VESTIBULAR ANATOMY & PHYSIOLOGY

Transcript of Lecture by Dr. Habib Rizk, MD, MSc

0:00:11.6 Dr. Habib Rizk: Good afternoon, everyone. My name is Habib Rizk. I'm a neuro-otologist at the Medical University of South Carolina in Charleston. As a board member of the Vestibular Disorders Association, we're partnering with the AMA Educational Hub to bring more awareness and clinical content about the vestibular disorders we treat on an everyday basis. The title of this talk is The Anatomy and Physiology of the Vestibular System. And during that talk, we're going to also talk about clinical findings and clinical pearls that could be pertinent for physicians of any specialty interacting with dizzy patients. These are my disclosures. The outline and objective of the talk is to go over the anatomy and physiology of the vestibular system, to understand site of lesion and mode of presentation of vestibular disorders, to define a peripheral vestibular disorder and differentiate it from a central vestibular disorder, understand and describe the vestibulo-ocular reflex, which is at the basis of the physiology of the system, but also at the basis of most of the clinical symptoms we encounter.

0:01:23.3 Dr. Habib Rizk: In a second part of the talk, I'm going to talk about the aging of the vestibular system, which is particularly pertinent in our current-day society and the aging society we are facing. Those are patients who are going to present with more balance and dizziness than a few decades ago. So, the inner ear and the vestibular system within the inner ear are housed in a bony labyrinth. And the bony labyrinth is located within the petrous bone, which is the portion of the temporal lobe that I'm delineating right here. And if we look at the bony labyrinth, it contains the cochlea, which is the hearing organ, but also the balance organs that are consisting of five structures: three semicircular canals and two recesses, the elliptical recess and the spherical recess. Within the bony labyrinth, we have a membranous labyrinth, which is the actual tissue that contains the sensory organs of balance. So, we have three semicircular ducts: the superior duct, the horizontal duct, and the posterior duct. And we have the utricle housed within the elliptical recess and the saccule housed within the spherical recess.

0:02:39.0 Dr. Habib Rizk: And interestingly, the saccule connects with the cochlea, the hearing component, through this structure called the ductus reuniens. More interestingly, as well, within that small space that contains less than one milliliter of fluid, it's actually highly metabolically active and highly immunologically active. Those utricle and saccule structures, they connect to form a utricular and saccular ducts that join to form the endolymphatic duct that opens up as the endolymphatic sac. The endolymphatic sac is the immunologically active portion of the inner ear. When we look at the innervation of the vestibular system, we also find certain interesting characteristics. We have the vestibular nerve, which is a portion of the eighth cranial nerve that separates into a superior branch. The superior branch goes to the utricle, the lateral or horizontal semicircular duct, and the superior duct. And then we have the inferior branch that goes to the saccule and to the posterior semicircular canal. And that will have significant impact on a lot of the clinical disorders we see, and particularly vestibular neuronitis. And I will talk about it in a second.

0:03:58.7 Dr. Habib Rizk: Vestibular neuronitis is a viral inflammation of the vestibular nerve, usually related to a flare-up of the shingles or the herpes virus in the vestibular ganglion. And when the virus wakes up again, we have a degeneration of the vestibular nerve when it affects the nerve. Usually, it's the superior branch that is affected, and that creates the symptoms of intense vertigo that would last for a few days, followed by imbalance for sometimes up to a few weeks. When the superior branch is affected on its own and the inferior branch is intact, some patients would develop a different type of vertigo several weeks afterwards. And that type of vertigo, it's called benign paroxysmal positional vertigo, BPPV, which is related to the otoliths or the crystals falling from their place in the posterior semicircular duct. And that's why it's important to keep in mind that patients may have multiple vestibular disorders at the same time. And as clinicians assessing those patients, understanding the anatomy and the physiology and interpreting the clinical exam findings will allow us to get there.

0:05:20.3 Dr. Habib Rizk: Additional information to know from the anatomy without going into a lot of details: the saccule and utricle are perpendicular to each other and allow us to sense direction of gravity. So the vestibular system, as I said, contains five structures. The three semicircular ducts are responsible for us sensing a rotational movement, whereas the saccule and utricle are responsible for sensing translational movement, like moving in a car for the utricle or moving up and down the elevator for the saccule. And within the saccule and utricle, we have a hair cell layer where you have the actual hair cells that sense the movement. You have a gelatinous layer and membrane called the otolithic membrane, on top of which we have the actual crystals, which in our lingo would be more called otoliths, stones in the ear. And these are the structures that are responsible for one of the most common causes of vertigo, the benign paroxysmal positional vertigo.

0:06:26.2 Dr. Habib Rizk: The otoliths are motion sensors. They are formed of calcium carbonate crystals embedded in a matrix of protein. And when the head is moving, the crystals will shear the top layer of that otolithic membrane. And by shearing that top layer of the otolithic membrane, they can differentially affect the top of the hair cells, creating more or less information to flow through the hair cells and down into the vestibular nerve, creating a sensation of movement. Like we discussed earlier, the crystals are present in the saccule and utricle usually. So when they fall out of place, they can fall into any one of those three semicircular ducts and create symptoms and clinical findings. When we look at the three-dimensional structure of those ducts, this is how they would look like, actually, after 3D printing of the temporal bone. And this is how they are configured in space. And you can see that, and the color coding is to show that the semicircular ducts on each side are paired with the other side.

0:07:30.5 Dr. Habib Rizk: We have the horizontal ducts are paired together on the right and left side. We have the superior duct paired with the posterior duct of the opposite side. We call it the RALP and LARP plane: right anterior, left posterior, and left anterior, right posterior. Within the semicircular duct, the structure is slightly different. We have this crista ampullaris where the nerve basically ends, the nerve endings. And then we have, instead of an otolithic membrane, we have a cupula, which is the gelatinous layer that goes across the lumen of the duct to the other side of it. And around it, there is endolymph flowing. The endolymph is the fluid that is filling those ducts. And depending on how the head is moving, the endolymph is going to move the cupula, which will create a shearing of the crista ampullaris hair cells and excites the ampullary nerve. So it's the same mechanism with a different structure, creating similar propagation of information.

0:08:32.1 Dr. Habib Rizk: And again, without going into a lot of details, the hair cells, there's a couple of types of hair cells within the inner ear structures. And the cell would recognize if it's an excitatory impulse or an inhibitory impulse, depending on the direction of bending of those hair cells. What is a different or important mechanism to remember when we look at the function of the vestibular system is that both vestibular systems are working even when we're not moving. There's a resting state discharge of electric impulses through the nerve that are telling the brain that we are actually static. And what is also a second tenet of vestibular physiology is that movement of the head will create an excitatory impulse on the side to which we're turning, but at the same time, it will be an inhibition of the side we're turning away from. This is what we call a push-pull mechanism. And if you push more on one side than on the other side, that can create a sensation of vertigo or a fall.

0:09:40.7 Dr. Habib Rizk: Our understanding of vestibular physiology is not that old. Unlike other structures, we started recognizing the function of the vestibular system in the late 19th century. A French physician started making experiments on pigeons. And the reason he did that is because they have an accessible otic capsule in which the inner ear is housed. At that time, in 1842, it was thought that all of those ducts were responsible for hearing and that any sensation of dizziness only comes from the brain. So this gentleman, Dr. Flourens, decided to destroy selectively each of the ducts. And instead of developing hearing loss, his animal models, his pigeons, started developing weird symptoms. When he destroyed the horizontal ducts, they started running around in circles. That's because they were chasing how they were feeling like they were moving, so they were having vertigo, and so they started moving around in circles. When he destroyed selectively the horizontal, the posterior canal, or the superior canal, they started developing those torticollis-type attitudes. To feed themselves and drink, they had to move their head in a specific way.

0:10:52.5 Dr. Habib Rizk: And then he let go of those experiments, didn't engage more in that. And 50 years later, Ewald, who is considered the father of vestibular physiology, went back to those experiments, and instead of destroying the otic capsule and the semicircular ducts, he started stimulating each of those ducts. And he came up with those three laws that allow us to understand almost any finding we have when a patient walks in with dizziness coming from the inner ear. Stimulation of the semicircular canal causes a movement of the eyes in the plane of the stimulated canal. Meaning, if you stimulate the horizontal canal, you're gonna have a tonic movement that is horizontal at the level of the eyes. In the horizontal semicircular canal, when the endolymph flows toward the ampulla or the crista ampullaris, we will have an excitatory impulse, and the opposite is true in the vertical semicircular canals. A flow of endolymph towards the ampulla is going to be inhibitory rather than excitatory.

0:11:59.6 Dr. Habib Rizk: And while that sounds like basic right now, at the time this was described, there was no understanding of the correlation between the vestibular nerve and the oculomotor nuclei. We did not know that the oculomotor muscles are paired with each semicircular duct. This was a very astute observation about the relationship between the vestibular system and the eye movements. And then, another 50 years later or so, Robert Bárány, who is a Hungarian physician, described the caloric reaction. This was kind of serendipitous. He was cleaning the ear of his patients who presented with wax, with flushing them like it's done in most clinics where there's no available microscope. And he started noticing that some of his patients, depending on the temperature of the water, they would develop vertigo. And the caloric response and the caloric tests that we do in routine vestibular clinics is based on those initial observations, where if you stimulate the vestibular system with a temperature colder than body temperature, you can create a vertigo with eye movements going opposite the direction of the ear that you stimulated. And the opposite is true when you use warm stimulus with temperature higher than body temperature.

0:13:27.0 Dr. Habib Rizk: Eventually, in the mid 20th century, 1950s, 1960s, we finally understood the pairing of the vestibular system with the oculomotor muscles. And now we know that the superior semicircular canal is paired with the bilateral superior recti muscle and the contralateral inferior oblique. The posterior semicircular canal is associated with the ipsilateral superior oblique and the inferior recti muscle. And the lateral semicircular canal is associated with the contralateral lateral rectus. And that's important because that actually drives the findings of nystagmus that we're seeing in clinic. And depending on the direction of the nystagmus in clinic, we can determine which part of the inner ear is being stimulated when it's a peripheral vestibular pathology. So this is an example of a posterior canal benign paroxysmal positional vertigo. The crystals from the utricle get out of place, and they fall and get trapped into the posterior semicircular canal.

0:14:28.8 Dr. Habib Rizk: When the patient starts going into a position of the head that triggers symptoms, it means the crystals are moving. And as you can see, the crystals are moving away from the ampulla, which, according to the third law of Ewald, is responsible for an excitatory event. In those cases, the patient will develop an upbeat torsional nystagmus that is beating toward the ear that is being tested or stimulated. And that's because of the third law of Ewald that we defined earlier. When the patient goes to sit back up, the crystals or the otoliths start flowing down and push the endolymph toward the ampulla, which creates an inhibitory response. And they will have a reversal of their eye movements that is downbeat away from the ear that we just stimulated. And that response is going to be much weaker than the initial response we had when we laid patients back. When you look at it in real-life, this is a patient, you lay him back, let's say, on his right side. And actually, in this case, it's going to be on the left side. They will have an upbeat torsional geotropic nystagmus toward the left that starts after a latency of a few seconds because you need the crystals to start moving before seeing that nystagmus.

0:15:47.1 Dr. Habib Rizk: The early theory about BPPV is that it was due to crystals being stuck on the crista ampullaris. Now we know that the crystals don't need to be stuck, although they are sometimes, and they create much worse symptoms. Most of the times, the crystals are free-floating within that duct, and just the movement of the head in specific positions can create a centrifugal effect on the endolymph. And as the endolymph moves, it can create the excitatory findings that we just described. If the crystals fall into the horizontal canal, it can create a different type of eye movement. Like you see it here, it's purely horizontal because the horizontal canal is paired with the lateral rectus muscle. There are other reasons why you could develop a positional nystagmus, and just a segue here, alcohol can cause a positional nystagmus not related to the crystals. So anything that can theoretically affect the density of the endolymph, whether it's the crystals if they fall out of place, certain products like alcohol, inflammation like seen in migraine, CNS inflammation, or infections, can create a change of endolymph around the cupula that can lead to a nystagmus.

0:17:04.7 Dr. Habib Rizk: So, a third type of benign paroxysmal positional vertigo, which is also extremely rare, is when the crystals get stuck in the superior semicircular duct. And in that case, as you can see, different than the other types of eye movements, we have a nystagmus that is downbeating rather than upbeating or horizontal. And that's because the superior semicircular canal is paired with the inferior oblique muscle and the superior recti muscle. Now, I said earlier that in certain cases, if you have a vestibular neuronitis, you can develop a different type of vertigo several weeks later. And that's due to everything we just discussed. If you have a vestibular neuronitis that affects the superior vestibular nerve but preserves the inferior nerve, it's not unlikely that you'll develop a posterior canal BPPV in the weeks following that neuronitis.

0:17:59.1 Dr. Habib Rizk: So if a patient comes in initially with a dramatic vertigo event that is lasting days and you are suspicious of a neuronitis or labyrinthitis if there's a hearing loss associated with it, and they get better, but then they come back with a complaint of vertigo, make sure to ask if this is a positional vertigo. Make sure to examine them in the appropriate maneuver that we call Dix-Hallpike, where we lay them back and look at the eye movements. And if you elicit symptoms and a nystagmus that is upbeat, torsional, geotropic, then you know you have moved on from the neuronitis to a super-added BPPV pathology. One thing we touched on earlier as well is that even though it's a tiny space that contains less than 1 cc of fluid, this is a highly metabolically active structure that contains a lot of ion channels, a lot of steroid receptors, beta-blocker receptors, aquaporin receptors.

0:18:58.6 Dr. Habib Rizk: So, a lot of metabolic disruptions and a lot of pathologies can affect the inner ear. One of them is migraine, or any inflammation in the CNS can theoretically affect the inner ear. So whenever you have a nystagmus, the initial information that the nystagmus would give us is allow us to figure out what structure or what pathway of the inner ear or the vestibular system is affected. But other than BPPV, like I said a couple of slides ago, certain metabolites can create similar findings like alcohol-induced positional nystagmus, or more frequently in clinical practice, migraine. Migraine is an inflammatory process and is strongly associated with a positional nystagmus that we need to differentiate from the nystagmus of BPPV. A lot of patients come in, walk in with a diagnosis of BPPV, and they've had many repositioning maneuvers with physical therapy to no avail. Actually, have migraine, and the positional nystagmus is not due to the crystals, and it will not respond to repositioning maneuvers.

0:20:11.2 Dr. Habib Rizk: When we talk about vestibular physiology, the first section I wanted to clarify how important it is to understand the anatomical connections between the ducts and the oculomotor muscles. But the tenet of vestibular physiology is something we call the vestibulo-ocular reflex. The vestibulo-ocular reflex is, in its basic form, you move your head to the right, your eyes go to the left. You move your head to the left, your eyes go to the right. This is like the doll's eye reflex that tells us that the brainstem is functioning because it is actually routed around the vestibular nuclei. However, in order to be able to be functioning human beings, when we move our head, we want our eyes to move with our head to track a target. Those are slightly more complex structures above the vestibular nuclei that control that, and they suppress the vestibulo-ocular reflex to allow the eyes to stay on target. And this gives us a way to evaluate the integrity of the inner ear system. The head impulse test relies on that suppression of the vestibulo-ocular reflex.

0:21:20.0 Dr. Habib Rizk: And basically, if you have a patient who has a weakness in, let's say, the left inner ear, when you move their head quickly toward that left side, since the vestibular system is weak on that side, their eyes will slip and then come back to the target. We call it they have a positive head impulse test because we are documenting a presence of a saccade. In this case, this is a patient who has a weakness on the left side. And as you can see, you move her head to the left and her eyes drift and then come back, whereas when you thrust her head to the right side, her eyes stay on target all the time. So, she has a weakness toward the left side. We can also evaluate the vestibulo-ocular reflex suppression by visual fixation, by having a patient look at a target or their thumb, overextended thumb, in the chair that you can move in clinic. And a patient who has an absolutely intact inner ear system and brainstem and cerebellar system is able to suppress the vestibulo-ocular reflex and keep their eyes on that target as you're moving the chair.

0:22:34.2 Dr. Habib Rizk: If somebody has a problem in the brainstem or the cerebellum, they're not able to keep their eyes on target as you're moving them because they're not able to suppress the vestibulo-ocular reflex. Another insight into what's going on when we're moving our head and how it's connected to eye movements is a characteristic of the vestibular system called velocity storage asymmetry. Imagine having the brain decode every single movement of the head you make in real time. It's going to be impractical. Nobody can move until the brain processes every single thrust of the head or movement of the head. What the brain does actually is predictive modeling. And by doing that, it allows us to do multiple movements of the head that are then stored. The information related to them is stored at the level of the brainstem, and then processes them and makes corrections and troubleshooting to the movement. That's why balance is something we don't think about in real time. But once there's a breakdown in the balance mechanism, there's a total breakdown of the process that we see in those chronically dizzy patients.

0:23:48.8 Dr. Habib Rizk: And the initial information that is detected is the change of velocity. It's the speed of the head movement that is the information or the variable that is being detected by the vestibular system. By the time it gets to the vestibular nuclei, so the higher levels of processing, that velocity, that speed variable, is changed into a position variable. And that's how the brain can detect our sense of position and where the head is located. So when we're moving very quickly, if the movement is stimulating both sides kind of equally, and then you go to stop, there will be a cancellation of the input coming from the right and the left, and you will still feel steady. That's why when we're moving around, we don't always feel like we're dizzy. Imagine going, like this is a video recorded in a park. We're spinning that child, who happens to be my child, and we're spinning them in a clockwise manner. So we're stimulating one system more than the other. And eventually we stop. And if you look at what happens when we stop. So she has a velocity storage asymmetry because we overstimulated one side compared to the other, and then we stopped it. This was not done on purpose. We were just chatting and playing at the park. And we happened to record that, and I felt it was a good educational moment.

0:25:18.3 Dr. Habib Rizk: And so she had a left-beating nystagmus following a significant stimulation of the left side by the clockwise rotation. And then when we stopped, the central nervous system, the higher levels, decided that there's an imbalance between the input coming from the left compared to the input coming from the right. And it showed it to us by showing us that post-rotational nystagmus. If you were to examine a patient in clinic who presents with dizziness, and you would shake their head right and left about 20 times and then stop and look at their eyes, if they have a left-beating nystagmus, chances are that their right vestibular system is weaker than their left vestibular system. This is called the after-head-shake test, and it's one of the clinical items that we look for when we're doing our evaluation of patients. So now that we got an overview of some of the mechanisms we use to understand some of our clinical findings, what do we do when we have a patient in front of us in clinic?

0:26:23.5 Dr. Habib Rizk: The first tenet of any evaluation of any clinical complaint is to define the symptoms. And in dizziness, it's particularly challenging because patients come up a lot of times with very creative ways of describing their symptoms. But usually and classically, we have to try to determine, put them into certain categories. One of the categories is lightheadedness. Are they talking about a lightheadedness or a pre-syncope? Is it more of a disequilibrium and unsteadiness on their feet rather than a true dizziness? Or is it a mix of both? Is it vertigo? And what is vertigo? Vertigo is an illusion of movement of oneself or the environment. The vertigo of neuronitis and benign paroxysmal positional vertigo is an illusion of movement, spinning of the environment. But there are other types of vertigo that are non-spinning, like a rocking sensation, like you're on a boat. Those are things we see in migraine patients. So not all vertigo is spinning, and not all vertigo comes from the inner ear. But a lot of vertigo that is spinning comes from the inner ear.

0:27:34.1 Dr. Habib Rizk: And the fourth category is something called oscillopsia, which is a subjective illusion of visual motion. It's a very hard symptom to elicit from the patient. They're not going to come tell you, "I have oscillopsia." But one way to try to determine it, vertigo, you can still feel it with the eyes closed, whereas oscillopsia only happens when the eyes are open. The Bárány Society, which is basically the society that deals with most vestibular disorders and has a committee that creates consensus documents, created a consensus document about a decade ago for classification of the vestibular symptoms. And it's interesting because it separates the categories into something we call internal vertigo, which is a sensation of movement of oneself, not of the environment, that can be spontaneous or triggered.

0:28:25.6 Dr. Habib Rizk: Second category is dizziness, which we define as a sense of spatial disorientation. So if somebody tells you they're lightheaded, it's important to differentiate lightheadedness pre-syncope from lightheadedness spatial disorientation. Vestibular visual symptoms that contains the external vertigo component of BPPV and neuronitis, it contains oscillopsia. And oscillopsia can happen when you're moving your head, and that is usually in line with a vestibular weakness in both ears. Or it can happen without moving your head. And that usually, when a patient is telling me that that's what they have, I start thinking, even before examining them, that they may have a downbeat nystagmus or an upbeat nystagmus or something going on that is pervasive and continuous. They can also have what we call a visual lag. You move your head to the left, your eyes don't follow. That's another symptom of a breakdown of the vestibulo-ocular reflex, the VOR, which we showed the head impulse test for. So if a patient has a tumor in their left ear on the vestibular nerve, a vestibular schwannoma, they probably will have on the exam a positive head impulse test. And sometimes they may have a visual lag if they're experiencing a hypofunction on that side.

0:29:46.7 Dr. Habib Rizk: A visual tilt is another type of vestibular visual symptom, and it's rarely related to an inner ear process. Usually, it's something we see in migraine. And one of the structures of the ear we talked about are the utricle and saccule and are responsible for our sense of translational movement. They are also responsible for our perception of gravity and usually any disruption to the utricle and saccule or to their pathway connecting them to the brainstem and higher centers in the brain can lead to a visual tilt sensation. And migraine is one of those pathologies that selectively affects the pathways of the utricle and saccule. And movement-induced blur, that can be many things. It can be a significant downbeat nystagmus related to a cerebellar pathology. It can be a vestibular hypofunction. Because of the visual lag, they start getting blurry vision when they move, and they cannot have a good dynamic visual acuity, visual acuity when they're moving.

0:30:43.3 Dr. Habib Rizk: And the fourth category of symptoms is postural symptoms. That includes unsteadiness, near falls, falls, and what we call directional pulsion, or another word for it is drop attacks. This is an example of oscillopsia. Obviously, it's like you have a GoPro on your forehead and you're running down the street. It's kind of you have a movement-induced blur. It occurs with head movements when it's related to inner ear pathology. But if it's happening without inner ear pathology, without head movement, it means it's usually a sign of a downbeat nystagmus. So now that we reviewed how the symptoms can be categorized, and I've talked briefly about how vestibular neuronitis, for example, and BPPV can cause external vertigo, there are other pathologies that can present with multiple types of those symptoms throughout the natural history of the disorder. One of them is Meniere's disease. And we will do another lecture on Meniere's disease. It requires significant time on its own.

0:31:43.3 Dr. Habib Rizk: But to be simplistic about it, in Meniere's disease, there's a significant changes of pressure within the inner ear fluid. The endolymphatic fluid regulation of the pressures is not adequate anymore, and that can lead to clinical symptoms. And in the early phases of the disease, we have hearing loss, and we have external-type vertigo symptoms. But in late stages of the disease, we can develop directional pulsion and drop attacks. So drop attacks in Meniere's disease are called Tumarkin crisis, and they're related to sudden shifts of pressure across the utricle and saccule. As I said earlier, the semicircular ducts are responsible for rotational perception, whereas the utricle and saccule are more responsible for translational movement perception. And the same way the semicircular ducts are paired with the oculomotor muscles, the utricle and saccule are paired through the vestibular spinal reflex with the truncal extensors, with the extensors of the trunk.

0:32:46.4 Dr. Habib Rizk: And when you have a sudden shift of pressure and function across the utricular pathway, you may have a sudden inhibition of the truncal extensors, which can lead to a fall. Now, other than in Meniere's disease, which is very difficult to, thankfully, to witness those drop attacks, I mean, they're pretty dramatic. Patients don't lose consciousness, but they fall to the ground in a second. And typically, I've never had a patient get really hurt. Sometimes they've had bruises, but it's not like they get into a car accident or... They usually fall in the shower, or against the wall, or talking to somebody. They can fall, basically. That's the summary of it. But it can also happen when you're doing a canalith repositioning maneuver for BPPV. So a patient has gone in this video through a benign paroxysmal positional vertigo repositioning through an Epley maneuver. And as they sat the patient up, those otoliths and crystals fell back into the vestibule and hit basically the utricle, which is the purpose of the repositioning, bring them back into the utricle. But if they fall pretty dramatically inside the vestibule, they can lead to sudden changes of pressure across the utricular macula. And in this case, you see that patient developing a significant, a drop attack.

0:34:11.2 Dr. Habib Rizk: Another example of a drop attack, I'm going to show it on this hyperlink. It was published on the JAMA Neurology website, and it was obtained on a surveillance camera of a store. This is what a drop attack can look like in real time for those Meniere's patients. Drop attacks remind us that the inner ear is related to our function in a gravity environment. But what happens when we don't have gravity around us? The fact that we're upright and we have truncal extensors is due to the fact that we live in an environment where there is gravitational force. And the vestibular system and the nervous system connected to it had to adjust to that. Caloric experiments were some of the earliest scientific experiments done in deep space. And in microgravity, the caloric response is not as prevalent or as present as what we see in clinic. And that's because the fact that in microgravity, we don't have convection currents, which require density change due to temperature change of the fluids. There's only a thermal effect that is extremely mild and weak.

0:35:30.0 Dr. Habib Rizk: Most of our function in deep space, in microgravity, is related to the otolith organs, the utricle and the saccule that sense gravity, as we discussed. I want you to listen to this astronaut describing their first spacewalk. "The way I get about 15 meters away from the space station, space station itself starts looking like a little tinker toy over there, getting too far, feeling detached from it, not feeling part of it. And just as if you were flying in an airplane and someone said, 'Get out on the wing,' versus being inside that cabin, all of a sudden, when I hit a spot I called no man's land, I felt totally detached. I didn't feel part of that space station anymore. I also felt like I was falling. Felt similar to free-fall parachuting, only going maybe 100 times faster." This astronaut, who happens also to be a physician, is describing symptoms of what happens when we have a significant stimulation of the otolithic organs of the utricle and saccule. He's basically describing a drop attack in space. But other two elements to listen to is the use of the word detached.

0:36:40.7 Dr. Habib Rizk: A lot of our vestibular patients who present with affliction of the otolithic pathways, the utricle and the saccule, whether it's peripheral or central, coming from a migraine pathology, use the word, "I feel like I'm floating. I feel like I'm detached." They're not crazy or anxious. Their symptoms are related to the fact that the vestibular system anchors us in our environment. And in the absence of good input from the vestibular system, we have a spatial disorientation of where our body is in space. The other important element is that his symptoms in microgravity started only when he was no longer able to visually fixate on the space station, which tells you how many redundant mechanisms there are to help us overcome some of those disturbances and pathologies and why, by the time you have symptoms, that means you've reached a tipping point where those compensation strategies are not helping. So the vestibulo-ocular reflex does not function in microgravity the same way that it would function on Earth. And we see that. We see a lot of changes in the velocity storage mechanism that we discussed. There's also changes because of the density changes. There's changes in how the cupula and the shearing mechanisms I showed earlier would function.

0:38:04.5 Dr. Habib Rizk: Astronauts, when they come back from space into Earth, they have oscillopsia because their system is not functioning back to the normal level. In weightlessness, the utricle and saccule no longer provide meaningful information regarding where the head is oriented in regard to the body. They only act like accelerometers and only detect linear acceleration. That's why he had that sensation of free fall. So when astronauts return home, they experience some aftereffects from this disruption. They have difficulty walking around corners. And interestingly, neuronitis can cause similar symptoms in the early phases. Vestibular migraine, which is a migraine variant that creates, is one of the most frequent causes of episodic vertigo as well, can cause similar symptoms. And we get back to that sensation of the head being detached from their body. When a patient is saying that, listen to them. They are definitely anxious. This is a very anxiety-provoking condition, but there is an actual anatomical and physiological explanation to that symptom.

0:39:12.9 Dr. Habib Rizk: On top of that, we know that in space, proprioception fails because there's no static muscle tension and the vestibular spinal reflex is reduced. So basically, all of those information that we got from astronauts, from experiments in microgravity, shed a light of what happens when you have a disruption of the vestibular system in our normal everyday environment. And I sometimes like to say that those experiments in weightlessness or vestibular migraine patients are basically our model of what would happen to our system if we were in microgravity environments for a long period of time, because a lot of the symptoms can join, can be common to them. And now I want to move on a little bit to talk about the central vestibular system. So when we talk about vestibular system in all of our psyche, we always think about the inner ear. But the reality is more complex than that. The inner ear is a portion of the vestibular system. It's the sensor, the gateway, it's the peripheral vestibular system. But the vestibular system is a pleiotropic mediator that is widespread across a vast network of neural connections.

0:40:25.1 Dr. Habib Rizk: And it receives communication from multiple aspects: from the cerebellum, from the cortex, from the thalamus, from the opposite side of the inner ear, from the spine, from the oculomotor nuclei. And that creates for a complex pathological presentation. And like I said, there are so many redundancies that patients basically can mask symptoms until there has been significant disruption to that network. The cerebellum is at the heart of the central vestibular system. It plays a major role in motor coordination, and the middle part of the cerebellum, the flocculus, nodulus, vermis, coordinates movements of head and eyes and regulates the vestibular system. So a lot of patients can have a cerebellar pathology, can have dizziness related to a cerebellar pathology, or ataxia related to a cerebellar pathology without having the normal findings of the cerebellar signs on exam: no dysmetria, intention tremor, or dysdiadochokinesia. They can have just a problem in the vermis, and they present only with imbalance. That's more common in our clinic, and those are patients who can sometimes be mistakenly diagnosed as having Meniere's disease or BPPV because they have motion-induced vertigo, but the problem is elsewhere.

0:41:48.5 Dr. Habib Rizk: And what is fascinating about the central vestibular system is that there's so much complexity coded in those pathways as they travel from the inner ear up to the cortex, to a point where we recognize that there are specific, specialized collection of cells that can map the border of the environment we find ourselves in, that can determine the place of our head and of our body and the relationship of the head and the body in relation to an object in our environment. They can detect body motion related to where the inner ear is located. And all of those specialized functions can be disrupted and create a host of symptoms that are sometimes difficult to simplify into that model where I said we need to categorize into four categories, and patients present with various phenotypes, if I may say. But what we need to know is the central vestibular system and the connections can be parsed out into what I have on this slide. The thalamus and the cortex are responsible for sensing and perceiving the head movement. The vestibular spinal pathways, which are usually mostly connected through the utricle and saccule, send motor commands to the muscles of the neck, upper torso, and lower limbs to maintain balance.

0:43:14.8 Dr. Habib Rizk: And there's cortical efferents and cerebellar efferents that can modulate it, and this is related to drop attacks. And then finally, the vestibular ocular pathways, which are the connections between the semicircular ducts and the oculomotor muscle, is responsible for the vestibular ocular reflex. A deficiency of the vestibular ocular reflex is responsible for most of the symptoms we see in peripheral vestibular disorders, whether it's the external vertigo, the visual lag, the movement-induced blurriness, and so on and so forth. So two questions always come to mind. If somebody has had a damage to the end organ in the inner ear, can they recover from it? This is a case of vestibular neuronitis. This patient happens to be myself without having prior medical problems. I started feeling like I was spinning when I would lay on my left side one day after clinic. And this would get better when I laid flat. And for that night, I thought I was having BPPV. I would lay to one side, get dizzy, turn around, I wasn't dizzy.

0:44:21.4 Dr. Habib Rizk: A couple of days later, I developed a constant vertigo even when I was looking straight ahead. An examination during that time shows that I had a left-beating nystagmus that was horizontal, beating to the left in all directions of gaze, which is in line with a disruption of the vestibular system on the right side. So the right side being weaker than the left side, I have a left beating nystagmus, or that there is something irritating the left ear, like a vestibular schwannoma, for example, or the first attack of Meniere's disease or vestibular migraine. But more than likely, when you have somebody presenting with a spontaneous direction-fixed nystagmus, they are more likely to be having a weakness on the side opposite to where the nystagmus is beating to. And in unilateral vestibular lesion, neuronitis, or a tumor, the spontaneous nystagmus has a fast phase beating toward the healthy ear, so away from the damaged ear. And the slow phase is greater when the gaze is directed toward the healthy ear.

0:45:35.4 Dr. Habib Rizk: So if you want to elicit a nystagmus, you see a left-beating nystagmus in center gaze, and you suspect this is a neuronitis, that nystagmus is going to be much stronger when the patient is looking toward the left, toward the healthy ear, because it creates a further imbalance between the two sides. We did what we call a video head impulse test early on, which is the equivalent of the bedside head impulse test, where we were looking for a correction of the eye movements to stay on target. And to interpret that graph, the blue is the left, and the red is the right. And we have the head movement on the right side, which is that sinusoidal curve. And in a subject who has absolutely no weakness, you will have an eye movement which shows an opposite sinusoidal curve that is a mirror image of the head movement. Obviously, on the left side, you can see they are mirror images of each other. On the right side, you start seeing a breakdown of that curve with those, what we call, overt and covert saccades, where the eye is trying to correct itself into the right position.

0:46:40.8 Dr. Habib Rizk: And that gain down there is down to 77% on the right, 95% on the left. And that was on day one of symptoms. As the vertigo started subsiding, the subject started noting falls to the right side. And when he turned his head to the right or when he tried to do this movement of the head for the ear to touch the shoulder, relying on perception of neck position, he felt like a drop. And those are patients sometimes who are going to come and tell you, "I feel like I'm falling, but I know I'm not." And that's related to a disruption of the vestibulospinal reflex. And that was a few days later. There was a disruption of the function down to 23%. And you can see on the right side, there's almost no recognizable curve. Everything is, the brain is not recognizing the head movement, and the eyes are basically all over the place. As the recovery process started, the spinning vertigo stopped. Balance started to be the main issue. And you can see already on testing that there is a beginning of a recovery where those saccades are starting to bundle up, bunch up together, because the brain is starting to recognize a pattern and trying to predict where the eyes need to fall.

0:47:55.4 Dr. Habib Rizk: There are setbacks during those recoveries, and your patients will have setbacks during recovery. In this specific case, it was a jet lag. Sleep disturbances can create significant setbacks in the recovery from vestibular injury. So if we look at the timeline from day four of symptoms to month eight, eventually, toward the end at month eight, there's barely any recognizable injury. The curves are back to being mirror images. There's those spikes that tell us something happened. But most patients we see present like that at that level. And short of a good history to collect the symptoms, we may not be able to always determine why do they have those spikes, which are corrective saccades of the eye movement, telling us that the vestibular ocular reflex is not working 100%. What is interesting in the recovery process is patients who have bilateral vestibular hypofunction who lost it suddenly because of toxicity due to aminoglycosides or, in the old days, tuberculosis medication, or in chemotherapy, which is much more rare but still can happen. If they have a concomitant loss of both sides, it's very difficult to recover from it. Those are patients who have oscillopsia. They are absolutely miserable.

0:49:14.9 Dr. Habib Rizk: However, there's a phenomenon called the Bechterew phenomenon. If you have a sequential loss of one side and then the other, interestingly, the recovery is much better. And those were experiments done on squirrel monkeys where a labyrinthectomy was performed on one side, and the animal was given enough time to compensate and recover like we do from a labyrinthectomy or a neuronitis. And then a couple of months later, an opposite side labyrinthectomy was performed. And you would think that this patient doesn't have any more labyrinth on either side. And yet they developed a nystagmus when they destroyed their second inner ear, similar to what you would have if you had a neuronitis on that side. And that's because of the absolute powerful compensation strategies that occur at the level of the vestibular nuclei. And that's a phenomenon called the Bechterew phenomenon. And I encourage whoever is interested to look up this article from the New England Journal of Medicine. This is written by a doctor who was also a patient and who developed bilateral vestibular hypofunction following streptomycin for tuberculosis. It was in the 1950s. And this gentleman describes the slow descent to hell with the symptoms being as acute as they are, as they were, and then the recovery process that happens.

0:50:46.6 Dr. Habib Rizk: We encourage our patients to go through physical therapy because no matter how bad the injury, there are so many redundant mechanisms that can help alternate systems, as this author names it, that will help us accomplish a better balance function. And even though he was still disabled, he was able to develop, use the vision, use the proprioception as compensatory strategies that were able to give him some quality of life back. The second question that comes to mind, do we have vestibular implants? Kind of like cochlear implants for profound sensorineural hearing loss. Are there vestibular implants available to recover the function? There's a lot of clinical trials happening, three major centers, one in Seattle, one Johns Hopkins, and one in Maastricht in Europe, that are looking into that. There's a few patients who have been implanted across those centers with promising results. The problem is we still haven't figured out how to preserve hearing while restoring the balance function with those implants because of the nature of the position of the semicircular duct in relation to the cochlea.

0:51:56.4 Dr. Habib Rizk: And that's the purpose of a current clinical trial happening at Johns Hopkins, where they're trying to figure out how much hearing we can preserve when we're doing those vestibular implants. So they're not ready for prime time yet, but they might be a tool in the future to recover some function back. The second question that comes to mind is, can peripheral vestibular end organ pathology affect higher cortical functions? A lot of patients with dizziness, especially chronic dizziness, they describe brain fog, they describe that floating sensation. They have difficulty concentrating. And some of them, it's due because of the comorbid depression and anxiety that can come with any chronic disorder. But is there actually a link between the vestibular system and cognition? A lot of our findings related to that go to aging literature. And we know that there's marked age-related degeneration in nearly every type of hair cells in the vestibular system that starts after the age of 65. The saccule seems to be the most affected, as well as the utricle. These are the first elements of degeneration that can occur.

0:53:12.7 Dr. Habib Rizk: Age-related decline leads to an inability to correctly detect head position and motion in space, and that can lead to increased falls. Early studies did not show direct correlation between histology and degeneration of the hair cells and abnormalities on paraclinical testing in the early vestibular testing tools. But now we have a little bit more modern tools to detect the vestibular function. We have some more evidence that comes with tests called vestibular evoked myogenic potential, which tests for the utricular and saccular function, the video head impulse test showing higher prevalence of abnormalities with age. And as I said multiple times throughout the talk, central compensation occurs until a tipping point is reached. So once a patient presents to you with significant balance and you're suspicious of a vestibular dysfunction, the likelihood is that they've kind of passed the point of no return. And this is where vestibular therapy can help because it can boost central compensation again.

0:54:22.6 Dr. Habib Rizk: Epidemiologically, we know that there's an increase of the prevalence of dizziness from 22% in the sixth decade of life to over 40% in adults over the age of 80. And about two-thirds of adults over 60 experience dizziness and loss of balance on a daily basis. And about 20% of imbalance and half of dizziness complaints is due to a vestibular problem. And the breakdown of the pathology is about 20% to 50% of patients have a peripheral disorder. So a substantial amount of patients have a vestibular disorder, and the rest have a multitude of things, including cardiovascular disease, or systemic infection, or polypharmacy. The lifetime prevalence of vertigo due to a vestibular disorder is around 8%, with the one-year prevalence of vertigo being around 5%, much higher in the patients over the age of 80. If we look at a general population level, the incidence of vertigo is about 1.5%. A third of adults over the age of 40 in the US have evidence of balance dysfunction, and 85% of individuals over the age of 80 have evidence of balance dysfunction.

0:55:25.2 Dr. Habib Rizk: In addition to the physical consequences of those disorders, dizziness is a major cause of absenteeism and partial or full disability and an increase in healthcare utilization. A few years ago, the Bárány Society published criteria for something we call presbyvestibulopathy, which is age-related vestibular disorder. And those are patients who have to be over the age of 60 and present with a chronic vestibular syndrome lasting at least for three months with postural imbalance or unsteadiness, gait disturbance, chronic dizziness, and recurrent falls with a mild hypofunction, mild weakness of the peripheral vestibular system documented by some of our paraclinical testing. And most easily is the video head impulse test that shows a gain between 60% and 80% on both sides. And presbyvestibulopathy is at the intersection of a disruption of this vestibulospinal reflex and the vestibulo-ocular reflex. And as we know, a lot of patients in that group, in that age, also have neuropathy or other reasons to have weaknesses like arthritis.

0:56:53.1 Dr. Habib Rizk: So it's a compounding effect and dramatically increases the chances of a fall and injury. And why is that important? It's because nowadays, children born now, their longevity is expected to be above the age of 100. And as we said, our system seems to be holding up up until the age of 80. Until we're 80 and above, we start having a marked degeneration. And chances are that as our population ages, we're going to be dealing, and treating, and recognizing more patients with vestibular disorders. So with all of this, what is the link with cognition? A lot of older studies showed that perilymphatic fistula, which is one of the peripheral vestibular disorders, extremely rare, can lead to memory impairment. And patients who have had gentamicin toxicity to the ear developed concentration difficulties. Patients with neurofibromatosis type 2 who develop tumors on the vestibular nerve bilaterally at a young age, and they used to be treated, and sometimes have to be treated with bilateral vestibular nerve section to take the tumors out, seem to have a reduction in spatial memory and spatial navigation as well as reduced hippocampal volumes, which are known to be associated with disorders like Alzheimer's.

0:58:11.3 Dr. Habib Rizk: A lot of studies looking at aging confirmed that there's a relationship between reduced vestibular function and scoring on multiple neurocognitive tests. Imaging studies showed that Meniere's disease can be associated with hippocampal atrophy. And about 20% of patients in other studies, 20% of patients presenting with vertigo have reproducible and significant cognitive error in arithmetic abilities, short-term memory, and performance in specific visual environments. And the arithmetic ability is kind of a, scientifically, in order to be able to do good math and order numbers, you have to have a good spatial cognition. And it's kind of an interesting study to look at performance in math and vestibular pathologies. And one of our colleagues in Nebraska at Boystown is doing a study looking at learning disabilities in children with vestibular disorders and/or cochlear implants. So there is something there and the science is still young in it, and we're still discovering every day interesting stuff about it.

0:59:22.6 Dr. Habib Rizk: Alzheimer's disease patients are twice as likely to have vestibular impairment compared to healthy control. And Alzheimer's disease patients with vestibular impairment have disproportionate reduction in spatial cognition compared to Alzheimer's disease patients without vestibular loss. So there's a possibility that vestibular disorders can lead to a specific subtype of Alzheimer's patients who are wanderers and who tend to get lost more often than those who don't have a vestibular loss. Which brings us back to that slide that I showed earlier about how many specialized functions and cells there is along that pathway that goes from the sensory organ in the inner ear up to the cortex. And this wide dissemination of the vestibular signal could have been an evolutionary process to create a neural network with sparse coding, which allows us to reduce energy cost, and allow us to have a large storage capacity, and can be tolerant to degradation until you reach a tipping point or a point of no return.

1:00:23.6 Dr. Habib Rizk: And usually we are taught in medical school and in residency to think in terms of peripheral vestibular disorders versus central peripheral disorders based on anatomical lesions. But we know, and I hope I showed in this talk, how much overlap there is in clinical presentations, no matter where the disorder ends up affecting, the inner ear or the pathway to the brain. And in a different lecture, I will talk about evaluation of the dizzy patient to kind of go over the clinical tools we use in everyday clinic to get some answers to this. But it's important to understand that there is an overlap. And while nystagmus is a marker of a disruption of the vestibulo-ocular reflex, that disruption is not always meaning that the inner ear is the cause. And really good sleuthing, collecting of symptoms, and a careful clinical exam oftentimes, if not always, will lead us to the diagnosis. And this is a laundry list of certain things that we think now are variants of vestibular disorders.

1:01:31.0 Dr. Habib Rizk: For example, at the level of the cerebellum, a downbeat nystagmus, episodic ataxia type 2 that responds to acetazolamide, upbeat nystagmus are types of vestibular disorders coming from the cerebellum. At the level of the brainstem, you have sometimes drop attacks, room tilt illusion, or vestibular migraine. At the level of the cortex, we have spatial hemineglect, and spatial memory deficits can be associated to some extent. And if we're thinking about the vestibular system as this widespread network of connections, that could be a type of vestibular disorders.

1:02:11.2 Dr. Habib Rizk: So I want to stop here about this topic. I went over the anatomy and physiology of the main functions of the vestibular system, and hopefully, that can help start, when you encounter a patient with dizziness, you can start thinking along the lines that we've described in this talk. Other talks that are more indepth for each topic are necessary, and we will be presenting them sequentially, and we welcome any feedback or any questions regarding that. We have a, Vestibular Disorders Association has a registry. We encourage our patients to go fill it. Even though these are frequent disorders, we have a lot of times not enough data to understand the natural history of those disorders, and we're working on that. There's multitudes of studies that are present in many locations that we encourage patients to participate in.

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