Hearing Health Hour

Ménière's Disease: Definition, Evalution, and Intervention

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ANIL LALWANI - Well, hello, and welcome to our Hearing Health Hour Webinar. I'm Dr. Anil Lalwani, and I appreciate you joining Hearing Health Foundation for this Hearing Health Hour Webinar this evening.

Today's topic is Ménière's disease, which is an inner ear condition that has hearing loss as well as balance issues. These symptoms, they can fluctuate, and usually affect only one ear. And these symptoms include vertigo. Sometimes it can be quite severe, and you can have nausea and vomiting. Other symptoms include hearing loss, ear fullness, and ringing in the ear, or tinnitus. Now, we're going to learn how Ménière's disease is detected, diagnosed, and treated today.

This event has a live captioner and it is being recorded. You can enable closed captions by clicking the CC button right at the bottom of your screen. Now, if you need any other assistance using Zoom, please do follow the link to the technical guide shared in the chat.

By way of introduction, my name is Dr. Anil Lalwani. I'm a professor and vice chairman for research in the department of otolaryngology-head and neck surgery, or ENT, as well as associate dean for student research at Columbia University Vagelos College of Physicians and Surgeons. I'm also a board member at Hearing Health Foundation, where I oversee the Emerging Research Grants program, also affectionately known as ERG.

Now, ERG is a competitive program that awards funds to researchers, like our speaker today, who conduct cutting-edge research in hearing and balance. Now, these grants have supported many leaders in our field to become successful scientists, including our illustrious speaker today that I just mentioned now. The ERG program that provided seed money to scientists just starting out in their field, their research is only possible through the generosity of supporters like you. If you'd like to support our work on hearing loss, tinnitus, and other related conditions, you can do so today at hhf—Hearing Health Foundation—hhf.org/donate.

Let's get to our program. Our presenter today is Dr. Wafaa Kaf, MD, PhD, a 2015 ERG recipient, who was funded by the Estate of Howard F. Schum, for her project investigating a novel Ménière's disease diagnostic method. Now, Dr. Kaf is a professor in the department of communication sciences and disorders at Missouri State University. Her presentation today will cover both foundational and current research about Ménière's disease, and its clinical

manifestations, and audiologic evaluation and intervention. Without much further ado we'll move to Dr. Kaf's presentation. Please do ask your questions to the Q&A box linked at the bottom of the screen, that we'll try to answer following the presentation. Dr. Kaf.

WAFAA KAF- Good afternoon. It's a pleasure to be here. Thank you Dr. Lalwani for the introduction, and for moderating this webinar. Many thanks to Hearing Health Foundation for funding our research in 2015. I would also like to thank both Yishane Lee, the director of marketing and communications, and Dr. Chris Geissler, the director of program and research support, at Hearing Health Foundation, for their invitation to present today.

For today's presentation, these will be the outlines. I will give a quick overview on the inner ear anatomy and physiology then we'll talk about Ménière's disease. Looking at the ear, we know the ear is made up of three primary parts: the outer ear, the middle ear, and the inner ear. And if we give a close look at the inner ear, we see that it has interconnected, fluid-filled chambers. The cochlea, the snail-shaped structure, is responsible for hearing, and the vestibular labyrinth is responsible for balance. Both the cochlea and the vestibular system have two types of fluid, a perilymph that looks like in light blue, and the endolymph in dark blue.

If we have a cross section of the cochlea we can see three chambers. The top one is scala vestibuli, the bottom is scala tympani, and both have perilymph. The middle chamber, or compartment, is a scala media which has organ of Corti, the sense organs of hearing, is filled with endolymph. Both endolymph and perilymph have different ratios of sodium and potassium. The perilymph has high sodium, low potassium, and the endolymph has high potassium, low sodium. This is very important for the health of the hearing and the balance function. If we have any conditions that affect the stability of that sodium potassium ratios such as Ménière's disease, the patient can end up with vertigo attacks, nausea, vomiting, ear fullness, tinnitus, or hearing loss.

Another structure that I want to point out is endolymphatic sac, and the endolymphatic sac is a part of the inner ear that is accessible to the other space outside the inner ear. So the endolymphatic sac, with the endolymphatic duct, has endolymph, and they are housed in a boney-like canal, the vestibular aqueduct is filled with perilymph. So the endolymphatic sac is very important for, again, the production, the absorption, and regulation of the endolymph. And also it helps with the immune regulations, so it serves as an immuno-defense mechanism of the inner ear and it helps with the removal of any circulating debris or antigens that may enter the inner ear.

Now, we will talk about Ménière's disease, starting with definition, manifestations, causes, and pathophysiology. As Dr. Lalwani mentioned at the beginning, Ménière's disease is a clinical condition that is defined by a triad or tetrad of clinical manifestations. The first one will be spontaneous vertigo attacks. Each attack will last 20 minutes to 12 hours, no more than 24 hours. The patient will have fluctuating low-to-mid frequency sensorineural hearing loss in the affected ear, also the patient will have fluctuating aural manifestations like pressure in the ear, ear fullness, and tinnitus. And the tinnitus usually is a roaring type of tinnitus because of the low-frequency hearing loss.

So we will have these manifestations—vertigo, tinnitus, hearing loss, and ear fullness—and we really need to ask in the history about any new history of nausea, vomiting, sudden attacks of falls or drop attacks because these could be related to other causes not related to Ménière's disease, maybe in migraines, or in rare cases, to vestibular schwannoma. Some

might ask how often that will happen. The vertigo attacks may occur over a short period of time, could be several weeks, or may come a month or even years apart. It's unpredictable.

Ménière's disease is a genetic disorder with variable expression. That's why each patient will have a different kind of clinical manifestations. The cause of Ménière's disease is unknown. We really do not know the main cause, and in this case we call it idiopathic endolymphatic hydrops. In other cases we have theories or associations of other diseases that could lead to Ménière's disease, and these will include autoimmune diseases, migraine, infection, viral bacteria, allergy, vascular problems, any problem that affects the ionic homeostasis function of the inner ear, anomalies of the endolymphatic sac, or trauma tumors of the endolymphatic sac, or even genetic mutations that affect the ion channels.

If we have a defected endolymphatic sac that is responsible for the endolymph production, we can have either extra production of the endolymph or decreased absorption of the endolymph. And in this case we have an endolymphatic hydrops, increased amount of the endolymph in the membranous labyrinth, so the volume will increase, the pressure will increase, the membranous labyrinth will expand because of the hydrops, and maybe even the pressure would lead to a rupture of Reissner's membrane as one of the theories.

And because of that rupture of the Reissner's membrane, we will have a mix of the endolymph with the perilymph, and this will lead to that abnormal recycling of the potassium and sodium. We do not have the same normative ratio anymore, and the patient will have the vertigo attacks, and the tinnitus and hearing loss, because of the potassium intoxication and sodium intoxication.

Now we will talk about evaluation and diagnostic testing. I know this might not be promising, but we do not have specific diagnostic test available yet. There is no marker for Ménière's disease. It's mainly based on the detailed clinical and medical history, and triggers like stress, certain foods that trigger Ménière's disease, or trigger the attack. Also physical examination, head and neck examination. The physician can order some tests to rule out other causes like autoimmune disease, thyroid problem, syphilis, kidney problem.

Imaging would be also helpful to rule out maybe tumors, or enlarged vestibular aqueduct, or dehiscence of the semicircular canal. Then the audiologist will do additional evaluation, including pure tone testing, vestibular test battery, auditory brainstem response, and electrocochleography.

I will just focus on the pure tone testing and the ECochG. Pure tone testing and speech audiometry is the most important test that should be done in any patient who is experiencing dizziness. And early in the disease, in the acute stage of the disease, the patient will have fluctuating low-to-mid frequencies, sensorineural hearing loss, normal hearing in the high frequencies, then with the progression of the disease, with more attacks, the hearing loss will get worse, and also the high frequencies will be affected, and with more progression of the disease, all of the frequencies will be affected with the severe degree of hearing loss, and the patient may end up with a profound hearing loss. The fluctuation can happen in the first and the second stage of the disease, where hearing can return back to normal, but in the repeated attack, hearing won't go back to normal, it fluctuates.

So when we have these clinical manifestations of episodic attacks of vertigo, aural symptoms, fluctuating low-to-mid frequency sensorineural hearing loss, this is classified as definite Ménière's disease. If we do not have documented fluctuating low-to-mid frequency

sensorineural hearing loss, it is a probable Ménière's disease, not definite, of course, after ruling out other causes. The other audiological evaluation that we do is electrocochleography, or ECochG. ECochG is an auditory-evoked potential for objective assessment of the inner ear and auditory nerve in response to loud sounds, could be click sounds or tones. The patient is relaxed on a recliner, and we place some electrodes on the head and behind the ear.

One of the electrodes will be placed in the ear canal. This is a tiptrode that we really do not recommend using that. It's better to use an eardrum electrode or tympanic membrane electrode, a piece of cotton connected to a wire and the silastic tube. We can make it in the lab or we can purchase it. And we place that electrode very close to the eardrum, and present a loud sound, and record the response.

So here is the normal ECochG. So what is a normal click ECochG when we present click sounds at say seven clicks per second? We get a very small, tiny summating potential response. It's a wave. We get it from the inner hair cells of the inner ear. So it's generated from the inner hair cells. And we get a large action potential wave that's generated from the auditory nerve, the hearing nerve. But in a patient with Ménière's disease, we can see that the summating potential response is actually as big as action potential, is getting abnormally large compared to that small summating potential. And because of that we can get also abnormally large summating potential to the action potential amplitude.

Another sign is we are getting widening of the area of the summating potential relative to the action potential. So we get also normally large area ratio. These are signs of endolymphatic hydrops and Ménière's disease. The problem is standard EcochG using click and using slow rate is not sensitive and not highly specific. We can diagnose maybe 69% of cases and we misdiagnosed 31% of cases who have actually Ménière's disease.

And this because maybe the click stimulus that we are using, not really assessing the apical part of the cochlea that is responsible for the low-frequency hearing. Also the timing of the testing. Are we using the test recorded during early stage of the disease versus late stage of the disease, and also the resulting, abnormally summating potential action potential ratio may not correlate with the severity of the endolymphatic hydrops. So we have some limitations.

Before in 2015, we received funding from Hearing Health Foundation to conduct a series of research studies to improve the sensitivity of standard ECochG and our aim was to assess different adaptation properties of the ECochG components, mainly the summating potential and action potential at fast click rates. So we do not want to use low click rates, we want to record ECochG to fast rates. This is like a stress test to the inner ear, similar to asking a patient who has heart problem to run. So now we have stressed heart. So when we present fast stimulus we are stressing the inner ear, so we can identify a problem. So when we recorded ECochG to fast click rates, up to 507 clicks per second.

Remember, the slow rate that is used for standard ECochG is 7.1 or 9 clicks per second. So when we do that we get a very complex response, overlapped waves of summating potential action potential, we cannot really label them or identify the response to interpret it. So for our funding study that we got, we used a novel continuous loop averaging deconvolution technique, or CLAD, to unwrap and deconvolve these complex waves. And this is how it looks like after we used the CLAD technique to devolve these complex responses. Very nice, summating potential action potential responses at all of the rates including the 507 clicks per second. We will talk about the results in the next slide.

So the first result that we have seen, we have seen a separation of the summating potential and action potential waves at faster rate than at a slower rate. You can see summating potential is a very small hump before the action potential starts. That will be very difficult for unexperienced audiologist to identify, but here is easy to identify.

So this was the first finding. The second one is when we go higher in rates there is no change in the summating potential amplitude at latency, relatively stable because it is a presynaptic response, it's not a neural response. But the action potential is getting smaller in magnitude and delayed in latency. So this study was the first study to assess the physiological neural adaptation of the actual potential amplitude as a function of fast click rate using CLAD. Compared to our normative data and Ménière's disease, patients have shown significant decrease of the action potential amplitude as a function of rate in our study and in Bohorquez et al., 2006 study.

We can see that significant degradation of the action potential aptitude as a function of stimulus rate. So now we have documented that patients with Ménière's disease will have abnormal neural adaptation of the action potential. Another finding, we have seen a separation of the action potential amplitude, reduced response when we use rarefaction compared to the condensation polarity, at a slow rate and mid rate of click, how many clicks per second.

Also the action potential latency have been shifted when we record to condensation versus rarefaction. That big separation and shift when we record ECochG to either condensation and the rarefaction is a significant sign of endolymphatic hydrops, or patients who have Ménière's disease. These studies have been done on only six patients with Ménière's disease, with definite Ménière's disease.

To improve the test sensitivity of ECochG, and instead of using click stimulus, we can use frequency-specific stimulus, again, to target those frequencies that are affected with Ménière's disease early in the disease process. So Ferraro and colleagues have done several studies, and they have shown a large summating potential amplitude when we use a 2,000 hertz stimulus in patients with Ménière's disease but normal summating potential, very small, very tiny as we would expect in patients who have sensorineural hearing loss but not Ménière's disease. The limitation is that we are still using slow rate, we are not stressing the ear.

We conducted another study to improve the sensitivity and specificity of the frequency-specific ECochG using CLAD to quantify the effect of stimulus rate and stimulus duration on the frequency-specific ECochG. So we use 500 hertz and 2,000 hertz tonal stimulation with different durations, 12 millisecond, 6 millisecond, 3 millisecond, and at different rates, from slow up to 234 tonal stimulations per second. Our results showed that the summating potential amplitude are larger at fast rate, look at the last traces in each section, larger to fast rate, and to short duration.

So the bottom traces for short duration, we're getting a larger summating potential than when we use a longer duration stimuli. So this was another study that we have normative data for the use of frequency-specific ECochG to fast rate. Again, audiologists are using the standard ECochG and we conducted another study to standardize the electrode type and the electrode side. So we conducted ECochG using an eardrum electrode recording, a Lilly Wick electrode and the homemade electrode versus an ear canal electrode recording. Our results show that the summating potential action potential area ratio for the tympanic membrane electrode

recording are very consistent and reliable over time than the use of the TipTrode. We have also larger cutoff and larger variability.

Our recommendation for audiologists who are doing ECochG is to use tympanic membrane electrode recording. For differential diagnosis, any dizziness can be a symptom of anything, from dehydration, to hormonal imbalances, to tumors, in rare cases. So the physician can help you to distinguish Ménière's disease from other inner ear disorders including vestibular migraine, or other disorders, autoimmune diseases up to multiple sclerosis.

There is a big list that you have to see a physician to be able to know why you have sudden repeated attacks of vertigo and aural manifestations. For treatment, there are a lot of treatment approaches available, mainly and simply because we really do not understand the pathophysiology of Ménière's disease. That's why more research is needed for evidence-based diagnosis and for early and appropriate treatment.

Your physician will treat the underlying cause if it is an autoimmune disease or a vestibular migraine. So they will treat the underlying cause first. If there is no known underlying cause, like in idiopathic Ménière's disease, then there are different conservative approaches can be done to reduce the frequency of the vertigo and to reduce the severity of the attacks as well. They can start with lifestyle modifications that are already tailored to each patient's need, and dietary modifications, including salt restriction. Oral medications that could be a betahistine or diuretics, could be intratympanic injection of steroids, or even gentamicin. Patients who have hearing loss, audiologists will fit them with hearing aids.

Others may suggest to use a Meniett device but we do not have good randomized controlled trials to support its benefit, and the surgical treatment will be the last option to be done. Patients need to be assured that their vertigo will be burned out, maybe, after seven years of the onset of the disease. These surgical approaches, again, can be conservative approach to cure 95% of your vertigo, endolymphatic sac decompression, vestibular nerve sectioning, or could be a destructive invasive surgery labyrinthectomy where they remove the end organ of hearing and balance, the membranous labyrinth, and this will also cure vertigo but the patient will have no serviceable hearing to use a hearing aid. If the patient wants to hear it will be a cochlear implantation.

For future research, this is so important because without research and without funding, really, we cannot help patients to understand the pathophysiology and the cause of Ménière's disease. We could use animal model for Ménière's disease, not the endolymphatic hydrops, this has been already documented, postmortem and in animal models. We can use immune-mediated, migraine models, genetic mutations to understand the pathophysiology. We need to improve the ECochG research using CLAD at fast rate.

We also need to assess family members of patients with Ménière's disease. This was a pilot study by Ferraro et al. in 2019 that found 80% of family members may be at risk for developing endolymphatic hydrops if a family member has Ménière's disease. Also, we need to investigate if Ménière's disease will progress to cochlear synaptopathy.

And as I have shown you earlier, patients who have Ménière's disease will have significant neural degradation of the action potential amplitude compared to normal physiological neural degradation. With the large summating potential amplitude, they will have an abnormally large summating potential action potential amplitude and area ratio and neural degradation of the action potential.

These findings are very similar to patients or individuals who have cochlear synaptopathy, where the site of lesion is in the synapses between the inner ear cells and the auditory nerve. So we really need to know are they the same thing? Is the neural degeneration with Ménière's disease fits the same cochlear synaptopathy as patients who have noise exposure, or aging, or medications without Ménière's disease symptoms? This is research that should be done. Thank you so much, and I really appreciate your staying later to attend this presentation.

ANIL LALWANI - Well, thank you so much for a really a wonderful, wonderful talk that widely covered the symptoms of Ménière's disease, the differential diagnosis and the treatments, and your contributions in how we can have greater diagnostic specificity with the CLAD test. There was a question from Andrew who asked whether ECochG and CLAD can be used now by an audiologist to help diagnose. Is this something that can be used to diagnose now or do you think is still an experimental stages, you're still collecting data or is this ready for prime time?

WAFAA KAF - No, not ready yet because Bohorquez et al study that I presented, they use a transtympanic electrode recording. So the more invasive way of recording ECochG. So it has to be done with a physician to place the needle electrode, the audiologist won't do that. So maybe if I get funding I will do more on big sample of patients with Ménière's disease definite versus probable using an extratympanic recording. So where we put that electrode on the ear drum. So it's not ready yet for clinical use.

ANIL LALWANI - And how about the contralateral ear? There's some questions about bilateral Ménière's disease, how common that is. Can you use your CLAD to identify a clinically silent Ménière's disease in the opposite ear?

WAFAA KAF - Okay, great question. Yes, it's like two questions in one question. Usually Ménière's disease, we know it starts in one ear, and maybe in 28% of patients can develop Meniere's disease in the other ear. If the disease starts early in life, not later, maybe the second ear can have the disease, maybe up to 50% or sometimes 78%. We see it more when the disease starts early because now the life expectancy, and we can see that the other ear is affected.

Can we see changes in the other ear when we do not have a hearing loss? Maybe the neural degeneration using CLAD will be more of a marker than just the standard ECochG. Again, more research is really needed in that area because again, this is a stress, it's a stress test for the inner ear. So if the inner ear has Ménière's disease won't tolerate that fast sounds, then it'll decay, the neural responses will decay, then we can see a change.

ANIL LALWANI - Sylvie and others ask whether Ménière's disease can go away or is it forever once you experience it. And I think the second half of that question, it looks like you're getting two for one question now, so one is, will it ever go away or do you have it for the rest of your life? And number two is how much can those symptoms change over longer spans of time?

WAFAA KAF - Okay, will it go away? I think Ménière's disease is a permanent condition. The symptoms will come in stages according to Shea, in 1993, he has like five stages of Ménière's disease. Like Stage 1, you might have hearing loss, the fluctuating hearing loss, the tinnitus, the ear fullness, maybe vertigo doesn't start in the first stage of the disease, it could start in the second stage. Then in the fourth stage and the first stage vertigo will decay,

it burns out. Maybe the stria vascularis and the membranous labyrinth will be already exhausted from the intoxication that happens.

Although the vertigo burns out, could be even within two years of the disease, but usually within seven years, eight years of the disease starts. But the hearing loss will progress. It fluctuates but it'll progress. It could end up with a severe hearing loss or a profound hearing loss. Did they answer the first part of the question?

ANIL LALWANI - Yeah, I think so.

WAFAA KAF - The second part of the question, can you repeat it please?

ANIL LALWANI - Yeah, and how much the symptoms can change over the span of time, I guess, mild to severe, how much can they change? I think you partially have answered that question.

WAFAA KAF - Yes, yeah, again, Ménière's disease has a genetic component. It could be an autosomal dominant with variable expression. So what is variable expression? Is that each patient will have different expression of the manifestations. Maybe, some will have repeated attacks within weeks, some may have more spaced attacks, so it's unpredictable. No one can predict when these symptoms will be repeated. And I think this is a devastation that people will be under stress, and that's why stress is a triggering factor as well.

I always remember this if I go to Seven [Six] Flags, for example, I have that ride that takes me very high up then drops me. I would just scream all the time. Then before it takes me up again and drop me back, I start to scream again, I'm waiting for that drop. So this is what patients with Ménière's disease will experience. They are under stress for their next attack. Although my recommendation for them is to live a normal life in between the attack so they are not exhausting themselves, because their stress can cause an attack.

ANIL LALWANI - There was a earlier question about how young can a patient be to get Ménière's disease? Do people under age of 18 get Ménière's disease?

WAFAA KAF - It's not common. I do not have the percentage, but usually it is an adult-onset problem. The peak of the Ménière's disease will be around 40 to 60 years of age. It'll be a small percentage for those who may have a Meniere's disease at age 18 or younger.

ANIL LALWANI - And does it matter how severe or not severe the disease is in terms of the value of your test, the CLAD test? Does the CLAD test result depend on the severity of the disease?

WAFAA KAF - Yeah, great question. Not necessarily the severity of the disease, is the severity of the hearing loss. Yes, so I need to know-

ANIL LALWANI - Yes, that's the point.

WAFAA KAF - What is a degree of the hearing loss, because with this evoked potential, the maximum sound that I present into the ear is like a 95 dBnHL, and if they have a 70 dB hearing loss, severe hearing loss, this means I do not have enough sound to trigger a response from the inner ear and the auditory nerve. So it should be done early, actually, and this is maybe the purpose. We really need to detect it early, not at a later stage of the disease.

ANIL LALWANI - Well, if you have the answer to the next question it's a Nobel Prize-worthy answer. The question is, Judith and others ask about potential medications in the future, of course, to treatment Ménière's disease given the complex mix of potential causes, your differential diagnosis had many different things and many people say that the common pathway of the end is endolymphatic hydrops for different things. What might future medication targets be most likely? So either a Nobel Prize or certainly billions of others of earning.

WAFAA KAF - No. Maybe, you need to invite a colleague. I think he is practicing in Texas. His name is Sami Melki. Melki et al., did a study in 2010 on a mouse model, with induced endolymphatic hydrops. They used a medication that is anti-inflammatory, antioxidant, it's called dimethyl sulfoxide, DMSO.

What they have found with the DMSO, that anti-inflammatory antioxidant medication that it really protects from the hearing loss. It was interesting, it protects from the hearing loss, not necessarily the vertigo, but if you can protect from the hearing loss, this is great because we have other medications, the current medications can really control the vertigo attacks, and vertigo again could fade away within few years from the onset of the disease.

So this is what I can think of but I know that there is a way that we can introduce the medications into the ear. I need to remember it was a pharmacy colleague who used a specific technique, it's nanotechnology, to introduce the medications directly into the inner ear. So it caused the effect more efficient with less side effects to the rest of the organs, using nanotechnology.

ANIL LALWANI - Now, you spoke about treating hearing loss, you talked about treating the vertigo and so on, and so there was actually an earlier question by Abdul Razak who said, Instead of using the classification to guide treatment, in terms of the different categories of Ménière's disease, should you be focusing just on a symptom such as hearing loss or vertigo? And I think you may have answered this, but your just general philosophy in how do you treat Ménière's disease with respect to their different symptoms they're having?

WAFAA KAF - If I understand the question correctly, we really need to know Ménière's disease to be able to provide the treatment, because if it is a vestibular migraine, maybe patients will improve with the use of the migraine medications. So it depends on the clinical presentations of the symptoms, what the patient have, it will be more symptomatic treatment to reduce the frequency of the vertigo attack and reduces severity, keeping in mind that you need to treat the triggering cause.

If it is an autoimmune disease, then the patients will respond very well to corticosteroid medication. So if it is a Lyme disease, for example, that causes Ménière's disease, we need to treat the Lyme disease. If it is a vascular causes we need to treat that cause. So who can tell that? It is a treating physician. So these patients really need to seek medical attention when they develop disease symptoms because, again, it could be very simple, it could be very severe.

ANIL LALWANI - Actually that's a wonderful segue to the next question that Katherine was asking, and you've already partially answered it, of course, in your wisdom, but nonetheless I'm going to ask this question which is, what kind of markers would help distinguish Ménière's disease from other conditions that have sometimes been taken for it? And just to go back to your talk, Ménière's disease, of course, is the idiopathic constellation of symptoms you talked

about, the episodic vertigo, the fluctuating hearing loss, the tinnitus and fullness, and in part you said things like Lyme disease test, autoimmune disease test, can distinguish some of those other conditions. In general, I think, you're thinking, and please elaborate further, is that you realize some of the common things that mimic Meniere's disease, and when you don't have any of those things, you treat it idiopathically even though it may still be a mixture of a lot of different causes that cause it.

WAFAA KAF - Yes, so if it is like a Lyme disease, for example, the patient well experience a history being bitten by a tick or being on the West Coast, or have some rashes, very characteristic rashes, that is characteristic for Lyme disease. If it is an autoimmune disease, it could be now other manifestations. So the patient will have lupus, so other organs of the body are affected, it could also affect the eye, so we have abnormal shape of the cornea of the eye. So there are more toward those other diseases. If it is a benign paroxysmal positional vertigo, for example, these patients who have frequent attacks of dizzy spells, the duration of the dizziness is very short and it's repeated, it could be related to eye movement or postural movement.

The clinical history is so important. Patients need to use very detailed kind of diary. You really need to know when did it start, what triggers it, how long does it stay, what helps to trigger it, what helps to reduce it? When you lie down, does it help to suppress your dizziness? when you fixate, look at a fixed object, does it help to suppress it? Because this can help me know that it is not a central lesion that affects the vestibular system. Does it accompany a throbbing headache? If there is more throbbing headache during the attack, maybe it's a migraine attack. So the clinical manifestations are very important.

ANIL LALWANI - You mentioned some genetic component. One of the attendees asking whether we know which genes are involved.

WAFAA KAF - Oh, there are 100 genes that are involved with sensorineural hearing loss, in general. Maybe a gene is an ion channels mutation that affects sodium potassium exchange, could be implicated with the endolymphatic hydrops, or a gene, I think, it's TMC-specific genes.

ANIL LALWANI - Got it. Is there a difference in how Ménière's disease affects women versus men, or another way to ask the same question, are there hormonal influences to Ménière's disease?

WAFAA KAF - Okay, actually it's like a myth. First we thought that it affects women more than men, and maybe because we label those who have vestibular migraines as Ménière's disease. Vestibular migraine is a new diagnosis that we came across in 2013. Before that, patients who have the stabler migraine was diagnosed as having Ménière's disease. So it looks like women have more, but in reality they do not have more incidence or prevalence of Ménière's disease. The other question is?

ANIL LALWANI - Is there hormonal influence? It's just the other half is it.

WAFAA KAF - Yes, other half. Like menopause, for example, or during menstrual cycles, again, it's a stressor. It could increase or a precursor for an attack, and this will be, maybe, more frequent attacks in women than in men, and maybe that's a why woman will seek more attention because of the vertigo attacks that comes periodically. Men do not have to do that.

ANIL LALWANI - There's a question about the CLAD test and the influence of migraine headaches. Is your test affected by the presence of migraine headaches? Does it complicated the issue or-

WAFAA KAF - Yes, it was part of my funding that I got from Hearing Health Foundation is to follow up with another study to assess patients with vestibular migraine. And on our pilot study we have found no significant changes compared to inner-ear status from healthy individuals. So we have three groups, healthy individuals, patients with Ménière's disease, and patients who have the vestibular migraine. The vestibular migraine presented normal physiological neural adaptation of auditory nerve similar to the healthy individual, but we have seen degradation of the neural adaptation.

Currently, we are doing research on migraine, so just migraine, using animal model, in rats, to see, does it affect the hearing? And with the animal model, with our pilot study, we have seen mild to moderate sensorineural hearing loss. Also, we are doing a parallel study on human beings who have episodic migraine versus chronic migraine. And what we have seen, hearing was not affected when we have tested them during that attack, but we have seen very significant hyperacusis, hypersensitivity to sound, very significant. Their hearing is, say, a 10 dB, and their intolerance, uncomfortable level to sound, was at 40 dB, very, very restricted range.

ANIL LALWANI - Levi asks whether the prevalence of Ménière's disease has increased or is it just simply being diagnosed more frequently because you're doing such a good job of educating us? But just to let re know, we're down to our last few questions now, near the end of the hour, we worked you very hard. Anyway, incidents increasing or are we just diagnosing it more?

WAFAA KAF - I think with the advance of technology, with the advance of knowledge, with the advance of funding to do research, we get to understand, and do a good job, and distinguish between different conditions. So we are able to not necessarily diagnose more cases of Ménière's disease, but at least you know that this is Ménière's disease, not vestibular migraine. So the advances that we do helps us to know the medical conditions. And it depends also on the clinical reports. Because in Finland, for example, they have higher incidence and prevalence of Ménière's disease than in the United States. So why do we do that? Maybe because of the health system itself that you have more patients who are reporting dizziness symptoms that we do not have here in the US.

ANIL LALWANI - So I think the last question for you really is can you offer us any hope... And this is really a combination of multiple questions for different people. Can you offer us hope with respect to treatment in the future? I know your talk was about diagnosis, but our attendees are interested in, what are some of the future directions in terms of therapeutic? Either directly leading for your diagnostic ability and precision, or any frontiers to give us hope.

WAFAA KAF - We cannot live without having hope in life. We understand that Ménière's disease is a devastating disease, is a progressive disease. It's not pleasant at all to have the vertiginous attacks that could affect the quality of your life. But again, patients need to be reassured that vertigo will burn out with time. It won't be that intense with time. The medications can get rid of 95% of vertigo. And again, we do not just go into surgery. I do not do the medical intervention. I am an audio vestibular physician, but I do not practice here in the United States as a physician. So again, even with conservative treatment like restricting

salt and have certain dietary restrictions will improve the devastating sensation of dizziness. With more research, I believe we will find a treatment for tinnitus, could be, again, using that nanotechnology that could really attack the inner ear directly without just a pill to take or injection, or just infusing the steroid or gentamicin inside the middle ear, not necessarily in the inner ear.

ANIL LALWANI - Well, with that positive note, I so want to thank you for this really informative presentation, Dr. Kaf, and also want to thank all our attendees. We're so grateful to you, our community, for your support of the Emerging Research Grants program. Remember that you can donate to our efforts to advance better treatments and cures for hearing and balance conditions by going to hhf, that's Hearing Health Foundation, hhf.org/donate. And again, thank you, and please do enjoy the rest of your day, your evening, and thank you for joining us. Dr. Kaf, thank you again.

WAFAA KAF - Thank you so much Dr. Lalwani. Thank you, I appreciate it.