the importance of really listening to the parents as experts on their children, that their child was responding more consistently without the hearing aids them with them. And the audiologist who was seeing this patient is looking into whether or not hearing a compression might possibly be to blame and is gonna continue to evaluate the benefit and really plan forward to determine whether hearing aids need to be discontinued at this time. So the next case that I'm going to discuss is

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different than the first. This is a three year old who presents with an absent ADR on the left, which you can see, I'm gonna pull up my pointer again. You can see here, they had a normally ABR on the right. So I'm not showing that and, sorry, it's right here. It's slightly noisy, but it is normal. And then their MRI which was completed showed a complete aplasia according to the report of the auditory portion of the eighth nerve on the left side and the vestibular portion of the eighth nerve and the seventh nerve appeared normal on the left side as well. What's interesting about this case though, was that when corticals were tested, they had a present CAEP on the left ear. So the imaging would have suggested that we would not necessarily expect to see anything present on that left ear, considering that it was reported as a complete aplasia, but an ABR was completely absent with again, that faster stimulus, but the CAEP was present. So some things that are important to understand is that an absent or incomplete eighth nerve is a form of auditory neuropathy spectrum disorder that just happens to have a known etiology.

A lot of people sometimes think that these as completely separate, but they actually fall into the same category. Could other nerve fibers, something that we always ask ourself and that our research team is looking into, is could other nerve fibers be taking over for absent auditory nerve fibers? The ANSD is really at its core a timing disorder, more than an inability to hear soft sounds. A slow rate, which we test with CAEP, electrophysiologic measure is more likely to elicit a response that a fast one. So a CAEP is more likely to be present in these patients than an ABR, and maybe more able to accurately represent a child's hearing ability, which is one of the reasons like I said, that, yes, we do the ABR for the initial diagnosis, but following it up with a CAEP and then doing it again over different intervals of time is extremely helpful for being able to track and measure, not just diagnosis, but kind of translating that over to actual handicap and how much the child might actually be able to hear, which has always been a big question in auditory neuropathy spectrum disorder, especially in very young children. For this particular child, hearing aid benefit was very difficult to assess behaviorally due to language and developmental delays. And so this is the

representation of the aided versus unaided sound field cortical results. So here you see this particular patient's unaided cortical being represented here and then you can see within the left ear with the hearing aid in use, you see the significantly greater amplitude. So in the 80 condition, the amplitude is significantly greater than the unaided greater than 20%, which was being used as an indicator of larger amplitude, consistent with reports from the family and the use of different behavioral questionnaires, such as the little ears, outcomes questionnaires like the little ears showing benefit. So it's an objective measure that can be used to show if benefit is present. So that wraps those particular cases. I wanna thank everyone for their attention, and I want to thank the amazing team. I'm so fortunate here at Nemours to have a plethora of amazing audiologists and teammates from other departments, such as Dr. Parkes and Dr. Hoffman, who were able to join for this grand rounds. There were so many amazing staff members and so many amazing cases to choose from. I hope you enjoyed the ones that we chose to bring to you today. And we have approximately eight more minutes for questions. It looks like we have one coming up here. Which conditions commonly co-occur with a diagnosis of misophonia? So I will omit my mic and let either Dr. Pellicori or Dr. Hoffman.

- [Jenna] All right, so I can obviously talk from the audiologic perspective, and then I'll also let Dr. Hoffman touch from the psychological perspective 'cause I think there's a little bit of overlap from both of our disciplines. So in regards to misphonia, there's definitely have been some studies in regards to co-occurring conditions. And one of the big factors that we've seen is that tinnitus and hyperacusis can commonly co-occur with misophonia. And there were a couple of studies that were conducted by Pawel Jastreboff and they had really highlighted that there is a high rate of co-occurrence amongst those conditions. And in fact, he had conducted a study from Emory Tinnitus and Hyperacusis Center from 2013 and out of approximately 200 patients with decreased sound tolerance disorders, approximately 28% of those participants had a comorbid diagnosis of misophonia and hyperacusis, suggesting obviously that the conditions may frequently coexist together. I know he also did a little

bit further research for looking at the prevalence of tinnitus and misophonia, and unfortunately, I'm unable to call the exact statistics, but I do know again, that there was a very, very high co-occurrence rate between those conditions. The other thing to keep in mind as well is, is that phonophobia, which is technically considered a decreased sound tolerance disorder is really more so of a psychological condition, but it's often a consequence of hyperacusis and misophonia. So it's not uncommon for patients with decreased sound tolerance disorders in general to develop some form of phonophobia along the way because of the fear that the sound provokes. So phonophobia would be another common co-occurrence as well. Those are really the ones that I'm most familiar with in regards from an audiological perspective as being frequently co-occurring tinnitus, hyperacusis, and phonophobia. And I would be happy if you wanna reach out to me privately as well to share some of those studies that I was referencing by Dr. Jastreboff if you are interested at all. And then I'm gonna let Dr. Hoffman takeover from the psychological perspective since there can be quite a bit of comorbidity and overlap over there as well.

- [Michael] Hi, Denise, that was a great question. So the long and the short of it is we don't have enough research to really say confidently what diagnoses within the behavioral health realm or the psychological realm co-occur with misophonia. There was one study out there that had not what I would not consider a fairly large sample size and the most common disorders that they had pointed at were usually things along the anxiety spectrum. Most typically obsessive compulsive types of behavior disorders, not necessarily full-blown OCD, but something along that realm or anxiety. I haven't yet to see any studies, if anyone knows of any that have looked at rates of comorbid psychological diagnoses within pediatric patients. And so based on that, but I have to fall back on is purely anecdotal and what I've seen in our clinic and the most common ones that I have seen among children would be either ADHD, which creates a really nasty blend of children having the sounds that are really triggering for them and then difficulties with general emotion with behavioral regulation. So they'd have these major blobs. And then the other one would be some sort of generalized anxiety

disorder or some sort of social anxiety. Those are really the most common ones that I see. Good question.

- [Jenna] This is Jenna. I'm just gonna chime in one more time here as well. One of the other pieces, which really isn't an audio logic condition, but interestingly, there has been some research on, is also the possibility of the ASMR to have some overlap. So ASMR stands for autonomous sensory meridian response, and it's basically the complete opposite of misophonia. So those with ASMR typically experience feelings of deep relaxation and euphoria to specific sensory stimuli, often of the auditory modality and you may have even possibly seen or heard ASMR clips trending online with individuals recording themselves in highly sensitive microphones, eating pickles, and doing different things like whispering. And they do that because it basically creates this very euphoric experience and sometimes can create tingling such sensations throughout the body. There's not a ton of research out there in regards to ASMR as it relates to misophonia. However, there were a couple of studies that were conducted that actually showed that patients with misophonia sometimes do demonstrate behaviors and characteristics consistent with ASMR. So despite having certain sounds that they cannot stand and that cause a rage response and cause these feelings of anxiety and anger, there are also occasionally some sounds that they find extremely pleasurable as well. So I just thought I would add that in as well.

- [Yell] Thank you, Jenna. Yeah, so to answer the question that came up. So we're actually able to do threshold corticals to set our amplification for children with ANSD, so that just like an ABR, you can lower your stimulus and measure the threshold of the cortical. And it is believed to be more reliable when looking at these particular patients than ABR thresholds. We also if we do behavioral in the booth, there's literature and suggestion that narrow band stimulus provides more reliability than pure turn stimulus for these patients. And before we had corticals, we had a very what's very conservative approach for the way that we fit hearing aids on patients with ANSD, where we would not rely purely on the ABR because the ABR often wasn't giving the most reliable

information that could be a talk in and of itself, going over all the different ways to fit hearing aids. But we are for case one, when we talk about setting the amplification, we used threshold cortical testing. Andy, Dr. Lau, it looks like, what is a test of vestibular neural pathway?

- [Andy] Yeah, sorry. I mean, if you're looking at the tests in terms of the pathway, the VEMPS will be the inferior neural path looking at the inferior vestibular nerve. And then the superior parts will be anything that goes with the VLY testing. So if you'd like to V-HIT, your caloric, all of those who attach onto this superior portions of vestibular nerve. Does that seem to help answer the question?

- [Yell] See if the individual over back. While we're waiting, I can respond. So from my clinical experience, there's certain factors when we have a child that identify with a ANSC at birth, we look to see what their genetics says. So from a genetic perspective, they have certain mutations, like the auditory mutation, there's been enough literature that suggests that those children are not going to be successful with hearing aids. So we would progress them through, we would still do our protocol and do cortical testing, et cetera, but we'd feel a lot more confident with those types of patients moving forward with implants without a little bit more of the evaluation that we do with others. You know, even with corticals, what we're looking to see is we don't want kids to be like, "Okay, well, you're doing somewhat decent with hearing aids and so there you go, you're gonna stay with hearing aids." We still wanna be making sure that we're making the best possible choice for these children. And if they can't have a synchronous signal, if they can't ultimately develop appropriate speech and language and make appropriate gain in speech with the signal that we're giving them, then we do move forward with cochlear implantation. So with a team approach, looking at their speech progress, as well as the critical progress and whether or not that system ultimately maturing, that helps us to make that decision. And I know that we are actually at the 1:31 mark, there was a great question about whether CAEP responses are different in children with misophonia? There's not a ton of research out there,

though I know our center was hoping to get a grant to do this type of research very soon to see if there is a biomarker and very specific key results for these children. We've seen it in a few, but probably not enough to say that there's a definitive answer out there. Dr. Pellicori, this would be the last question before we have to break off.

- [Jenna] Sure. So yeah, as Dr. Inverso had said, we did conduct some, what we would say preliminary research at Nemours, where we were having some of our patients with misophonia undergo cortical auditory evoked potential testing. So when we're looking at cortical auditory evoked potential testing, obviously, we're looking to see how the auditory system is functioning starting at that external ear canal and ending at the early auditory cortex. And then with OAE suppression testing, we're evaluating a reflex within the ferret auditory pathway, basically from that medial oligarchy complex to the cochlea, which is basically designed to enhance speech sounds in the presence of background noise. With that being said, a lack of a functional reflux or poor suppression with the OAE suppression testing, typically means that speech and background noise may be perceived at the same intensity, which can often result in children feeling overwhelmed or sensitive or distracted by noise and auditory information. And in some individuals, instead of actually suppressing noise, the system can even abnormally increased noise. So with that being said, our small sample size was relatively consistent with findings from Schroeder and colleagues in 2014, where they had conducted an oddball paradigm and their oddball paradigm in patients with misophonia thesis a control group had basically revealed that there was a smaller and one amplitude. So there was a smaller recorded end one neural generator response in patients with misophonia and no significant differences were observed for the P1 or P2 components. And with that being said, the n1 primarily represents the patient's sub attentionability to detect a change. So it allows us to kind of reflexively offer our focus towards more relevant auditory information. So that study has suggested the possibility that basic impairment and auditory processing and auditory attentionabilities in patients with misophonia and in regards to what we found that Nemours, ultimately, we did see that with the OAE suppression testing in particular, that a lot of our patients

were demonstrating asymmetries between ears. And again, we do have a small sample size or group. So we did submit a more formal proposal to try to get a research grant to look at this further. But what we receive less with the OAE depression was that there wasn't asymmetry. And then in regards to the cortical responses, they varied from being absent, reduced, or delayed. I don't think, and Dr. Lau feel free to correct me if you think otherwise, but I don't think we had any patients with ISA demonstrate a completely normal cortical response. It was either one of the three scenario, so it was absent reduced or delayed. Again, we are looking at a small sample size, so we wanna carry that over to a larger group. So there's more power behind the numbers.

- [Yell] That is true, yes. In our small sample, all of the results were at least in some way, abnormal, which just goes to show that we need to keep moving forward and keep doing research and keep studying. And we hope that today's presentation lit a fire or struck an interest for someone out there. Thank you to everyone for their attention. I wish we could keep talking forever, but I wanna respect everyone's time, it's 1:35 and, yeah. Our information is available through the general web and LinkedIn and those types of places, please reach out and have a wonderful, wonderful day and stay safe out there.