Dr. Jason Barnes:

Hey there. Welcome to another episode of ENT In A Nutshell. My name's Jason Barnes, and today I'm joined by endocrinologist, Dr. Marius Stan and rhinologist and skull based-surgeon, Dr. Janalee Stokken. And today we'll be discussing thyroid eye disease. Dr. Stan, Dr. Stokken, thanks so much for being here.

Dr. Marius Stan:

Thank you for inviting us, Jason.

Dr. Janalee Stokken:

Yeah. Thanks for having us.

Dr. Marius Stan:

Pleasure.

Dr. Jason Barnes:

I first just wanted to start with presentation. Dr. Stan, most of these folks will be presenting to your clinic, and I was hoping you could tell us how a patient presents, not only with thyroid eye disease, but with Graves' disease, and then how you work up the eye component of their pathology.

Dr. Marius Stan:

The thyroid eye disease is present in a subgroup of patients. But as you're alluding, majority of patients with Graves' disease, and I'm going to call Graves' disease the overactive thyroid, majority of those patients do not have eye manifestations of concern. So they typically come with complaints of palpitations, tremors, increased heat intolerance. And that's what typically leads to testing, which is TSH, T4 and so forth. Out of this category I will say that probably about a quarter to a third will have eye changes of concern at the time of diagnosis of hyperthyroidism that would raise the question about concomitant thyroid eye disease.

Dr. Jason Barnes:

And what questions are you asking patients to tease out if they have eye involvement?

Dr. Marius Stan:

The most typical thing that patients will report is a concern about foreign body sensation, concerns about dryness that might be present as well as a pressure behind the eyes, or an obvious change that they've been told about that the eyes look more protruding or that they look as if they're staring, because typically the upper eyelids are retracted in these patients.

Dr. Jason Barnes:

And is there a particular course or clinical course that this follows from a timeline standpoint regarding the eye presentation?

Dr. Marius Stan:

I would say that fortunately for the vast majority of patients that have thyroid eye disease, the disease tends to follow a mild course with these symptoms, going through an evolution over six to 18 months,

somewhere there. There's an inflammatory phase at the beginning. And I guess we'll talk about this in more detail later, but it's a bit of an increase in the symptoms for the first few months, followed by a natural resolution of the symptoms. And for most patients, this becomes really negligible in the longterm, that is a year and a half out, but not for all.

Dr. Jason Barnes:

And what are some other questions that you're asking them in terms of risk factors or other symptoms that they might be experiencing?

Dr. Marius Stan:

Right, that's a very important aspect. We know that smokers are at a high risk of having eye disease. And those that have the eye disease and are smoking are at high risk for progressing to more severe forms of disease. So this is one aspect that we try to elicit in everybody and try to address as much as possible. It's not unfortunately one of the successful things that we can brag about is stopping smoking, but it's important that patients are aware. And a minority is making big improvements in that direction. The other thing that's helpful from a biochemical perspective is the antibody titer. The TSH receptor antibody correlates fairly well with the course of the eye disease. And it's a good marker to use as to how severe the disease is likely to become. So prognostic value is there in that antibody, as well as the severity of the thyroid disease per se. Seems to be that the more severe the thyroid disease is, the eye disease follows to some extent that pattern, but not always.

Dr. Jason Barnes:

And when someone presents presumably with hyperactive thyroid and eye involvement, what are you looking for on physical exam when you first evaluate these patients?

Dr. Marius Stan:

First of all, the thyroid disease can be a big hit for a number of individuals. So it's very important to understand how much of a toll it took on them from the perspective not only of tremors and jitteriness, but also of muscle wasting, of really the cardiac implication. Some of these people come in the office with a heart rate between 110 and 140, and that is at rest. So obviously there's a risk for arrhythmia, and we have to make sure they don't have already atrial fibrillation. And in a small group of patients, there's a risk for congestive heart failure. And this unfortunately is not only for those with preexisting heart disease, but it can occur in patients in their thirties or forties. So cardiac status, muscle strength, which tends to be lost in many of these individuals are important elements to consider.

And beyond that, we're looking at on exam how the thyroid shapes up. Tends to be that a very large thyroid will not respond easily to therapy. So, that's a useful element. We also besides the eyes, we also want to make sure that there's no involvement of the lower extremities. What we've read in our textbooks, the pretibial dermopathy is there and tends to be there in patients that have eye disease, as well as an assessment of their cognitive status because sometimes this overactivity leads to a difficulty in following a train of thought and making informed decisions. So when we present them with treatment options, we have to make sure that they are in the position to understand those treatments well. And sometimes they are actually not there yet until we bring the thyroid levels down before we ask them to commit to some major interventions, as we'll discuss later about thyroid eye disease, surgery, and so forth.

Dr. Jason Barnes:

And what specifically are you looking for on eye exam?

Dr. Marius Stan:

The eye exam has a number of components, and I would start by saying that the most important element at the beginning is to see if we're dealing with a sight threatening form of the disease, which really should be either the obvious form of globe subluxation or luxation, or an infection of a corneal ulcer. So those probably for most patients, for most physicians that have seen these patients will be fairly obvious. But then the one that we want to keep in mind is also the possibility that the optic nerves are compressed. So optic neuropathy, which in the office setting for you and me without a lot of ophthalmological tools at our disposal, is just the assessment of colors, particularly red and blue. And the assessment of clarity of vision. Visual acuity is something that we should ask. And we should in a fairly quick manner, we can assess in the office.

Dr. Jason Barnes:

And can you tell us about the use of an exophthalmometer?

Dr. Marius Stan:

So once we've ruled out the presence of sight threatening disease, which obviously is a medical emergency, we would move down the list of deciding on the exam are there signs of inflammation? And here we have that clinical activity score that goes around the features that we all know for inflammation, pain, redness, swelling. And we're talking about eyelids, we're talking about caruncula. We're talking about the conjunctiva with chemosis with conjunctival injection, and we're talking about pain behind the eyes or pain with eye movements. All those would fill up seven points on a scale of clinical activity score. And then from the severity perspective where we're about proptosis, which is what's measured with the exophthalmometer. And basically this tool, which is based on assessing the most forward aspect of the globe by using the lateral bony orbit as the reference point.

So it really depicts how many millimeters in front of the orbital bone is the globe exposed or measured. And it's something that might be symmetric, or it might be asymmetric. The right might be more than left or vice versa. And sometimes it's really unilateral, which can be confusing to people that only one eye is affected, and therefore this cannot be thyroid eye disease. And yet I would say, yes, it can be. So we have to be careful about this. Besides the proptosis, we obviously want to know about double vision. That's another measure of severity. We want to know if they can close the eyelids fully because the opening can lead to dryness and that can lead to complications. And I think those would be the main features of a severity, proptosis, lagophthalmos, double vision, and then the optic nerve assessment as we discussed earlier.

Dr. Jason Barnes:

And Dr. Stokken, when someone presents to your clinic for evaluation of thyroid eye disease, we'll talk about surgical intervention towards the end of this talk, but what are you looking for in clinic when you're considering intervening in these folks?

Dr. Janalee Stokken:

Yeah. So in addition to the eye exam, which is usually well-documented by my ophthalmology colleagues, we also want to ask about the nasal history. Any history of nasal obstruction or sinus symptoms because a portion of this surgery to decompress the orbit will happen through the nose. So we'll have to get a good history of their sino-nasal symptoms and get an exam to see what their nasal

structures look like. We may adjust our surgery if there are polyps or signs of chronic inflammation in the nose. And then we may also have to add a septoplasty if their septum is deviated to one side or the other to allow access. So the ENT focus of our exam is really on the nasal structures.

Dr. Jason Barnes:

And do you perform nasal endoscopy in these folks when you evaluate them?

Dr. Janalee Stokken:

Yeah, I usually do. I find that the easiest way to know if I'll have access to the ethmoid cavity is to use nasal endoscopy to look at the superior septum. And when I look with a zero degree endoscope, I'm looking to see if I can see the attachment of the middle turbinate to the lateral wall, that area we call the axilla. If I have good visualization of that structure, I'm pretty confident that I'll be able to do a decompression without septoplasty. However, if I'm not able to see that axilla very well, then I usually talk with the patient about septoplasty in addition to the decompression.

Dr. Jason Barnes:

And Dr. Stan, when you see these folks, it seems like they have a pretty straightforward clinical history, but what else might you consider on differential diagnosis apart from thyroid eye disease?

Dr. Marius Stan:

So it's unfortunate practicing along with Dr. Stokken in this format where we have our colleagues in ophthalmology also joining us in the thyroid eye disease clinic that we have perspective from different angles about the eye component. We always consider that if the disease is unilateral in particular, that might be another intra orbital process that needs to be excluded being that a real tumor, a pseudo tumor, a form of vascular malformation, a meningioma. So all these are on our list, and it's not unusual for us in unilateral disease, or when there's a question about the etiology of the disease to obtain CT imaging of the orbits, which probably also helps a lot, Dr. Stokken and your colleagues in deciding how to approach a potential decompression down the road.

Dr. Jason Barnes:

And can we now move on to pathophysiology? Dr. Stan, can you remind us a little bit about the pathophysiology of Graves' disease, and then speak a little more specifically to what the orbital involvement is here?

Dr. Marius Stan:

I will try. Fortunately, we're living I think in a time when we have learned a lot more than what I learned when I was in the training stages. But probably it's more that we've learned about the thyroid eye disease in the recent years than the thyroid disease per se. That we still think that it relates as we all know to an autoimmune process where the TSH receptor on the thyroid cells is being basically stimulated by an antibody, as opposed to the typical TSH signaling that we all have from the pituitary. In the case of Graves' disease, we have an antibody against the TSH receptor that obviously doesn't follow any feedback. And as a result of this continuous stimulation of this receptor, we have continuous production of thyroid hormones from the thyroid, which as expected like somebody going to the gym seven days a week is going to have bigger muscles, these people are going to have bigger thyroids.

So goiter is present. The impact of the thyroid hormone is then felt on the tissues that we discussed earlier. The result of these antibodies at the eye level is a little more complex though. So we think that the same antibodies, the TSH receptor antibodies are the main culprit when it comes to the thyroid eye disease, and they lock on TSH receptors on the orbital fibroblast. And one possibility of that, one result of that interaction will be that the orbital fibroblast transforms into a fat cell, into adipocyte that takes a lot more volume than the initial fibroblast. So that's the reason for the expansion of the tissues in the orbit, A, or B, is that these fibroblasts in the muscles, in the extraocular muscles secret glycosaminoglycans, hyaluronic acid, the most common one. And that fills up these muscles making them as we've seen them on CT imaging to have those large bellies that are also very stiff muscles now.

So they lead directly from this stiffness we're seeing the double vision, the inability for them to follow the nerve stimulus appropriately. So we have large muscles and maybe a lot more fat than initially. And this all leads to an increase in the orbital volume. At the same time, it decreases the venous return from the orbit. So you end up with congestion. And it retains the cytokine that's triggered by the stimulation from the antibody. This leads to mild inflammation, but it's not something that can be easily cleared out of the orbit. So you have a pro-inflammatory milieu decreased venous return that keeps it there, along with the increased intraorbital pressure. So it's a bit of a ticking bomb there.

Dr. Jason Barnes:

And if this goes untreated, what are the possible complications that folks would experience?

Dr. Marius Stan:

From my perspective, the changes that are triggered by this initially are those of appearance with swelling, with redness, with the eyes being more protruding. This leads to the exposure. So when people complain of dryness, it's because the eyes are not properly covered by the eyelids. And that leads to a fairly quick drying process. It leads to what I mentioned, the muscles being stiff, and that they are not reacting in synchronism when we're trying to look to the sides. So the double vision is the result of this motility that we're seeing in the extraocular muscles. But the most feared complication is the fact that the optic nerve, which travels from the globe towards the pituitary area, is going to be compressed by the increased intraorbital content with optic neuropathy. And that's another area where Dr. Stokken has helped a number of patients along with our ophthalmology team in trying to rapidly decompress that area.

Dr. Jason Barnes:

Moving on to workup, you have a patient who comes to your clinic and they have a history of thyroid disease and now are presenting with eye symptoms. Dr. Stan, could you tell us what laboratory studies you will obtain and what it tells you about the activity of their thyroid eye disease?

Dr. Marius Stan:

The thyroid levels are probably very well summarized through a TSH, a free T4, so free thyroxin, and a total T3. The antibody level that we typically obtain is now a combination. We obtain what's called the thyrotropin receptor antibody or TRAB, but we also obtain the thyroid stimulating immunoglobulin. We look at both measurements because I think the latter, the thyroid stimulating immunoglobulin can be informative in the early stages of the disease, while the TRAB is better at quantifying and predicting down the road how the disease will evolve. We also like to obtain liver tests, which are helpful because the thyroid disease itself can affect the liver. And it will affect our choices of therapy, particularly the medications that we can use, as well as a CBC. Occasionally, this autoimmune problem goes along with

neutropenia, and that obviously has a number of implications, including again, the kind of medications that we can use for thyroid disease. So thyroid tests, thyroid antibodies, TRAB and TSI, liver tests and a CBC would be my biochemical approach.

Dr. Jason Barnes:

And you talked a little bit about eye examination already. Could you tell us, when you perform the exam with an exophthalmometer, what are the ranges that you're looking for, or what is concerning for proptosis from a measurement standpoint?

Dr. Marius Stan:

This is something that fortunately is now well-described in a number of guidelines in both the American Thyroid Association, and then a very well established group in Europe called EUGOGO, European Group for Graves' Orbitopathy have outlined there. But it has to start with defining the type of patient in front of us from a racial perspective, because the normative value differ and they are lower for Asian groups. As low as I would say 17 millimeters in Chinese individuals. And the maximum tends to be in African Americans where we can see in males values up to 24 millimeters being normal. Caucasians are in the middle at somewhere up to 19, 20 millimeters for women, and 21, maybe 22 for men. Keeping in mind that this is a range. So if one started at 17 and is now at 20, it might still be within range, yet abnormal for that individual.

Dr. Jason Barnes:

And you also mentioned the clinical activity score. Could you again tell us what these points are and what they mean in terms of disease activity and how we move forward with treatment?

Dr. Marius Stan:

The idea of using a clinical activity score is to sort of dichotomize the disease into an active phase. When there's inflammation that we can hit with anti-inflammatory agents versus an inactive phase where we think the scarring is already going on and it's the time to talk about rehabilitative interventions, which are typically surgical. So the clinical activity score aims to do this, to separate active disease, which is at least three points on this scale of maximum seven points. And if you'll look at any of these depictions of clinical activity score, you'll see pain either in primary gaze one point, or with extraocular movement, a second point. Followed by redness of the eyelids, swelling of the eyelids, each one point. Conjunctival injection, another point, swelling of the conjunctiva, what's called chemosis, another point.

And then inflammation of the caruncula, the triangular medial aspect of the covering of the globe, that's another point. So a total of seven can be obtained at any examination. There are three extras that can be obtained during followup that mainly look at progression of disease. And if the score is three out of seven, or at followup four out of 10, we consider the disease to be active. That is there's enough inflammation to use an anti-inflammatory agent.

Dr. Jason Barnes:

And Dr. Stokken, can you speak to imaging that's obtained in these patients and how you use it in pretreatment plan?

Dr. Janalee Stokken:

Yeah, in general we typically get a CT sinus scan without contrast. A CT orbit scan will also give us the information that we need. This is mentioned before as particularly important when there is unilateral disease. So unilateral Graves' is not uncommon, but we definitely want to make sure you rule out any underlying mass lesion or other etiology. The next reason we use the imaging is to get an idea of how much fat versus muscle is hypertrophied in these patients. It doesn't change our planning a ton, but if we know that there's more fat hypertrophy, a lateral decompression will probably accomplish more by removing fat than it would in someone who has more muscle hypertrophy.

The last thing that imaging is important for, and this is where a CT sinus scan would be more beneficial than the orbit scan, is if you use image guidance navigation. So anytime I'm doing surgery that involves a total ethmoidectomy, I like to have image guidance navigation available. And this will help make sure that I've taken down all the septations I need. I'm up to the skull base and I've skeletonized that lamina well.

Dr. Jason Barnes:

And Dr. Stan, taking all of these things together, is there an official diagnostic criteria for thyroid eye disease?

Dr. Marius Stan:

That's a good question because sometimes we jump to that diagnosis. But I think that almost everybody in the field would agree, you need to see thyroid autoimmunity. And that doesn't mean hyperthyroidism. That could mean hypothyroidism, as Hashimoto's thyroiditis with positive antibodies. And in that case tends to be TPO antibody. Or we can see even individuals that have normal thyroid levels and yet have positive antibodies that I mentioned earlier, the TRAB or the TSI. So with evidence for thyroid autoimmunity, the presence of eye changes, and I would say at least two eye changes, not only lid retraction, but presence of soft tissue swelling, presence of double vision, redness. I think those changes would then qualify an individual for having thyroid eye disease. It is probably important if there's an element of uncertainty to obtain CT imaging, because the signature would be the presence of the extraocular muscle enlargement. And if that's not present, then we should go back to the drawing board.

Dr. Jason Barnes:

Moving on to treatment, Dr. Stokken, can you tell us some of the indications for surgical intervention for patients with thyroid eye disease?

Dr. Janalee Stokken:

Yeah. When I think about offering a patient surgery for thyroid eye disease, I really break it down into three components. One that has been mentioned previously is optic neuropathy. So if a patient's losing vision and is not responding to anti-inflammatories, surgery in a fairly urgent fashion will help spare the pressure that's being placed on that nerve and help patients regain vision. The second indication is secondary to the proptosis, but could be from irritation to the conjunctiva or corneal ulceration or keratitis. Things that are secondary from not being able to close the eyelid.

Surgery can help move the globe back in place where the eyelid can close and they can protect their eye and keep it healthy. And then the last indication for surgery is restoration of cosmesis. Many of these patients, when they come in they bring pictures of their eye and how they looked prior to the disease. And they really want to go back to how they feel they should look. A lot of times people wonder, is this going to be covered by insurance and that sort of thing? And we really try to reassure

them that this is something that's restorative. It's not cosmetic in a sense of plastic surgery, that sort of thing. So those are the three things that we usually talk about in a clinic visit.

Dr. Jason Barnes:

Sure. And we're kind of talking around eventual surgical intervention, but before a patient is prepared for surgical intervention, Dr. Stan, what are some things that you consider and maybe ways you prepare both mentally and medically patients for surgery?

Dr. Marius Stan:

The connection between thyroid disease and eye disease is there. So it makes sense for us all to make sure that we've already addressed the thyroid component, because if the patients are still hyperthyroid or hypothyroid, then it's very unlikely that our interventions for the eye disease will have a suboptimal result. So normalizing thyroid levels is step one in my mind, then eliminating as much as we can the impact of smoke exposure. And I'm sometimes surprised how we limit the interview to, are you smoking yes or no? But smoke per se, secondary exposure, as well as some hobbies that sometimes I find patients they take advantage of. And particularly a welder that surprised me of not being aware that he was exposed to smoke every day.

So smoke exposure should be minimized as much as we can. And then we have medical therapies when the disease is active that are becoming actually quite effective. And many of us have been impressed by this new agent called [inaudible 00:29:06] that has been reported now on two randomized clinical trials as being quite effective at both decreasing the inflammation and improving proptosis by reportedly on average of three millimeters. Besides that though, I should say that steroids are a strong anti-inflammatory agent that we use for these patients. And the intravenous form seems to be more effective and less prone to adverse effects than the oral steroids. The other agents that have been used are with their ups and downs in response, but probably [inaudible 00:29:46] is one that we've been impressed with here at Mayo. And that's an agent that I would still consider along with steroids and [inaudible 00:29:57] at this point.

Dr. Jason Barnes:

And is there a timeline that you consider in terms of stability regarding active disease, at which point you say they've been stable long enough that they're ready for surgery?

Dr. Marius Stan:

That's a very important question. And as you've heard from Dr. Stokken about patients going to surgery particularly for rehabilitative interventions, we want to see that the disease is not in a progressive phase. So we want to see probably about three months of stability. Sometimes if we have the luxury of the disease is not threatening in any way, three to six months is ideal because obviously shooting at a moving target makes it quite unpredictable in regards to the results down the road. So we want that stability at a minimum of three months I would say.

Dr. Jason Barnes:

And Dr. Stokken, we've talked about it enough, let's move on to surgery. When you evaluate these patients, they're stable from a thyroid eye standpoint, and you've talked to them about surgery. Can you explain a little bit what the surgery entails, what your goals of surgery are, and who else you're working with in this intervention?

Dr. Janalee Stokken:

Yeah, so surgery is always a decision that's made in our multidisciplinary group. When we see these patients, we work with ophthalmology in addition to Dr. Stan. And we make a decision as a group whether the patient will benefit, and what type of surgery they'll benefit from. In general, we have many options. And the options for surgical intervention somewhat depend on how severe the proptosis is. So there are several patients who have minimal proptosis and they may not need a large decompression to get the outcome that they want. Say they have noticed a subtle difference in the way they look and they don't have any exposure, keratitis or visual compromise. They may benefit from just a medial orbital decompression. And so those types of patients, we will plan to do an endoscopic approach where we take down the ethmoid cavity, expose the medial orbital wall, and take down that bony structure, but keep support of the globe itself by keeping the medial inferior strut in place.

And that we find is really helpful in limiting postop diplopia. In patients who have more significant proptosis, we will do as a combined procedure. I'll again do the medial orbital decompression. And then the ophthalmologists that I'm working with will often do a lateral decompression. And that is a procedure that's formed with an external excision, and the lateral orbital wall is taken down and fat is actually removed. And the goal of doing both of those together is that the way the globe falls back is more balanced. What we want to try to avoid is the most common adverse effect of surgery, which is worsening double vision or new onset double vision. And so the team will look at the degree of proptosis and the other symptoms that a patient has and make that decision prior to surgery.

Dr. Jason Barnes:

And Dr. Stokken, from a surgical standpoint, how do you counsel patients on outcomes and expectations in terms of how improved their proptosis will be both with medial decompression by itself, but also with the medial and lateral together?

Dr. Janalee Stokken:

Yeah, that's a good question. I think we usually think about getting somewhere from two to three millimeters of decompression per wall. And if needed, we could even add a floor decompression to get an extra few millimeters in patients who have severe proptosis. And so we'll usually counsel them somewhere along those numbers. Again, that can be very variable based on how much fat there is that's hypertrophied versus how much muscle there is that's hypertrophied, as well as if they've had previous surgery, or if there's just more scar tissue within the orbit, that kind of thing. So it's not a consistent number that we would really promise a patient. But again, we would kind of tailor our surgical approach based on the degree of proptosis that they had prior to surgery. The other things we counsel patients on of course is the risk of worsening diplopia.

So we're not perfect at making the eyes fall back symmetrically in the exact same way. So the literature reports up to 30% or so worsening diplopia rates. So patients all are aware that this is possible, and that they may need a strabismus surgery even months after their decompression surgery if this were to happen. We also talk to them about similar risks that any endoscopic sinus surgery would have. So the risk of bleeding, which is about 1%. The risk of CSF leak or vision loss or things that we would describe with our patients who have sinus surgery that are all under 1%. From the lateral aspect, we always make sure they understand that there'll be postop swelling and bruising, and that that can last for several weeks. And then of course that they'll have an incision that the risk of infection and other things that can happen with a skin incision.

Dr. Jason Barnes:

And Dr. Stokken, how do you follow up with these patients in terms of postop cares? You've performed some sinus surgery, so how do you counsel them on rinses and that kind of thing?

Dr. Janalee Stokken:

Yeah. So with any endoscopic procedure, we like patients to use saline irrigations. And we'll provide patients with a bottle or a device to perform these irrigations, make sure that they don't use well water, city water. They should be using distilled water with a salt packet or their own salt mixture. We have them do those twice a day postoperatively, and then probably plan on doing them for about a month afterwards. I do not use packing when I can get away with it in the OR because we're really trying to make space for the eye. We don't want to put something back into the sino-nasal cavity that will work against us. So the irrigations are largely to flush out any blood or scabs and crusting that form in the postop period. That way when I see them back at the one week or two week mark, depending on the patient's schedule and where they live, that the debridement is limited.

At that endoscopic debridement, somewhere around 10 days after surgery we'll make sure that the middle turbinate hasn't lateralized. I'll suction out the maxillary sinus and make sure that it's nice and patent. And then largely not do a whole lot more. I find that they heal well because they don't have underlying inflammatory disease. And that thorough debridement is less helpful than it would be in a patient who's had polyps or some sort of inflammatory sinus disease.

Dr. Jason Barnes:

And Dr. Stan on your end, what's your followup like with this? Does this disease eventually burn out from an eye disease standpoint?

Dr. Marius Stan:

That is the expectation, and that will happen, but the time course that it might take to reach that burnout or inactive phase is not easily predictable. I think the antibodies help us to some extent. Seeing a titer of antibodies that declines is a very good indication. We know that when the titer of antibodies is less than five, that's probably very likely that we're not going to have significant problems down the road. And I would say in the opposite sense, when the antibody titer is more than eight, that's a predictor of a more severe disease. But there's a lot of individuals that are in between this cutoff point. And we cannot say that this will be in six months or 16 months.

So we look for this progression aiming from my perspective to keep their thyroid levels in normal range, minimize their risk factors. And again, we have to do this in a group that has the expertise to decide when we want to pull the trigger for a more aggressive course, based on the fact that most patients will improve. So we have to be mindful that sometimes observation actually is the better choice as opposed to a more aggressive course. And that's a case-by-case scenario.

Dr. Jason Barnes:

Well, thank you all both so much. This has been a hugely helpful conversation. Before I go into our summary, is there anything you'd like to add?

Dr. Marius Stan:

No, I'm okay with what was said so far.

Dr. Janalee Stokken:

Yeah. Dr. Barnes, you've done a nice job.

Dr. Jason Barnes:

Great. Well, we'll go into our summary. Thyroid eye disease affects close to a quarter, but up to even 50% of patients who experience Graves' disease and is characterized by an active phase and an inactive phase, which can be variable in length. The cause of thyroid eye disease is an autoimmune reaction that leads to the accumulation of fibroblasts, glycosaminoglycans and adipogenesis in the orbit. Clinical workup includes evaluation of proptosis using exophthalmometer as well as assessing severity using the clinical activity score. And from an ENT side of things includes history taking in terms of sino-nasal symptoms, as well as rigid endoscopy. Laboratory evaluation is helpful in determining how active the disease is, as surgical intervention is not often offered during active disease unless it's in certain cases like trying to prevent optic issues. Surgery is offered to improve cosmesis, but it's also offered in the setting of optic neuropathy, keratitis and ulceration. Surgical intervention includes endoscopic medial orbital wall decompression, and our ophthalmology colleagues can also perform lateral wall decompression for a more comprehensive decompression. Dr. Stan, Dr. Stokken, thanks so much. Anything else that you'd want to add?

Dr. Marius Stan:

Thank you for inviting us to participate. I would say that we're, both Dr. Stokken and myself fortunate to be in this multidisciplinary environment in which we can operate with expertise from all angles. And I would say that that is the desired way in which these patients should be managed in a consultative fashion with all the disciplines that we've discussed about.

Dr. Jason Barnes:

Well, I'll now move into the question asking portion of our time. As a reminder, I'll ask a quick question and then wait a few seconds and then give the answer to the question. So the first question for this episode is, what are the components of the clinical activity score used to evaluate thyroid eye disease?

So as a reminder, Dr. Stan went over this, the seven initial elements are pain at rest behind the eye, pain with eye movement, redness of the eyelids, redness of the conjunctiva, swelling of the eyelids, chemosis, also known as edema of the conjunctiva and swollen caruncula, which is the triangle at the medial aspect of the eye. So those seven aspects compose the initial clinical activity score, and a score greater than three is considered active disease. Dr. Stan also mentioned a total of 10 points, which is an addition of three points for ongoing comparison with last visit. The second question is, what is the pathophysiology of Graves' disease and more specifically thyroid eye disease?

So as a reminder, Graves' disease is an autoimmune disorder in which autoimmune antibodies are typically directed at the TSH receptor, also known as the thyrotropin receptor. And the orbital pathophysiology more specifically is likely driven by the production of glycosaminoglycans and fibroblasts, as well as adipogenesis in the orbit that leads to proptosis. And finally, what are the surgical considerations when approaching thyroid eye disease? As we discussed with Dr. Stokken, we can offer a medial and lateral orbital wall decompression. Medial wall decompression is performed endoscopically by the ENT folks. Whereas, lateral wall decompression is performed with our ophthalmology colleagues. And as we said, this should often not be done during active disease, unless we're trying to save vision. Additionally, diplopia can be an adverse effect to this, and patients might require strabismus surgery following this if they are continuing to struggle with residual diplopia. Thanks so much, and we'll see you next time.