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LAWTON SNYDER: Welcome, and thank you for joining us for the sight-and-sound bites webinar series brought to you by the Eye & Ear Foundation. This series began actually in April of 2020. And we are going to keep it going even as things are starting to open up again, which we're all happy about. But this series highlights the research at the University of Pittsburgh School of Medicine. Today's topic is innovative treatments for nasal obstruction and chronic rhinosinusitis.

I'm Lawton Snyder, the CEO of the Eye & Ear Foundation. The Eye & Ear Foundation supports research to advance care or vision, hearing balance, voice, and cancers of the head and neck at the two world renowned departments of Ophthalmology and Otolaryngology at the University of Pittsburgh.

The funds we provide from Eye & Ear Foundation support goes to research. And it's only made possible because of the philanthropic support that we get from our donors. I'm going to thank everybody who's supported the Eye & Ear Foundation who's on today's call and certainly welcome anybody who'd like to know how they can support programs like you're going to hear about today.

Just some housekeeping rules. This Zoom webinar-- we do not use chat. So you may recognize chat on here. But we disable it.

But we do ask you to type in questions throughout the program through your Q&A app down at the bottom. The little bubble on the bottom, it says Q&A. When you type your questions in, I'll read those at the end of the program. Please refrain from asking very general, very specific questions about your own personal health that the rest of the audience wouldn't be interested in.

You'll receive a survey tomorrow about today's webinar. And we appreciate you responding to that and giving us that information. It's helped us find topics even like today's. And then you'll be added to our mailing list for future webinars as we move forward.

So to introduce today's speaker into this program, I'm going to bring on Dr. Jonas Johnson, our Chairman of Distinguished Service Professor and Chairman of the Department of Otolaryngology and the Eugene and Myers Chair at the University of Pittsburgh School of Medicine.

JONAS JOHNSON: Oh, thank you, Lawton. And good afternoon, everyone. Welcome to our program.

So I'm delighted today to introduce Dr. Eric Wang, who is a vise chair for clinical operations in our department. Eric is a rhinologist, which means that he specializes in taking care of people who have problems in their nose.

Today's topic is a terribly prevalent and important topic, and that is nasal obstruction and chronic rhinosinusitis. And Eric will share with us some new and innovative treatments that are helping people who previously have not been helped. So with that we're going to turn it over to Dr. Wang.

ERIC WANG: Thank you, Jonas. And thank you all for taking your time to come to this webinar today. This is a beautiful picture of our beautiful hometown.

And I want to just take a few moments to thank all of the people who contribute to this. It's not solely just the physician team. But we have a wonderful staff of nurses, physicians assistants, many of my partners who all participate in the treatment and care of this scenario here.

So one of the first things that we're going to talk about is how chronic rhinitis and rhinosinusitis are actually difficult things to diagnose. The concept if you have sinusitis is very prevalent, but actually probably not quite as accurately diagnosed as we want. So the four cardinal symptoms of these diseases are nasal obstruction, or the difficulty breathing out of the nose, nasal drainage, a decrease in your sense of smell or olfaction. And then some people have some facial pressure.

So even though these are our four cardinal symptoms, there's a really interesting study that actually showed even if you have all four of these symptoms, about 30% of people will still not have any findings on their CAT scan. So the symptoms and the objective measures of disease vary a lot. So just because people have the symptoms, sometimes it's very difficult for us to differentiate what is the underlying driving process because all of these things, like this Venn diagram from our grade school time, overlap a lot.

So oftentimes, then we have to start getting diagnostic scans. And this is a CAT scan of the sinuses. And on the top, you actually see someone with very significant polyps.

And on the bottom, you can see that the sinuses, which are underneath the eyeball, point out these big black spaces, or your maxillary or cheek sinuses right here. Underneath the eye sockets are perfectly black. And that actually demonstrates really good sinus health.

While in the picture above, you see all of this gray stuff. All this gray stuff represents soft tissue, which means very little to no air is going through. And yet both of these two patients of mine had very, very similar symptoms.

So that's one of the challenges that we face. And diagnostically, we really need to differentiate them once we get past our initial therapy. So first line therapy at least conveniently for both of these two diseases start with something like a topical nasal steroid, which is pictured in that green bottle onto the left, the most common of which is this thing called Flonase or fluticasone. This is now over-the-counter because it has a really wonderful safety profile.

It was actually designed very much in the 1980s. And what it does is it gives a very small amount of corticosteroid to the nasal lining. But that small amount actually doesn't get absorbed enough. So that you can actually measure any bloodstream effects.

And this is probably the biggest advent in the treatment of inflammatory diseases of the nose. And it was very, very popular. It had huge advertisements throughout the '90s and the early 2000s. And that profited to a whole variety of different kinds, like Nasonex, Rhinocort, Nasalcort. There's a lot of different brands now. But they all deliver the same thing, this idea of a very small dose, which builds up in your nasal lining, which reduces that inflammation to hopefully open up the nose, reduce the drainage, and make people feel better.

The other thing that has been very popular is saline sprays. So a sinus rinse actually has this historic story of people in India using the Ganges River water to flush out their nose. And it was believed to be very medicinal and therapeutic. And it was very specific to that river water.

But actually, over time, we've found that there's probably a mechanical property to it. And that by cleaning out the nose and washing out the nose will probably get rid of some of the irritants that bother us. We get rid of some of the inflammatory stuff that our nose makes itself, including mucus and some of these inflammatory products of chronic inflammation.

And in some ways, it probably just makes people feel better because it mechanically gets rid of some stuff. So first line therapy, which has actually a very high level of evidence for both chronic rhinitis, which is defined within the nasal cavity alone, and chronic rhinosinusitis, which involves the nasal cavity as well as the paranasal sinuses are actually very similar. But once we get past these first line therapies and people don't get significant improvement, then we really have to differentiate that.

And first, we're going to try to look at chronic or allergic rhinitis, which the term rhinitis essentially means inflammation of the nasal cavity. But when people come in with obstruction or difficulty breathing out of their nose, more often than not, they actually have two components to their difficulty breathing. They have that inflammatory component, which initially we very much try to treat with the medical interventions, like the Flonase or fluticasone.

But often people also have a structural impedance to their airflow, the structural anatomy of their nose, whether they have a wide nose or a narrow nose. And predominantly, the most important structure tends to be your septum, which is as midline wall of your nose. All of us have known someone who likely had a deviated septum, or you may have it yourself. And that can change the airflow from one side to the other side. So understanding and piecing out how much of the obstruction in the nose is a derivative of inflammation versus how much is dependent upon the structural aspect is actually a key component of our evaluation.

OK, so when we talk about the anatomical structures in addition to the septum, we also have this area called your nasal valve, which I'm going to show you a little bit some more pictures about that as well. And then beyond the actual static portion, we know our nose is a dynamic thing as well. So the dynamic thing is this external portion. So the cartilage of the external nose can actually collapse.

And I want to show you a few pictures of that. And as you can imagine, as you breathe deeply in, that collapse can narrow that airway and actually still make it difficult for you to breathe even with a correction of some of the other anatomical problems. And the inflammatory components, we definitely think of allergic as the most common. But there are people who also have these other chronic rhinitis whether it be irritants.

So all of us if we walk into a sawmill will have an irritant rhinitis because we're not allergic to that sawdust. But those little particles in there really irritate our nose. There's a process called vasomotor rhinitis, which I'm going to speak about a little bit more.

There can actually be medication-related rhinosinusitis and then sinusitis, which is how we're going to close our talk. OK, so this is a picture of an anatomical structural abnormality where this is the right nasal cavity. And what you see taking up the majority of screen left is actually the inferior turbinate.

And this nasal septum, which is supposed to be a structure that is straight down the middle, actually comes out into the nasal airway. And this septal deviation inhibits the breathing pathway. This is an example of inflammation where the septum is actually fine. It's actually in the middle.

But these side structures of your nose, called your turbinates, have swollen in response to these irritants, whether they be allergic or whatnot. And the inferior turbinate now takes up most of the nasal airway. So these are the two components that we can look at here.

All right, so after we get past the topical nasal steroid and we get some saline sprays going, our American Academy of Otolaryngology has a clinical practice guideline, which many of us and our department follow, which helps us, based upon the evidence, has been vetted not only with physicians but also with stakeholders, including patients who have these symptoms and patient advocacy groups. So first line therapy is a topical nasal steroid. Second line therapy is actually a pill, an antihistamine pill.

So the classic is Claritin, Zyrtec, Allegra. These are supposed to be non-sedating oral antihistamines or second generation antihistamines. Unfortunately, Zyrtec has lost its non-sedating description because of continued reports in the first 10 years after its practice. So it can no longer claim that it's non-drowsy. But it is very effective for some people.

So once you get past those first two lines of therapy, the third choices are actually all considered fairly equal by our academy. One third line therapy is actually using an antihistamine spray. That's pictured in the upper right hand corner.

It's generic name is Azelastine. Its proprietary name is Asselin. And this basically tastes a similar type of medication as Claritin, Benadryl, Zyrtec. And it puts them in a nasal spray form.

And for some people, it's a really fantastic medical therapy that really changes their quality of life. Unfortunately, it doesn't work in a large group of people. So it tends to be one of those things where and the people who get efficacy, they get a lot of efficacy. And those who have a little bit less unfortunately don't get much bang for their buck.

The other medical therapy is the idea of immunotherapy. So this has been around for a long time. And this is the idea of building tolerance to your allergies.

And basically what happens is we give a very small dose of the things that you're allergic to. And that dose increases and increases and increases with the idea that your body builds tolerance or can tolerate now these new things that, or this allergen that is bothering them. This is an effective therapy, not 100% unfortunately.

But it is also very costly from a time standpoint. Typically, it takes six months to a year to ramp you up to your appropriate dose where you get some symptomatic relief. And most people believe you need to keep it going about two to three years. So it's a long term strategy for managing that.

OK, so what do we do about the structural things? Well, so here is a preoperative image of a patient of mine. You can see how this septum fills up the airway. This is the right nasal cavity again.

This structure we're looking at the top is our middle turbinate. And we can see all the way back that sort of arch in the back is our airway that goes down to our throat and then to our lungs. But you can see how the septum fills up that space.

So a very simple and common surgery called a septoplasty, we can remove that cartilage in the bone that is deviating out into the airway and impeding the airway. And here you can actually see what it looks like after surgery. You can see it with a straight shot.

You can go straight down. You can-- this is a fairly large instrument called [INAUDIBLE] elevator that shows you that you have a new open airway. And even those 3 to 4 millimeters of space is a tremendous difference for people from their breathing.

So this is probably the most common airway surgery we do. I also still do rhinoplasty when it's indicated. But most people actually can get away with the septoplasty just fine. And they can have a really significant improvement in the anatomical aspect of that nasal obstruction.

So what happens? So the other option is we can actually reduce a turbinate as well. So this is that inferior turbinate.

So this is interfering with both the anatomic and the structural. So you can see that the inferior turbinate is what actually takes up the airway, the thing onto the side. This is on the left side.

And we can actually make this terminate smaller by removing the glands underneath this lining while keeping the bone intact. OK, so both of those things can help from a structural and to some degree an inflammatory response from the inferior turbinate hypertrophy.

So how do we measure this? Well, here at UPMC, we use this thing called the NOSE scale. It's very cleverly named. The Nasal Obstruction Symptom Evaluation.

You'll see that rhinologists really like these quirky acronyms a lot. So this is the NOSE scale where we ask patients to measure how they are preoperatively on a one through four scale. And then we can measure them post-operatively. And it assesses how we do.

And you're going to see that this NOSE scale is going to be used in a lot of these innovative therapies that we have moving forward. OK, and this is something we use here in our practice as well. OK, so what happens when you have a great airway and you've done what you can to fix your septum?

You've done what you can to reduce your turbinates. You've put them on great medical therapy. Well, what else do we have?

Well, to be honest with you, in the last 20 years, really not very much. It actually was pretty limited what was occurring between the 2000s to the 2020s at least as far as patients was concerned. But over the last 10 years, there actually have been a lot of research into the nasal cavity into the paranasal sinuses with some innovative technologies moving forward, which are now actually available to our patients.

OK, so I told you that I mentioned some other structural abnormalities associated with nasal airway obstruction. And this is one way we measure this area called the nasal valve. So the nasal valve is this small, or it's a triangular-shaped structure.

So if this was a patient's left nostril, it would be this upper corner right up here in the valve area. And we measure it using two maneuvers that, one, you can do very easily by yourself called the cottle maneuver where you actually just take the soft tissues of the cheek and gently pull them out as if opening up that narrow valve area. In our office, we tend to use something called a modified cottle where we generally put a small ear instrument and gently lift that sidewall out to see if that helps improve patient's nasal breathing.

And it's amazing how that small difference in your nasal valve can actually make a big difference in your breathing. The other way to measure it is actually you can just put some gentle pressure on one side of your nose right in that corner pocket between the lower and the upper cartilage. And you can feel how narrow that breathing is when you put that pressure in there.

And that's what some people live through all the time. And so traditionally, we had to deal with this with a rhinoplasty. And in a similar way, this external nasal valve collapsed. So this is one of my patients.

So you can see in his resting state, which is actually on your screen right, that the breathing-- this is how his airway looks. So you wouldn't think that he would have any airway problems. But when he takes a deep breath in, you can see how the left nasal, basically the left nostril collapses in on itself.

So this external or dynamic collapse can be another source. So even if you don't have a fixed nasal valve narrowing, you can have a dynamic nasal valve narrowing because the cartilage on the sidewall is too soft. So both of these problems, again, have traditionally been managed with a rhinoplasty.

Recently, this was some work actually that came pretty much from Northwestern University. But they started looking at could we use an implant into that sidewall to thicken it up, to give it some increased strength? And so the development of this particular device, which is an absorbable sidewall implant commercially known as the Latera, has now been commercially available for the last two to three years after about five or six years of research.

This uses a trocar system. So a needle system, which you can see depicted here in the bottom corner to gently implant this implant, which is shown here in the upper right hand corner, in between the skin and the cartilage. So you make a small nick incision into the nostril. So not too much external.

And then you gently pass this trocar up above the cartilage and then below the skin. And this now releases this implant, which is made out of a material that we have used in suture for a very, very long time. That's commercially known as vicryl. But it's a PGLA, which is another device that-- or another synthetic we'll talk about a lot because it's an area that people continue to use for biomedical engineering constantly.

And the way this is devised is this little fishbone aspect of it is placed onto the nasal bone to help secure it and hold it more rigid while the rest of the device has some small barbs, which hold it against the cartilage. And this in some people really, really helps prevent that nasal collapse. It can actually be done in the office.

Although, many people also do it in the operating room. And in its studies, you actually see that it really makes a very big difference for lateral wall collapse and in some patients that narrowing of the lateral nasal wall. So this was a study done on this where in the hash mark lines, you can see that most of the patients had extreme or severe nasal obstruction using that nose questionnaire and that the majority of patients actually moved to a mild-or-moderate moderate group.

It's interesting that no one gets completely better. But it is an adjunct that helps some people get significantly better. And you can see that it's fairly durable.

So how does something absorbable have such durability? Well, it's because that as the-- I'm sorry, the durability is shown here in the lower graphic where you can see-- the first week people get the most benefit, the first week to the first month.

As the inflammation settles down, they still get significant improvement of their NOSE score even at two years when the implant has largely absorbed and gone away. So what's interesting is that-- so this is actually from an animal model. So this is not in humans. So they could study it.

But this is the implant of that same device. OK, and one of the properties of this particular material is that as it absorbs, your body creates inflammation around it. And that inflammation actually creates scar, which they call remodeling in these pictures. So they want to make it sound better.

But basically, it forms a scar in this region. So facial plastic surgeons have taken advantages by doing injections in people. And that they know that over time the injection will actually take up more space and actually create scar to give people more youthful appearances.

In the rhinology world, we're taking advantage of this scar to help provide thickness to that wall so that the collapse no longer occurs. So the resorption has a dual fold of number one, getting rid of an implant because people don't really want implants in them. But number two is that resorption actually provides that long lasting durability.

OK, so this is the effectiveness studied in a meta analysis, which shows that overall, it improves quality of life. But unfortunately, 5% of people have a reaction to it. So this is unfortunately one of my patients who had a reaction to it. She had previously undergone a rhinoplasty by another surgeon.

Her septum could be used a little bit of revision work. But she really wanted to try this more minimally invasive device. And unfortunately, you can see in an early picture she has this redness and erythema, which is this skin reaction that happens to it. And unfortunately now, 12 months to 13 months after, she had this little pinpoint hole where the device extruded, part of the device extruded.

So this is really unfortunate and has dampened some enthusiasm. Like all things that we're going to talk about, nothing is a silver bullet. Nothing's perfect.

It definitely can be beneficial in the right hands and at the right time. But there are adverse events that we have to be cognizant about. But this isn't a therapy that we offer here at UPMC.

OK, so moving out of the realm of procedural interventions, there has been new research. And they've asked me to take part in this as well. I'm looking at the idea of using vibration, acoustic vibration, to relieve nasal congestion.

So I'll be honest with you when they first told me about this, I thought they were crazy because I didn't really understand how this could really work. And the idea is that you apply this vibratory signal to the nasal cavity. And you breathe in gently over three minutes.

And the oscillating respiratory vibrations balanced with the breathing in and out through this device, which provides some respiratory resistance, actually helps to open up your nose. So this sounds a little bit crazy, right, that the idea of this positive pressure, so breathing out against something that causes some resistance, which maybe some people could argue all our current masks provide that for us nowadays. But they couple this with a reverberation of an acoustic vibration back into the nasal cavity could have some benefits.

The reason I actually agree to start looking at this with them in preclinical models is because that there are people who actually really benefit from this in chronic lung disease. So using these acoustic vibrations in people with diseases that restrict the lungs usually from long term smoking actually has shown to have some improvement in their nasal airway. No one really understands the exact mechanism whether it increases things like nitric oxide, which are anti-inflammatories and antimicrobials, or its mechanical properties of the vibration.

There does seem to be some benefit. So this is a phase I trial performed at a single institution, not our own. They've asked us to consider participating in the phase II trials for this.

But basically what they showed is if you measure performance peak ability to breathe outward, at five minutes, they have a 15% increase. And if they use it more consistently for a few weeks, they actually have almost a third improvement. And again, that nose score that I mentioned shows a really pretty significant drop.

Although, this manuscript is only out there in peer reviewed now. So it's being evaluated right now. But I'm aware of it because of the individuals involved in the study. So this is something that might have some promise in people who really think surgery is not what they want to have and really might have some benefit there. So that's an exciting thing because it'll be non-operative.

So another procedure that actually takes advantage of something we've had for a long time but has done it with a more technologically advanced mechanism is the use of radial frequency. OK, so this is basically energy transfer. And that energy transfer causes the tissue underneath the surface to remodel or scar similar to the scar we talked about earlier. And that might actually help reduce some turbinates without the need for a surgery itself.

And the clever thing about it is these probes have ability to regulate the temperature in the area, such that the radial frequency gets to the deeper tissues, which we're aiming for, while preserves the mucosal lining of the nasal cavity, which we would love to spare. Now this procedure is solely done in office. And there are no incisions associated with it.

You float the device over the surface. Although, there is usually some injection of the numbing material. You do have to inject it with a Novocaine or a lidocaine very similar to your dentist. But the actual device is non-invasive.

So the idea of radial frequency is not new. It's, again, this alternating current. So that energy passes through a surface, which causes desiccation or heating of the surface underneath, which eventually will now create new scars.

So we think about this in rhinology a little bit more commonly now. But it's been used in a variety of different ways and a variety of different medical disciplines from cardiology, to removing liver cancers and tumors, to nerve ablation, and people with chronic back pain, OK. People are now using this temperature-controlled radial frequency to create scarring in other mucosal surfaces predominantly in people with incontinence. So that's actually where the other big area of investigation besides the nose is.

OK, so this is a device, which uses this temperature-controlled radial frequency to, again, float it over the surface and again, induce scar underneath that lining similar to that terminate reduction I talked about before. Except this does it in office without anesthesia. And it shows a significant improvement about 60% people's NOSE score.

And it can be used in people with very severe allergic reactions where their septum is actually pretty straight. But a part of their septum actually is swollen called the nasal body. And this can actually induce some scar in that region as well and help open up people's breathing.

So to be honest with you, I'm still trying to understand the benefits of this device. We don't offer it yet at UPMC. But we're looking into its benefits based upon these quality of life sites.

So this is actually fresh off the print. It actually is just in this week's print journal of the International Form of Allergy and Rhinology. But it was in pre-press. So I was able to read the article.

And this is what's encouraged me to think about it because it has a pretty durable effect. So up to two years, at least in this particular small trial of 40 patients, you can see that there seems to be a pretty lasting and significant improvement in the majority of patients, although not all. You can see up to 20% of patients still have quite a bit of difficulty with it.

But I think that it's worth considering and looking into. And so this is another study out of a Korean group that uses a slightly different device and again shows some significant post-operative improvements without hurting the lining.

So what this means, the grass off to the right are what measures of the function of the lining. This is called the ciliary beat frequency, which is basically how well does the lining continue to move things? And the [INAUDIBLE] test is how quickly we put some sugar in the front of the nose and people taste it?

And you can see that it actually is not affected after surgery. So this may-- or actually, after the procedure, excuse me. So this may actually be a very valuable alternative for our office.

OK, in addition to the nasal cavity, they are actually starting to market this same device for the treatment of nerve-induced nasal drainage. So when you see these three ovals here, well, the first two are the turbinate I was talking about. The last is actually well, they're not treating the turbinate anymore.

What are they treating? Well, they're actually starting to treat the nerves that innervate the turbinate. And maybe that this can make a difference.

So this is a process that we commonly call vasomotor rhinitis. So this is the idea that people can produce a significant amount of nasal drainage usually as thin, fairly clear in its nature without allergies. And it's believed to be driven by a nasal hyper reaction or a nerve imbalance.

OK, it's typically exacerbated by eating. And in my belief, I believe that this is almost all nerve driven, or at least the vast majority of it's nerve driven.

So I'm going to take us back to grade school a little bit and talk about how all of our body, including our nose is controlled by our nerves. So in grade school, you might remember that there was this thing called a sympathetic and a parasympathetic kinds of nerves.

So sympathetic are classically called the fight-and-flight nerves. So those are the things that supposedly help us get away from bears maybe back in the day or other kinds of things trying to harm us. And in the nose what that does is it shrinks down the lining. It reduces the drainage and it opens up the airways.

So that sounds great, right, except for the fact that now the nose isn't doing its job. It's not filtering out all the things that it's being exposed to the world. And the air that comes back into our nose, which our nose is amazing in its ability to humidify the air, takes whatever the air is on the outside. And by the back of the nose, it's now 100% humid. So it's great for our lungs.

But if you reduce all that, now it doesn't get that humidification. But it may help us run faster or at least a short spurt.

The parasympathetic is the reverse. That's our rest-and-relax time. And so that's when the nose starts to swell. And it produces more mucus and that allows it to clean itself, to continue humidify, and filter all the things that it does. And ideally, they live in a back-and-forth balance.

So I think what happens in vasomotor rhinitis is that the parasympathetic is really excessive and the sympathetic gets reduced. So the balancing scales are off. OK, and there are a lot of different causes for it. But unfortunately, the most common of which is actually just age related.

And it can be definitely exacerbated in people who are eating something because that's another resting and relaxing time. And some people will tell you about this profuse nasal drainage that they have while they eat. So we don't really have a perfect treatment for that nerve dysfunction yet. But we used to band-aid it or at least control it a little bit with something called an atrovent nasal spray.

So this is ipratropium. It's a drying agent. And in some people, that combats the nasal drainage aspect of that nerve dysfunction. And in some people, that's all they really need is they just need a nasal spray. And that controls them enough so that when they go out to eat with their friends, whenever we get past this COVID time and we get to go out and eat with our friends again that they don't have to be embarrassed by their nasal drainage.

OK, so this is a study that was started right before my fellowship at where I did my fellowship where they looked at where do these nerves, these parasympathetic nerves that give us this rest and relax time come out? And so they were able to study that it comes out right behind the inferior turbinate. And it comes out from this area that Dr. Stein and I operate in for tumors and other problems.

But these parasympathetic nerves come out right there. And they predominantly go to the inferior turbinate to make all this nasal drainage. So our first study actually was a surgical procedure, which we published on where we cut these nerves. And we put a barrier between them to help prevent people from having nasal and motor drainage.

And actually, it's relatively effective. It's about 70% effective or so. And we published this in a joint publication between us and two or three other institutions.

But it's still a surgery and still not everyone wants that for something that's principally nasal drainage. So then one of my really good friends got the idea that maybe instead of cutting the nerves themselves maybe we could just give it frostbite or basically freeze those nerves. And so from that thought and innovation came a series of studies and finally this commercially available device now.

Its brand name is called the ClariFix. But the idea is a cryo or coldablation of those nerves where basically we freeze or frostbite those nerves so that such that they don't function anymore. And so this is done in the office. And this is something in the right selected patients I do offer in the office where we use this device, which has basically a liquid nitrogen, like freezing agent in this capsule, which is this blue dial on the top of this instrument.

And it feeds this cold stuff into this balloon device, which then inflates. And you put it along the lining. And that bit of frostbite now freezes over the nose and freezes over the nerves.

And this can be done in the office. And it can be very effective. So this is the study that demonstrates this ability where, again-- so this is the total NOSE scale score. But it's similar into as the NOSE where you want a lower score.

So this is where patients were before. This is where they are after this cryoablation if you choose the right patients, OK. But you can see that the non-allergic patients do much better than the allergic patients in this subgroup.

And this was further studied in this multicenter group. And I think actually this has been more clear to my experience. So in the patients who do not respond to that after event, they really actually don't get too much benefit from this cryoablation.

And the patients who do respond to that nasal spray, that atrovent nasal spray, they also very much respond to this cryoablation. So it's unfortunate because that predictor is an ideal. We would love to have an intervention that worked in the people that didn't work with a medical intervention.

But this is where the data seems to lie. And this is generally my belief in it as well. If you respond well to it, I think that you're a good candidate for this if you want to get off the medications and to have a more durable and lasting effect.

All right, so with that, I'm going to spend a couple of minutes transitioning us to chronic rhinosinusitis and some of the research that's been done from our institution here. So despite a lot of people hearing that they have polyps, the actual prevalence of it is probably not very high. It's probably only about 2% of the population at most in the United States.

But they have a very, very high symptom burden. What that basically means is that in comparison to even most of the nasal problems, they have some of the highest challenges from a quality of life standpoint. And although people used to think that polyps were predominantly a smoldering infection that never got controlled, we now understand that chronic rhinosinusitis is really not an infectious problem.

It is an inflammatory problem where, again, we're talking about balancing. In our nose, we're supposed to have this idea of balancing between the ability to get inflamed to fight infections to clean our nose and the ability then to have that inflammation be reduced and for us to be able to breathe and have an open space. So most of this inflammation is mediated through these interleukins through type II inflammation. And in these patients, they really have a strong, strong imbalance where they have lots of pro-inflammatory signals. And they lack those regulatory signals to help the nose get back down.

OK, so previous to 2018, we were pretty limited in what we had. We had saline. We had topical steroid, sprays, which I've talked about many times. We use some antibiotics.

Although, to be honest with you, the efficacy was relatively poor. Although, there's some new data looking at this medication called azithromycin, not for its bacterial killing effects, but for its anti-inflammatory effects.

And then we had oral steroids, which are effective but really bad for the body, rest of the body. It helps the nose. But it makes the rest of the body pretty bad.

And then in the early 2000s through 2010, people started using an asthma medication off label to get more steroid in through the nose, which is a pretty significant advent. It was still something we use a whole lot of. This is called budesonide. And this is a medium strength asthma medication, which we borrowed and basically co-opted from our asthma colleagues to start treating people with polyps.

OK, so this is an example of a patient with nasal polyposis that I operated on just a week ago. So this has a component of the nasal obstruction from the septal deviation as well as all these polyps filling up the nasal cavity and making it nearly impossible for this poor patient to breathe. So this is like the classic scenario of someone who has a lot of challenges with their nasal quality of life.

So at the end of endosc-- so in this situation, historically, we've done endoscopic sinus surgery. I'm not going to do too many surgical pictures, mostly because it's everyone's lunchtime, at least on the Eastern seaboard, and not always so nice to have to look at that. But the basic idea of endoscopic sinus surgery is that it is not a curative surgery.

So it's not getting out your gallbladder and you're cured. Endoscopic sinus surgery is the idea that we're going to take apart all these little bony partitions and walls of all these little rooms that separate out our sinuses such that we can create a big, wide open cavity that makes it easier for us to distribute the medications from the nasal cavity into the sinuses and now treat the source of the problem. So instead, the way I joke with people is it's a little bit like a home renovation.

Instead of having all these little rooms all squished together, we're going to create one big open floor plan. And that one big open floor plan you have to keep the studs in the drywall to keep the face up. But we can now create this big open space. So now when we deliver medications, they're going to feel better. And we can control it long term with nasally driven medications.

So endoscopic sinus surgery makes a lot of people feel better. It's very important part of our armamentarium in treating patients. But it's not a curative surgery. It's an adjunct surgery.

OK, so most of the research in the last 15 years or so has mostly looked at things like this, like how do we help surgery along? This is the idea of a chitin-based spacer or a shellfish lining spacer that helps. You can deliver some medications with it. Additionally, there have been ideas of drug eluting stents and improvements in the surgical technique with this GPS-driven tool on the right side to help you find the right places, or even the advent of these balloons, which were very popular for a little while.

At first, people try to bill them as different surgeries. But they're not really. It's the same idea of taking that opening and making it bigger. It was just using it as a different tool. While it's still used in some places with a lot of regularity, the enthusiasm has probably dropped some and probably in an appropriate manner.

All right, so the biggest change in our armamentarium has now been a basic understanding of that inflammatory process. So this is a lot of research that one of my colleagues, Stella Lee, spent a lot of time working on, looking at this monoclonal antibody. It's a human-derived monoclonal antibody that blocks the receptor itself.

So this is an injection you get every other week where these antibodies are injected into you. And they can actually block that inflammatory cascade that happens. So that dysregulation can drop it all the way down.

And it's been shown when they compared a placebo, to reduce the need for both steroids and surgery. OK, so this is the study that was published in a big journal in Europe called *The Lancet.* This is mostly research that came out of Europe.

And what it shows here really is that it improves the amount of polyps. It improves patient's nasal congestion and their sinus [INAUDIBLE] when you compare it to placebo. OK, so this is now FDA approved, commercially available in the United States.

And in the right patient, it is a really, really powerful intervention. And a lot of this research was done here at UPMC as well. So this is an example of dupixent in the nasal cavity. You can see that it doesn't make all the polyps go away. But it certainly reduces the polyps that patients have.

Unfortunately, there are some disadvantages to it. It's an every two week injunction. And rarely it can unmask another problem that actually is very difficult. It's an autoimmune problem.

But its biggest downsides probably are that it's actually a very expensive medication. It's like paying for college every year. And the polyps recur as soon as you discontinue it. OK, so as soon as the polyps are-- as soon as you stop the medication as best as our early data shows, the polyps come right back. So it basically has to be maintained for a very long duration.

OK, the other area that we're investigating is this exhalation-based delivery system. And this is really a clever device. So this still uses topical nasal steroids. But the way this does it has a mouthpiece as you can see and a nasal piece.

So as you breathe out, what happens is your soft palate closes in the back. And so that causes the medication to recirculate into the nasal cavity. So instead of a whole lot of medication getting wasted in the throat, all the medication gets recirculated back. And it gets recirculated back higher into the nasal cavity where most of the polyp problems happen.

OK, so this was the placebo controlled trial of this, which demonstrates its clinical benefit. The blue is the placebo line. And the rest are varying amounts of this medication in a dose-response manner.

So this is actually a pretty-- this is the second FDA approved drug that's come onto the market for polyps. And all of this has happened since 2018. So we study this as well.

So this is a study, which basically shows that in patients who failed topical nasal steroids, even though the medication is the same in Flonase as it is [INAUDIBLE] or this exhalation delivery device, because it gets distributed better, patients have significant improvement in their quality of life using this metric. OK, so it's not really the medication itself. It's getting to the medication where it counts.

And this is especially so in patients after sinus surgery. So this is all about the distribution of that medication. OK, and this is the biggest quality of life one I can show you. So these are a variety of different surgical procedures and how much it improves people's quality of life.

So the one that is most beneficial is bariatric surgery for patients with extreme morbid obesity. But you can see [INAUDIBLE], which is not a surgical procedure, has a quality of life improvement that equals that of getting a cardiac catheterization or a hip replacement. So this is a pretty big quality of life improvement I think. And it shows you that if we can get things to the right place, that makes a huge difference.

So the last thing here is this is a sinuva implant. So what this is the idea that in some patients, rather than giving them oral steroids, we can deliver steroids through this dissolvable implant directly to a post-operative cavity. So this is a patient of mine where we're putting this sinuva implant into their polyps. You can see all their polyps beyond in the screen.

And we deploy this device. This is done in the office. The patient is awake talking to me.

And we deploy this here. And you'll see that the barbs come out. And as the body starts to resolve this device over 90 days, it continues to deliver steroids. And this can now help reduce some of that burden.

So we couldn't get this-- the topical steroids couldn't get through all that polyp. But through this device, we can get it through the polyp into the polyps itself. And it can help some people avoid revision surgery. Its biggest downside is that it needs to be removed. OK, so this is the trial of that that shows its benefit in reducing. And it has a quoted 61% reduction in need for revision surgery, OK.

The last thing I'm going to do is plug some work that we're doing here. This is preclinical with the same idea of delivering medication where it counts. So whether using-- so you could see that that device was OK. But it doesn't get things to the lining itself. It delivers it to the cavity.

Here we're coupling with some of our colleagues in chemical engineering. To look at this idea, which we call temps, so this has a provisional patent on it, which is basically that this is a thermal responsive microsphere delivery to the sinuses.

So basically what this is at a room-temperature state, it's in an liquid formulation. And these microspheres can now carry medication. Right now we're using steroids. But it's incredibly valuable, and it's very versatile.

And then we can inject this into the paranasal sinuses, particularly if you've had surgery. But we're looking into how maybe we can use it in nonsurgical patients. And then it can actually contour towards the sinus lining and then release the medication slowly over a month.

It's adaptable. It's adaptable to the sinuses, which are irregular-shaped things. But it's adaptable to other disease modifiers. So as we understand other medications or other interventions that may help treat that sinus lining, they can now modify the microspheres, use the same delivery device to now carry the latest innovations to the paranasal sinuses. And we have an NIH grant that's under review right now that's back in the study section looking at this.

And all of this work was essentially sponsored through the Eye & Ear Foundation. It's all the seed money from your generosity that really got us through these initial animal models that got us to the point where now we can apply for an NIH grant to continue to look at these innovations.

So again, these are my sincere thanks to the Eye & Ear Foundation and to all of you who've helped support us through these initial innovations and these initial studies. There are a lot of different ways that the department is working. But again, innovation is really driven through the philanthropy of the Eye & Ear Foundation. And I can't thank you enough for spending this last 45 minutes with me. I'll be happy to take any questions.

LAWTON SNYDER: Dr. Wang, thank you so, so much. That is-- I'm just overwhelmed by how many new advances there are in really just a short period of time, over the last, as you said, even the last 5 to 10 years there's been a lot. And are we getting to a point where you're seeing just a pipeline of new opportunities for these new therapies for your patients?

ERIC WANG: I think so. And I really hope so, Lawny. I mean, I think that for a long time, people thought the sinuses were just not that big a deal. But increasingly, as we see these quality of life impacts to it, both patients-- well, there's so many stakeholders in medicine.

But patients, the physicians, the pharmacy, even the NIH is beginning to say we really need to look at this more. We need to care about this more. And I think that that's really driving these innovations that are happening. And again, as I pointed out earlier, the latest innovation we're working on, this tempts device, is really solely driven through the Eye & Ear Foundation. We couldn't have done it without it.

LAWTON SNYDER: Well, that's what we're here for. So thank you. And we have questions from the audience that we'll direct both to Dr. Wang and Dr. Johnson. So Mayo clinic did research some years ago regarding cases of rhinitis and sinusitis caused by an immune response to fungus.

The body sends [INAUDIBLE] to attack the fungus [INAUDIBLE], but also irritates the lining of the nose. It technically isn't an allergy reaction. Has this research progressed in this area?

ERIC WANG: So Dr. Johnson, is it OK if I take this one? All right, so unfortunately despite-- so that was work by this guy named Jens [INAUDIBLE], who was really enthusiastic about this idea that maybe the silver bullet was fungus.

Unfortunately, what has shown over time is actually that that has not proven to be true. If you try hard enough, you can actually culture fungus out of all of our nose, Lonnie, me, Dr. Johnson, everybody. What was probably driving that big difference was actually the amphotericin that they were giving. So the medication that they were giving into the nasal cavity is an antifungal.

But many medications have multiple effects. And amphotericin is one of those. And it actually has a pretty strong anti-inflammatory effect. So it was probably more likely that the anti-inflammatory effects of the amphotericin were proving to be beneficial.

So when people-- actually, people were very enthusiastic about this amphotericin, irrigation or wash into the nasal cavity that you're referring to. And they did randomized controlled trials with it outside of Mayo clinic. And Mayo clinic does have a patent on it. So that should be disclosed as well.

And it has been proven over and over and over again that it's not more efficacious. And in fact, in the latest international consensus statement on rhinosinusitis that we're authors on, it actually has a recommendation against antifungals for that specific reason.

LAWTON SNYDER: And that's-- thank you.

ERIC WANG: But it was a great question because there was a lot of research poured into this in the late '90s and early 2000s.

LAWTON SNYDER: Yeah, thank you. Thank you for that question. By the way, folks, you can continue to ask questions. I see them coming in here. But remember, it's the Q&A bubble down at the bottom.

What causes sinus related headaches? The headaches are relieved by ibuprofen or [INAUDIBLE]. But what seems to occur with barometric pressure changes in weather? But it seems to curb, sorry, with barimetric changes in weather.

ERIC WANG: So sinus headaches are another tricky thing to be honest with you. What I tell my patients often is that the sinuses can cause facial pressure and headache. But they usually have to have a constellation of things around them.

So if you look at patients who have only sinus pressure-- and it's this classic four-quadrant pressure, like up above here and down here. If they lack the other constellation of things, a decrease in their sense of smell, nasal congestion, or nasal drainage, those four cardinal symptoms that we talked about, if you go back and look at how often their CAT scans actually show sinus inflammation or sinus disease, it's actually a very small percentage, something in the range of 5% to 10%. Increasingly, we're recognizing that actually atypical migraines is a very common cause of this pressure [INAUDIBLE].

In fact, it's actually now in the latest International Headache Symposium described as the third most common migraine variant. So the most classic is the one that we all know about where bright lights bother you, loud noises bother you. But this four quadrant pressure is really, really a common migraine pattern so much so that our headaches and our colleagues here in the Department of Neurology, they don't even get scans in patients anymore to look for sinus disease if they're missing some of the other symptoms because they believe it's likely to be atypical migraines.

As far as the pressure goes, sometimes migraines can be triggered by all sorts of different things, including external environmental changes. So that could be a [INAUDIBLE] of the driver. But you really probably need someone to evaluate and look in your nose or talk to you about your symptoms. It's not one of the easiest things to differentiate. But it is a very common complaint and common problem.

LAWTON SNYDER: Thank you. Again, thanks for that question. Do you have any experience in utilizing breathing methods, i.e., buteyko method to improve sinus health?

ERIC WANG: So my short answer is no. There are people who have looked into a lot of those kinds of things, whether it's meditation, acupuncture. The biggest group is out of UCLA where they actually do offer acupuncture for some people with sinus pressure.

And so certainly there's a lot that we don't know about yet. And you don't want to close your mind or close your doors to any of those particular opportunities. But I don't actually have a whole lot of personal experience with that [INAUDIBLE].

LAWTON SNYDER: The questions are still coming. So can problems with the teeth in the back of the mouth, specifically molars, cause these problems in the sinuses and drainage to the ear? How do you eliminate this as a cause in your diagnosis?

ERIC WANG: So that is a great question. I didn't dive into teeth-oriented sinusitis because it's a unique subgroup. But actually, we were one of the first groups to really publish on this.

And I will give credit to my former partner, BJ Ferguson. She was really one of the instrumental people in making everyone understand and recognize the importance of this odontogenic, or teeth-derived sinusitis.

That one unlike traditional chronic rhinosinusitis's is really an infectious problem where the top of the teeth, roots can bust into the sinus and actually cause an infectious problem. In the study that we published on and actually found that if the tooth problem is located and still contained within the cheek sinus itself, usually, either endodontic work, like a root canal, or tooth extraction coupled with antibiotics would treat the problem, and that would be that.

Unfortunately, when it spreads outside of the cheek sinus, like it gets to the other sinuses like your ethmoid sinuses or your forehead sinus, those often need endoscopic sinus surgery basically to drain the infection. We still have to deal with the tooth, the primary cause. And we work with our oral surgeons frequently in these kinds of scenarios to help treat that.

And the patients do need antibiotics after. But usually, it requires a combination of sinus surgery as well as management of that tooth to control that. But it's one of the more pleasant ones to deal with because once we do, you're actually all better. So that's one of the time sinus surgery is really a cure.

We don't get that very often in the sinus world. But it is one of those times where sinus surgery plus the dental surgery really does cure a patient. And that's a really-- that's a wonderful thing when we get to have [INAUDIBLE].

LAWTON SNYDER: All right, well, just a few minutes here, but we do have some more questions. What's your take on the neti pot?

ERIC WANG: So the neti pot is a sinus rinse. It's really just a high volume, low pressure salt water wash. It has all the same efficacy as a sinus rinse.

I find-- so this is just personal bias. You often talk about the things that you've done yourself. The sinus rinse is easier for me to do than the neti pot. Maybe I'm just not good at tilting my head all the right ways.

I tend to get it into my throat a lot when I use the neti pot while it's easier for me when I use the sinus rinse. But they're all about the same in that sense. And I'm happy for patients to use whichever works better for them.

LAWTON SNYDER: I guess another question here. I stepped away for a minute. Did you discuss DUPIXENT?

ERIC WANG: We did. DUPIXENT is that monoclonal antibody that we talked about that blocks the inflammatory pathway. It's FDA approved and is a very valuable treatment in severe polyposis.

Its biggest downside is it has a fairly significant cost associated with it. It's estimated to be between 25 and 35,000 a year. And unfortunately, it's not one of those medications that when we stop it, people are always improved.

So we stop it. But when we stop it, it seems like most people's polyps come back. So it needs to be maintained for a long time.

So I think that it is a huge advent as far as giving us an additional option. But it also is a very costly option. And so we have to balance all that out.

There was a study done at Emory that shows that you have to have sinus surgery every six months for eight years to equal the cost of DUPIXENT over five. So it's a pretty pricey intervention. It's not wrong. And I will tell you, I use it in some of my patients. But we have to be good stewards of that particular drug.

LAWTON SNYDER: Insurance doesn't cover that?

ERIC WANG: It does. But it's pretty expensive on the health plan. Right now DUPIXENT is being given away through this thing-- through the companies-- through something called DUPIXENT My Way.

But I can't imagine that they'll be able to continue that for very long. And I do worry about the copays that are going to be associated for my patients after. But with those caveats being said, I think it's a very important adjunct and something that we do deploy in the right person.

LAWTON SNYDER: OK, if you've got a minute, we have two more questions here if that's OK with you, Dr Wang? Are there any new or innovative treatments for [INAUDIBLE] in the nasal airways?

ERIC WANG: [INAUDIBLE] not so much. Unfortunately, they're still largely having to be removed. We're better at removing them through more minimally invasive corridors. But unfortunately, there's not really a way to get rid of them independently without surgical intervention at present.

LAWTON SNYDER: You mentioned eating as a trigger for sinus congestion. Is change in outside temperature equally a trigger? And what can be done for that?

ERIC WANG: That's really one of the toughest we have. So I definitely know patients who do get an irritation from cold air. But I also have other patients who love the cold air. And they love-- and they hate the humid hot air.

It's probably one of the most difficult things for us to study because people can't be confined in these areas for us to really study where their congestion comes from. I definitely believe that there is an irritant aspect of that, that whether your nose is triggered by the cold or triggered by the humidity, that your nose swells in response to that.

It's probably one of the most recalcitrant we have because we can't really control that environment. And none of our medications really [INAUDIBLE] in our treatments up to now have really made a big difference in that regard. There are people who are using that temperature controlled radiofrequency ablation, which is probably the one therapy we don't actually offer right now, but we're looking into for that specific reason. But the data is not out there yet. And I really want to understand what that data is before encouraging, or allowing our patients to see what that's going through because we're not on trial for that at all.

LAWTON SNYDER: And the last one, kind of just back to the neli pot, neti pot, I'm sorry. Is it safe, I guess, for people with nasal polyps?

ERIC WANG: It is safe. So this question may be referring to there was an FDA warning associated with it. So there were two cases of an amoeba getting into the brain via a neti potter sinus rinse. They were using tap water from the same water facility in an area of Louisiana, which really makes me think that they need to get their water authority to really look at that.

This is a well known amoeba that causes problem, though. Historically, some child in the upper, like the great plains region, like Minnesota, Wisconsin would swim into a lake, get this amoeba in their nose, and die of this amoeba infection every year. It is indigenous to North America.

So the recommendation has moved from allowing people to use tap water to principally distilled water because now you won't have any microbes associated with that. In some patients, they still choose to do boiled tap water. Although, I really discourage well water.

But again, it's very isolated, two incidents, same water treatment facility in the Louisiana state, the state of Louisiana. Well-known amoeba. I think it was just a bad place, bad time kind of scenario. That's my opinion about it. So I think it's actually very safe.

LAWTON SNYDER: Well, thank you. An absolute wealth of information, but also a topic that we saw a lot of interest in today. And I'm sure that we'll have more to come.

So thank you so much. And thank you, everybody, for attending. And we'll look forward to seeing some of you again on one of our future programs. Thank you again. Have a great day.

ERIC WANG: Thanks, Lawny.

[MUSIC PLAYING]