



# INTERVIEW TRANSCRIPT

DISCUSSIONS WITH WORLD-LEADING EXPERTS

## **Mast Cells: A Link Between Migraine, POTS & EDS?**

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**Introduction (00:05):** Some people with migraine also experience symptoms and diagnoses that go beyond or interact with their migraine. This might include symptoms like flushing, dizziness, fatigue, or joint pain. Mast cell activation syndrome [MCAS], postural orthostatic tachycardia syndrome [POTS], and Ehlers-Danlos syndrome [EDS] are among the conditions increasingly recognized alongside migraine. Today we're joined by Dr. Jennifer Robblee to help us make sense of these connections. What the science tells us so far and how understanding these links might influence care and management for people living with complex migraine presentations. Dr. Robblee, welcome to the Migraine World Summit.

**Dr. Robblee (00:40):** Thank you so much for having me, and very happy to be here.

**Kate May (00:42:50):** Thanks. So it's your first time joining us on the summit. Can you tell us a bit about your work and what led you into this field of migraine?

**Dr. Robblee (00:50):** Absolutely. So I'm an associate professor at Barrow Neurological Institute and my area of interest is in refractory migraine and status migrainosus. So I spend all day, every day, either doing research or seeing these patients who just have this disease that's extremely debilitating, and is extremely hard to get control of. And many of these patients have these three conditions that we're going to be talking about today.

**Kate May (01:19):** Brilliant. Thanks so much. I mean, I have so many questions to ask about your work, especially in status migraine, but let's unpack the topic we've got today. I'd like to dive in by talking about mast cells and migraine. What exactly are mast cells, and what do they do in the body?

**Dr. Robblee (01:33):** Yeah, so mast cells are, simplistically put, part of your allergy system. We do know that they are part of the underlying migraine pathophysiology, but exactly how directly connected it is to migraine is not clear. So the whole pathophysiology of migraine is extremely complex, but to put it simply, there's stuff that happens out in the periphery of the brain. That's where the coverings of the brain, like the dura, are and some of the blood vessels that are out there.

**Dr. Robblee (02:05):** And we know there's a bunch of chemicals that get released and that leads to a whole stream of things happening. So that's things like changes in the diameter of blood vessels, a bunch of proteins that get released, the pain receptors called nociceptors — those get activated and sensitized. And then one of the things that happens is mast cells become involved and can lead to something called mast cell degranulation. And all of that then feeds down and leads to the symptoms of migraine, like pain.

**Dr. Robblee (02:34):** So we know that they're there. We know that it's something that is seen when we look at all the little nuances of migraine. It's not the main driver of migraine, but it is a piece of the puzzle. And then when you're talking about mast cells in general, in allergy, it's one of those things that get, you can say, again, simplistically, they get activated as part of the allergy system.

**Kate May (02:58):** Yeah, interesting. I like what you said there about a piece of the puzzle. We know this is a complex condition, and there are factors and comorbidities and other things that can feed into that complexity. So I'm going to touch back on that later on. But I'd love for you to explain what mast cell activation syndrome is and how it might be diagnosed, how it might present.

**Dr. Robblee (03:17):** Yeah, so in 2022, there was actually consensus criteria that were created. So these are based on expert opinion and based on literature reviews. So they are not validated. There's definitely changes that will happen to it over time as we learn more. They're divided into three different pieces. The first part is about the symptoms. So it requires that you have episodic recurrent symptoms that are affecting at least two different organ systems.



**Dr. Robblee (03:45):** And they're all symptoms that they know are associated with symptoms that can be from mast cells and the associated chemicals. So the different organ categories that they have are skin, your gut, your respiratory system (nose and eye-type symptoms), your cardiovascular system, brain, and then systemic, so like whole body. The skin symptoms that they list are flushing, urticaria, and angioedema. So those are some allergy-type symptoms.

**Dr. Robblee (04:14):** The GI symptoms are things like abdominal bloating, cramping, pain, nausea, vomiting, and diarrhea. The respiratory symptoms are things that you might see sort of that make you think about asthma, like wheezing, chest tightness. The nose and eye symptoms are things like itching, stuffiness of the nose, the eyes getting bloodshot. The cardiovascular symptoms are drops in blood pressure, fast heart rate, chest tightness, or pain. The brain symptoms include brain fog and, of note, headache.

**Dr. Robblee (04:45):** And then the systemic symptoms are things like fatigue or having a full blown allergy reaction like anaphylaxis. The second part of the criteria are basically that you're having some sort of improvement in your symptoms when you're using a treatment that has an effect on the mast cells. So that could be histamine receptor antagonists, that could be antileukotrienes, that could be blockers of prostaglandins, mast cell stabilizers, or specifically a medication called omalizumab.

**Dr. Robblee (05:14):** And then the third part is that you have an increase in your biomarkers. So when you do a blood test or a urine test and you look at what your baseline is, and then when you test it in the middle of a mast cell attack, you should see that these are increased at least two times above your baseline. The one that is felt to be the most reliable, or the best, is your serum tryptase.

**Dr. Robblee (05:36):** But others that they look at are 24-hour urine histamine metabolites, leukotriene E4, and then something that's called your PGD2 metabolites [prostaglandin D2 metabolites]. And you basically are going to measure those; you want to have your baseline so when you're in between an attack, you can compare those two.

**Kate May (05:57):** That's really fascinating, I think. It's interesting to listen to what might be going on there and how it might respond to treatment and that process. But it also sounds like there's a lot of similarities with migraine, particularly with the head symptoms. How might you tease out whether it's going on or what can be attributed to migraine? What might be mast cells? Yeah, how do you pull that apart?

**Dr. Robblee (06:17):** Yeah, it's a tough one because if you look at all of this, nausea and vomiting, those are literally in our migraine criteria. I've definitely seen people who have migraine and they get some GI upset leading up to the migraine attack. And I've seen that even include diarrhea. It's not uncommon to have what we call cranial autonomic symptoms. So having a stuffy or runny nose, again, that's not uncommon in migraine. Obviously, headache is a big piece of it. And many people report brain fog and fatigue, especially when they have more constant symptoms.

**Kate May (06:47):** That's really interesting to hear. And we've had a lot of interest in this topic from within our community. Jessica from our migraine community has commented that many people might not be aware of mast cell activation syndrome and the link to migraine. Can you tell us how common it is? Is it something that's easy to miss?

**Dr. Robblee (07:03):** Yeah, it's a hard one because we don't actually have a good sense of its epidemiology. And that's really true for all of these. The hard part is when we get into talking about mast cell activation syndrome. There's actually five different subtypes. So there's the most uncommon, which is primary, like mastocytosis. There's ones that are secondary. There's ones that have a combination of the first two types. There's a genetic one that affects your alpha tryptase.



**Dr. Robblee (07:33):** And then there's the idiopathic, which is really what we're talking about in this conversation. And again, there's a lot to know. We don't have a sense. And there's a lot of people, I think, who get the diagnosis who haven't been tested. And then a huge amount of people who probably have this and just have not been tested.

**Kate May (07:49):** So what might a mast cell activation diagnosis mean when it comes to migraine management?

**Dr. Robblee (07:54):** I think it's an important question. Unfortunately, we don't have a huge amount of evidence to really guide us there. So what I'm saying is really just based on my experience and a little bit of anecdotal stuff. I do find these patients tend to be more sensitive to medications, so you do want to start at a much lower dose and really just slowly build.

**Dr. Robblee (08:13):** So for patients, if you've been on treatments and you find you're just not responding to anything, make sure you're being started on the lowest possible dose and you're not giving up on a medication too fast. So often I'm starting with a half tablet or liquid just so I can get their body used to it and slowly build the dose up. It's just going to take you longer to get up to a fuller dose in some cases.

**Dr. Robblee (08:35):** The other thing is, while it's much less common in idiopathic mast cell, it is possible to get anaphylaxis. So if you have patients who are really prone to anaphylaxis, you want to make sure that they're comfortable with the treatment; they have an EpiPen available for if they were to have a reaction. So there's some things to think about, about being more cautious with how you're approaching things like that. That would be, I think, the biggest piece.

**Dr. Robblee (09:00):** And then whether or not the treatment that they use for MCAS is going to have an impact on migraine, that part we don't really know. There's a little bit of observational data to suggest that it might, but nothing to say, you know, we should be using a mast cell directed treatment as part of treating migraine per se.

**Dr. Robblee (09:23):** But if you are on treatment for mast cell, then hopefully it'll help with decreasing the overall symptoms that you have related to migraine because those two conditions are going to interact.

**Kate May (09:33):** Yeah, fascinating. And you mentioned before, there are different treatment options and it might be a part of someone's picture. What are some best promising approaches to management if these two conditions might be going on?

**Dr. Robblee (09:43):** Yeah, so I mean, I have patients who are on all sorts of different treatments. Usually I see them first start with some sort of H1 or H2 histamine receptor antagonists. I see a lot of them on mast cell stabilizers. So things like cromolyn or ketotifen are really common ones. Sometimes things like aspirin get used. I find it doesn't get used as much more for the idiopathic. And then some people do end up on the monoclonal antibody, which I've definitely seen some people do well with.

**Dr. Robblee (10:16):** So things like that are often tried. I sometimes will try a medication that's old that we used to use in more pediatric migraine, cyproheptadine. I haven't had amazing success with it, but it's something that I can kind of, just thinking outside the box sometimes with these patients. A lot of these patients also try different sorts of diets where they're trying to remove things that they are more sensitive to, like, say, a low-histamine diet.

**Dr. Robblee (10:43):** And again, anecdotally, I've had patients report that they've had some benefit from that, but I don't have any strong evidence to suggest that that's something you should be doing.



**Kate May (10:51):** All right. So just for those who are listening along at home, can you explain what you mean by idiopathic versus a nonidiopathic presentation?

**Dr. Robblee (10:58):** For sure. So as I was mentioning, there's these five different phenotypes of mast cell activation syndrome. There's primary, where you have what are called clonal mast cells, and that's things like mastocytosis. There's secondary, where different components of your allergy system are involved, so things like your IgE, your IgG, your complement. There's combined where those first two, basically, there's elements of both of them. There's a hereditary form.

**Dr. Robblee (11:26):** And then idiopathic is basically when you don't, you're not part of any of those first four categories and we don't really know why you have it. Idiopathic is basically medical speak for "we don't know."

**Kate May (11:35):** So an unknown cause, it's just developed and can't clearly trace it, but it's going on and this is what we've got to do. Yeah. Yeah. That makes sense. Thanks for explaining that. So we've discussed mast cell activation syndrome, but I'd like to link into other conditions as well. Together with mast cell activation syndrome, postural orthostatic tachycardia syndrome, also known as POTS, and Ehlers-Danlos syndrome, sometimes known as the autonomic trifecta. What are these conditions and what links them together?

**Dr. Robblee (12:03):** For sure. So postural orthostatic tachycardia syndrome, better known as POTS, is a dysautonomia. By definition, you have a 30-beat-per-minute increase in your heart rate within 10 minutes of standing. So these patients will get this sudden racing heart. They get a lot of orthostatic dizziness where when they're upright, they feel more dizzy. And it's very commonly associated with mast cell. And then Ehlers-Danlos syndrome. So it's basically a whole bunch of different genetic disorders.

**Dr. Robblee (12:35):** And then there's this one that's called hypermobile EDS. And that one actually doesn't have an identified gene. But in 2017, they came up with this set of clinical criteria. And so right now, the diagnosis basis is based on those criteria. We do know that there seems to be this trifecta of the three of them, and they commonly go hand in hand. And there's a lot of overlap in the symptoms as well. So it gets a little bit messy.

**Dr. Robblee (13:01):** But at least one study where they looked at just under 200 patients found that almost a third of patients with both POTS and EDS also had mast cell versus when they looked at people who did not have those conditions, the rate was about 2%. So it seems to be that there's a much higher rate in people who have these other conditions. And then migraine is often thrown in as part of a fourth piece of the puzzle.

**Dr. Robblee (13:24):** We know that in general, there seems to be dysautonomia in migraine, and it seems like it's higher in those with more disability. And then we do know that people who have Ehlers-Danlos, there does seem to be higher rates of headache in those people. Migraine for sure. But then there's all these other things that make exactly what the diagnosis is a little bit unclear, like patients with EDS because of the ligament instability can get atlantoaxial instability.

**Dr. Robblee (13:55):** They can get CCI, where there is craniocervical instability. There may be an association with even some high pressure symptoms, low pressure where you're more prone to a CSF leak, maybe higher rates of Chiari [malformation]. But again, a lot of this is anecdotal.

**Kate May (14:10):** Thank you so much for explaining all that, Dr. Robblee. So there's a lot of autonomic dysfunction that could be going on here. Some of the symptoms of these conditions sound really similar to migraine. How might it make migraine symptoms worse or influence and interact with migraine?



**Dr. Robblee (14:25):** Yeah, so again, this is all anecdotal, but in my experience, when one condition is under poor control, often the others also flare. So one of the first things that I do when someone's flaring is try to get a sense of, is it that they're in the middle of status migrainosus? So then their POTS is also feeling really bad. Or does it sound more like that's been the primary issue and they're just, they're kind of having more headaches in the setting of that.

**Dr. Robblee (14:53):** And it can be really hard to tease apart where you should be focusing your management. And sometimes you end up just focusing on optimizing all three. So the honest answer is you can't right now. I don't have a good sense to tease them apart.

**Kate May (15:08):** Yeah, absolutely. I think I can imagine there are people listening on that may be experiencing that, that do find that difficult. And it's hard to manage when there are multiple conditions going on. You mentioned before that there's some things we do know, some things we don't know. Is this an emerging area of research? What's there still to learn in this space?

**Dr. Robblee (15:27):** I mean, I think there's still so much that we need to learn. One of the hard parts is that I don't know that ownership has been as well taken of each of these conditions. So for instance, for POTS, should this be more managed by cardiology? Should this be more managed by neurology? It's really hard to find an autonomic clinic where they really do focus on this. It's not uncommon a patient has seen a cardiologist, but they've never been worked up for this and had a tilt table test.

**Dr. Robblee (15:58):** And it's not uncommon that they've seen a neurologist. And they've got all this dizziness or these weird episodes, and they've been diagnosed as functional; or they've been diagnosed as it maybe being inner ear; or it's something cardio, so you should go see cardio; and just never being tested for some of these things. So that's a really common issue.

**Dr. Robblee (16:19):** They might have the diagnosis of POTS, but they haven't gotten the diagnosis of mast cell, and then you're going to need some separate treatments. And there is some overlap in what they might try, but one is very focused on managing the allergy system and one is very focused on managing POTS.

**Dr. Robblee (16:36):** And then when it comes to EDS, there's absolutely no one who owns EDS. I don't even know where to refer these patients to other than someone who is a physical therapist that is EDS aware. It's not really managed by rheumatology. It's not really managed by genetics because there is no genetic diagnosis. Right now, all we have is clinical criteria for it, and often they end up more in a pain clinic, but you don't want to just stick someone on an opioid for the rest of their life. There's a lot of other things to manage, so it's tough.

**Dr. Robblee (17:07):** There are definitely groups that are trying to do registries and trying to learn more and put out some guidelines to help manage, but I think the general trend is not enough movement there. I think one silver lining of COVID is that because a lot of patients post-COVID, as part of long COVID, had things like POTS; it's at least pushing that. And then because these all go hand in hand, it's also pushing along some of these other conditions.

**Dr. Robblee (17:35):** In the migraine world, we're starting to become more aware that we're starting to talk about it a little bit more, but I still don't think it's enough. If you go into PubMed — which is one of the places that we use to look up our scientific articles — and search migraine and MCAS, there's basically no study that comes up. So there's just not enough yet. And the hard part is when we don't have definitive criteria to rule in and rule out something like mast cell.

**Dr. Robblee (18:08):** And right now, what we have is expert opinion and some consensus criteria. The other question is, where is this moving? How do we know for sure that that's what the diagnosis is? Because right now, all we have is expert opinion. And so, what we use to diagnose it right now, if we look in five, 10 years, it might be a completely inaccurate diagnosis.



**Dr. Robblee (18:28):** So that's the other thing is even some of the studies that we do have now, we're not sure how those will be looked at in several years. So I think it's a hard time. I think we need to do the research. And I think a big piece of this is going to help with the disability. And the better that we can understand how all of these things interact would be good. But a first starting place is just even having a sense of how common all of these are, especially in the migraine world. Like, what is the epidemiology of these? And we honestly don't know.

**Kate May (19:01):** Yeah, it's fascinating. It just sounds like there are so many gaps in this space and what's maybe available for people that might be going through these symptoms in what we understand about this. You've mentioned a few times a lot of your examples have been anecdotal and that there isn't this huge evidence base for some of these things.

**Kate May (19:18):** So I can imagine it's incredibly challenging when someone might be going through these symptoms or some of these diagnoses to piece together what is actually going to be right for them. Any reflections from your experience in practice? What are the challenges when these things come up and how do you deal with it?

**Dr. Robblee (19:33):** Yeah, well, I think the hardest part is I'm not an expert in that, so I'm not an expert in POTS. I'm not an expert in EDS. I'm aware of them. I know how to diagnose POTS because I have access to a tilt table test. Often these patients already have such complex migraine that I don't have the knowledge or the time and space to help them with that part. But it's hard to get them into a clinic where they really can get those things well controlled, officially diagnosed.

**Dr. Robblee (19:57):** And then trying to make sure that you do that good collaborative care is just, it's really difficult right now. We just don't have a good enough system and set up for all of it.

**Kate May (20:07):** Yeah, it sounds really challenging to deal with in management and in treatment, as I'm sure it's incredibly challenging for people that are living with these conditions. I'd love your reflections on if someone is diagnosed with migraine and is experiencing mast cell activation syndrome, one of these other conditions, or perhaps some of the symptoms we've discussed. It could be an important piece in their puzzle. But with more than one diagnosis, different models of care, engaging research, I can imagine it's incredibly hard to navigate the day-to-day management. What advice could you give to someone who might be navigating this experience of diagnosis and management?

**Dr. Robblee (20:41):** Yeah, it's a good question. I think the first part is find some people who are willing to support you in that care and make sure that you get the correct diagnosis. There are criteria to diagnose each of these conditions. You may have symptoms that sound like these, but making sure you're actually getting the correct diagnosis is the first step.

**Dr. Robblee (21:04):** I definitely see a lot of people where they're given these diagnoses and they've never had a tilt table test. They've never had the mast cell activation tests. They've never had anyone go through the clinical criteria for EDS. And that's difficult because then are you actually treating the right thing or is something else actually the cause of it? And getting in to someone who can do all those things is important. I don't have great access to all the tests for, say, mast cell activation syndrome, so it's hard for me to, say, test for that.

**Dr. Robblee (21:37):** But an allergist is going to know all the right things and make sure you don't have something else like mastocytosis, but you need one who's willing to go down that path with you. And the EDS part is hard because, again, it's got these long clinical criteria. You need someone who's comfortable with knowing when you should have one of the other genes tested.

**Dr. Robblee (21:54):** And at the end of the day, a lot of the treatment for that is really going to be more physical therapy oriented, which I think is also one of the reasons why a lot of physicians aren't



owning it, because there's not a big piece that we can really do other than make sure there's nothing dangerous that it's causing. So looking for all the other associated symptoms, but often that's GI. So if you're a rheumatologist, you're not going to manage the GI stuff.

**Dr. Robblee (22:19):** Or if it's craniocervical instability, you're not going to manage that. And when do you know to send to a surgeon versus not? And should you? So it's a tough one because I think there's so much to learn, so much uncertainty that a lot of people just don't feel comfortable with it. So try to find people who are comfortable and at least with supporting you through the journey. Educate yourself on what is scientifically there, but know that there is a lot of things that aren't.

**Dr. Robblee (22:49):** So sometimes you're going to have to go outside the box and you're going to decide what your level of comfort is and weigh the risks with any potential benefit. And there are lots of studies and registries out there, so if you want to help move it forward, those are great ways to get involved. I know particularly for EDS, they had a really great registry where they were trying to get people with an official, and they needed a physician-confirmed diagnosis for you to enroll.

**Dr. Robblee (23:17):** But those are great ways to help move the field forward because right now, as I said, a lot of times we're just, we're doing the best we can, but the best that we can right now is not good.

**Kate May (23:28):** Sounds like a really tricky space. If someone was listening along thinking this is relevant to me or they had some concerns, where can they seek help? What types of doctors or health professionals? I know you've mentioned rheumatologists and allergists, but there's so many different types of doctors. It can be a bit overwhelming. Can you let us know where are some places people could look for help?

**Dr. Robblee (23:47):** Yeah, so I mean, there are some autonomic clinics around the world. I know in the U.S. there's a couple of different places that have them, but they're exceedingly hard to get into. So if you have access to one of those, I mean, that's a great place to start because they're going to be familiar with POTS, with other dysautonomia that might look like POTS but are not.

**Dr. Robblee (24:04):** And then with these associated conditions, because they're very used to diagnosing mast cell and Ehlers-Danlos and having a good sense of they're the ones who manage it, where to send you to. So that would be the ultimate is if you can get into an autonomic clinic, then that's the first go. Unfortunately, those are few and far between, and even if you know of one, they may not be accepting new patients. And even if they are accepting new patients, it just might be too far for you to travel for it to be feasible.

**Dr. Robblee (24:33):** So then it's trying to find people locally who are familiar with it. And it's going to be hard to tell, but they should be, if they're wondering about POTS, they should be getting something like a tilt table test or an autonomic reflex screen, or at least looking at your vitals once you've been lying down and standing up and seeing how your blood pressure and heart rate changes over the following minutes.

**Dr. Robblee (24:56):** For mast cell, again, there is some controversy about what the best blood tests and urine tests are to do for it. I've definitely seen people where there's some question about, are we even testing the right things? So do you absolutely have to get those blood tests to diagnose mast cell? I'm honestly not sure. But someone who's at least talking through about, scientifically, how do we decide that you have mast cell versus something else like mastocytosis, and why aren't they concerned about these other conditions? And why are they choosing the treatments they're choosing?

**Dr. Robblee (25:27):** So you want someone who's at least trying to take as scientific an approach as possible. And then for Ehlers-Danlos, it's going to be hard to find someone to give you an official



diagnosis. You should have some hypermobility, so at the very least, you should have what's called your Beighton score, depending on your age, should be high, and you can look up the Beighton score.

**Dr. Robblee (25:48):** It's basically going to be, can you touch your thumb to your wrist? Does your pinky go back at least 90 degrees? Are you double-jointed at your elbows, at your knees? Can you keep your knees straight, put your palms flat on the ground? So a significant number of those should be positive. Or if you're older, it might be that they historically were, but now because of changes in arthritis, you can't do it. And then your best thing there is find a physical therapist who is comfortable with EDS to help you with managing that.

**Dr. Robblee (26:16):** And then any associated symptoms, like if you have a lot of gut stuff, you may want to get in to see a GI specialist. If you have a lot of pain, then you may want to get into a pain clinic, but you also want to be careful that you're not getting to one where they're just throwing you on opioids and then you're not getting that full-picture management. You probably want to try to get into a headache specialist. With this constellation of things, if you can get a headache clinic, that's best.

**Dr. Robblee (26:40):** But again, those are hard to get into, so at least a neurologist. So often these patients are going to have multiple different specialists, and that's kind of the best that there is right now, unless you can get into an autonomic clinic where they're comfortable managing a whole constellation of symptoms.

**Kate May (26:57):** Thanks. Thanks for walking us through that. I think it sounds really tough to navigate, that there's lots of options, that options is really important when it comes to managing migraine. We've covered so much today, and I'm sure there's so much to learn in this space. It sounds like there's lots of gaps. Where is this field of research and practice heading, and what are you looking forward to seeing in the future?

**Dr. Robblee (27:17):** Yeah, I mean, I think some of the biggest things is having an easy way to test for what conditions you actually do have. I think we have a good way to say whether or not you do have POTS. I think we've got a good way to diagnose migraine based on your clinical criteria, but I don't think a lot of people are comfortable with the tests that you have to order for mast cell activation syndrome.

**Dr. Robblee (27:44):** And with those ones, you need a baseline and then you need to do them again when they're in the middle of an attack. And that can actually be really hard to get just feasibly; they're hard to get anyway. And so that's tough. I hope that eventually we get more than just expert consensus and we feel more comfortable with how to diagnose that.

**Dr. Robblee (28:05):** So if I have someone coming in and they have symptoms that sort of sound like that and I'm trying to figure out how to get them under better control, I have an easier way to say, not just, "Hey, you might have mast cell, do you want to see an allergist? Like, hey, we've diagnosed you POTS on tilt table, let's see if you have mast cell so we can see whether or not we need to get to an allergist."

**Dr. Robblee (28:20):** And then for EDS, that maybe eventually we do have an easier way because the clinical criteria are pretty cumbersome, and I don't know them well enough to do it myself, and I don't know where to send these patients. So my hope is that we start to get easier ways to direct, whether or not these patients have the diagnosis and where to have them go so that we have the next steps.

**Dr. Robblee (28:45):** Because it's not necessarily going to be your neurologist or your headache specialist that is managing these, but you do want them to be aware and be able to potentially identify because that might be the person who first recognizes that you have these symptoms that then correlate to one or all of these conditions.



**Dr. Robblee (29:00):** So that's where I hope it goes, is where I can start to just have a better sense of identifying patients, getting them into the appropriate referral. And then, hoping that we have a sense of whether or not that treatment actually improves the underlying migraine condition would be, I think, the other thing that I really hope that we understand. I do see a pattern of that, but I then definitely have people where they're like, "Yeah, my POTS is under great control, it's migraine," or, "Yeah, migraine's under great control, it's my POTS." So again, it's not a 100% thing either, as nothing is in medicine, of course.

**Kate May (29:33):** Yeah, fantastic. Thanks so much for summarizing that. I think there's so much to learn and lots of interesting things to look out for in the future for people that might be managing these conditions. Are you able to leave viewers with one key insight about how these overlapping conditions fit together and what it might mean for people's migraine management?

**Dr. Robblee (29:50):** I think it's important to know that these conditions are probably quite common. Again, we don't have perfect epidemiology for them, but you're not alone.

**Dr. Robblee (29:59):** And while some of what I'm saying sounds a little bit hopeless and frustrating, know that there is a lot that we need to learn, which means that even if things aren't great right now, there are new things that will potentially be on the horizon that will really help. And that there are physicians out there who are going to be willing to help you get these diagnosed and help you get these managed so that you can feel better.

**Kate May (30:23):** Well, thanks so much for joining us for this discussion. I know it's a tricky topic to talk about because there is so much more to learn, so I really appreciate your insights and reflections and teasing apart the anecdotal evidence versus what's in the literature and what the science tells us. I certainly learned a lot today and really appreciate your time and energy in this discussion. Thanks so much.

**Dr. Robblee (30:49):** Absolutely. Thank you.