

# Live Q&A Session

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[00:00:05] **Krissy Dilger:** Hello everyone. Welcome to our Q&A session with our experts, Dr. Kyle Blackburn, and Dr. Jonathan Galli. My name is Krissy Dilger, and I am the manager of research and programs at the Siegel Rare Neuroimmune Association. So first, I just wanted to say thank you both for joining us today and answering some of these questions.

[00:00:31] **Dr. Jonathan Galli:** My pleasure.

[00:00:35] **Krissy Dilger:** So, to start off, Dr. Galli, can you just tell us what causes TM and have any predisposing factors been identified?

[00:00:42] **Dr. Jonathan Galli:** Yeah, that's a great question. Whenever I'm meeting a patient for the first time, who's getting a diagnosis of transverse myelitis, what I like to explain to them is transverse myelitis generally is an umbrella term for an inflammatory spinal cord lesion. And what causes it can be one of many different diagnoses, one common cause of it is multiple sclerosis, but there are other rheumatological conditions, other autoimmune conditions that can cause it, but sometimes we don't find a cause if you will and it ends up being either -- sometimes it can happen post viral and sometimes you can get it post-infectious, things like that. Sometimes you can just develop it for no clear cause in which we call idiopathic.

[00:01:47] And so there's a myriad of different causes of transverse myelitis, although oftentimes again, it ends up being that idiopathic or post-infectious cause. And then predisposing factors, certainly there's a genetic predisposition for certain autoimmune conditions and things along those lines. But one thing that I always tell my patients who've developed transverse myelitis is that there was nothing really that you did that caused this because oftentimes that's something that I think patients come to me and they say, what did I do wrong? And really the answer is nothing. It was just something that happened on its own. I don't know, Dr. Blackburn if you wanted to expand on that at all.

[00:02:30] **Dr. Kyle Blackburn:** No, I absolutely agree with what you're saying, and you nailed it. This is a condition that actually has a number of different causes. And I think the way that doctors sometimes talk about it is a little different than the way that patients do. Because I think at the end of the day, our patients have been told they have transverse myelitis and they're often thinking of that idiopathic condition. But I always like to emphasize when somebody comes to us with that label, our job is to look for all of these other causes and make sure this is in even indeed inflammatory and not something else. So, we don't have neat underpinnings of what causes these, what we call idiopathic cases, the cases where we have not figured it out. But certainly, there are a number of causes that we have identified and as we continue to progress, we're going to find more.

[00:03:23] **Krissy Dilger:** Thank you both. Those are great answers. And I think hopefully, like you said, in the future, we'll expand on our knowledge from what we know right now. Our next question is, what does idiopathic mean? And what percentage of people with idiopathic TM have reoccurrence? Why does reoccurrence happen? And does it worsen with each occurrence? Dr. Blackburn, do you want to start us off?

[00:03:52] **Dr. Kyle Blackburn:** Sure. So, the word idiopathic, basically it's medical jargon for lack of a better term and it really just means a disease that does not have a known cause. So, for example, as we were talking about earlier, when doctors talk about the umbrella of what transverse myelitis is, there are diseases like multiple sclerosis and diseases like NMO which we talk about here at the SRNA, those diseases can cause transverse myelitis. But we refer to it as idiopathic when we've done all the work up and for everything that we've done and considered, we just cannot identify the cause. And that will be under that umbrella of idiopathic transverse myelitis or idiopathic myelitis depending on who you ask.

[00:04:39] There's a question about what's the percentage of patients that have idiopathic TM have a recurrence. That's a really interesting question. So, something that hasn't been investigated well but I really think most of us agree that rate -- for somebody that has true idiopathic TM is extremely low. And in fact, if somebody were to have a relapse, I think many of the people that we work with are going to be reconsidering that diagnosis and potentially somebody may be miss reclassified as having multiple sclerosis depending on what that new evaluation yields, they may be reclassified as having a type of neuromyelitis optica. Whenever somebody has a recurrent, it's actually a red flag to me that we need to reconsider that idiopathic label and really dig deeper.

[00:05:30] And then, they asked why does a recurrence happen? To address that, I think there's a reason. We don't understand why some of these conditions are relapsing, but what that typically tells me is that the immune system is for some reason, persistently confused. There's a tendency for it to want to go back to the nervous system again and again, and that can warrant a different treatment approach as opposed to most of our idiopathic and those post-viral things that Dr. Galli was talking about, they tend to only occur once. And then the question, does it worsen with each occurrence, I can't say that having one relapse may necessarily predict that the next one is going to be worse. Certainly, if someone's having relapses, that's a time when we may want to consider intervening. Dr. Galli, how do you feel about what I said there?

[00:06:27] **Dr. Jonathan Galli:** I completely agree. And I think the really important point that Dr. Blackburn is making is, if somebody comes in, we say yes, they have transverse myelitis. We do our work up; we don't see anything. So, our work up is looking for conditions that have a high risk of relapsing and causing further damage down the line if we don't do anything. Again, if it's idiopathic, I think of that as a one-off event, a monophasic event. And if I have a patient that I suspect has idiopathic transverse myelitis, they develop another lesion, I will definitely go back to the drawing board and ask myself, what am I missing because buy the books, if you will idiopathic or post viral, really shouldn't relapse. And so that's a really important thing to think about. Because generally if somebody's had idiopathic transverse myelitis, I don't necessarily need them on long-term immune therapy because it's not something I suspect to come back. However, if somebody does have a condition that is causing relapsing, transverse myelitis, that's somebody who I'm definitely going to totally change that management plan and think about putting them on immune therapy to prevent a relapse.

[00:07:48] **Dr. Kyle Blackburn:** And I wanted to elaborate on one other point you brought up Dr. Galli. I absolutely agree. I mean, the most of these idiopathic patients are not going to relapse and I have had people that have true idiopathic TM come to us and say I've had 4-5 relapses and we look at imaging and the symptoms they were experiencing and then we don't really find anything that clearly backs that up. And I often find in most of those cases, if we really dig that there's just a misunderstanding of a temporary worsening of symptoms that sometimes that you'll hear in MS world called Botox phenomenon and a relapse. And certainly, when

somebody's having a worsening of their symptoms, the obvious concern is this is a relapse, but the symptoms that these diseases cause can fluctuate wildly and can temporarily worsen with a lot of triggers. I'm in Texas today and it's about to hit 100 degrees. I'm not looking forward to it but many of our patients have learned over the years that they may notice worsening of their symptoms during those times and it's something that we try to counsel about because we certainly want to avoid people getting treatments they don't need because they're having a temporary worsening of symptoms due to a physical stress on the body.

[00:09:11] **Krissy Dilger:** Thank you so much. Hey, our next question is for someone whose TM occurred after receiving a vaccine and no other possible causes were found, can they get vaccinated after their TM onset?

[00:09:28] **Dr. Jonathan Galli:** Yeah, this is a great question. I generally will encourage my patients to get vaccinated. There's some suggestion that some of you can get post-vaccine inflammatory events. That data, certainly, in the MS world has not really borne out. And I oftentimes will tell patients, your risk of having this occur again is, in my mind, so low that the benefit of getting the vaccine and preventing something like influenza, or COVID now, that benefit outweighs any risk. And I like to also counsel patients and tell them, we also know that there could be neurological complications from things like influenza, COVID, and things like that. So that's generally how I go about counseling my patients.

[00:10:25] **Krissy Dilger:** Do you agree, Dr. Blackburn?

[00:10:26] **Dr. Kyle Blackburn:** Absolutely. If somebody comes to us with idiopathic transverse myelitis and then it seems to be closely tied to a vaccine, we tend to counsel them in the exact same way that is really thought to be a one-time event. And while it's completely understandable to be very hesitant about a vaccine in that setting, the data that we have and really the risk of this recurring seems to be exceedingly low. And even some of the data, I think from Guillain-Barre where there was some data to suggest that maybe a flu vaccine at some point may have been able to trigger a Guillain-Barre syndrome suggests two things. One that the risk -- I think is Dr. Galli has talked about the risk of having a neurological issue from the virus is higher than the vaccine. And then two that vaccinating down the road did not seem to have a recurrence. So, I tend to extrapolate that to our myelitis patients and say that this risk is very low, and I can only speak from experience but my patients that have gone through and gotten vaccinated really have never seen a recurrence.

[00:11:40] **Krissy Dilger:** Thank you. I think that'll be helpful for a lot of people who are trying to make these tough decisions. Our next question was a community question we got about advocacy for oneself in a clinical setting. So, what advice would you give to patients about how to advocate for themselves with medical professionals? For example, maybe something's not working for them, and the patient thinks that, they better understand what would work for them. Is there any advice you have about going about these conversations? Dr. Blackburn if you want to start us off?

[00:12:18] **Dr. Kyle Blackburn:** Sure. And this is always a really big struggle. There's definitely a power dynamic in a doctor patient relationship. And I think it's really important to try to diffuse that. If some part of a treatment plan isn't working for you, I think it's important that you as an individual feel imperative to speak up. I will say most of the time your doctor isn't actually going to be aware of that. If they're going to assume that you're taking treatment -- if for example, treatments is giving you issues and you're actually not taking it, they're going to assume that you're not having side effects unless you speak up to it.

[00:12:57] As you all may have experienced; it can be a pretty busy place to be a clinic. So, I always encourage people to be very vocal about what their needs are and how we can help. And I know sometimes that can be tough to do and sometimes it's even harder to be heard even if you are being vocal. And I think it's really

important to recognize that just like in other industries, it's really important to have a good relationship with your doctors and other providers and to feel comfortable with them. And if you're really feeling that you're not being heard, I think revisiting a second opinion and finding other places is appropriate at that point. So, I absolutely encourage my patients to speak up when there's issues and I really think people should.

[00:13:47] **Dr. Jonathan Galli:** Yeah, I really agree with that. And I will say this, and I will also preface it by acknowledging like, logistically sometimes this, what I'm about to say isn't possible from an insurance standpoint a location standpoint. But I think it's really important for that relationship between -- especially in our populations of these rare conditions that you find a provider that you feel comfortable with and really someone that listens, I think it's always probably a good idea to have a neurologist on board who at least on even if they're general because they should at least understand these basic symptoms and management.

[00:14:36] Dr. Blackburn and I see this day in day out. So, when I do an intake on a patient, I actually have a list of potential symptoms that I just commonly see that I run through. Like, so you don't even have to be like, oh, by the way, I'm having neuropathic pain, like that's going to be talked about. And like I'm going to address that every visit. And so, I think someone who's -- when you see a provider who's really comfortable with the condition, it's probably the easiest to have these discussions because we know what you're probably going through, and we've seen it. It's not anything that -- if I have a patient who's at transverse myelitis for 10 years and they say, my left arm pain is worse, again, I've seen that. So, I'm comfortable and I believe them.

[00:15:29] So like, I think just finding at least a neurologist I think is always helpful if you can and I always encourage if possible, seeking a second opinion if you're provider, and you just don't gel, or you don't feel listened to. I mean, I always tell my patients like if you want a second opinion, like doesn't hurt my feelings. So again, also logistically that may be challenging, and I understand that and it's hard. Probably what I would recommend.

[00:16:02] **Krissy Dilger:** It is hard. But these are important considerations. What percentage of individuals, women and men develop MS post-TM diagnosis? Can someone have a diagnosis of TM at the same time as a diagnosis of MS, NMOSD, MOGAD or another disorder? Dr. Galli if you want to start us off?

[00:16:30] **Dr. Jonathan Galli:** Yeah, I would actually have to pull up the data. I forget off the top of my head what percentage of patients with TM go on to develop MS. I forget the exact number, I apologize. But when I see somebody with transverse myelitis, MS is always on the differential if you will the potential cause of it. And how we risk stratify that, is really with brain imaging to see if you have lesions in your brain as well because those patients have a high likelihood of going on to develop MS versus if someone's got brain imaging and there there's no lesions, they have a very low risk in general of going on to develop MS. And part of the evaluation again as we -- and I'm trying to answer this and not confuse even myself here. But you can have transverse myelitis which leads to a diagnosis of MS, NMO, MOG and other things. So, you certainly can have them. Typically, we don't see like MS plus MOG plus things like that. But you can have transverse myelitis secondary to one of these conditions and it be your presenting symptom. So, I'm sorry, do Dr. Blackburn if you can clarify what I was just -

[00:17:52] **Dr. Kyle Blackburn:** No worries. This is something that I do talk about a lot in clinic too. So, I think as we were talking about earlier, transverse myelitis is an umbrella of several different diagnoses. So, somebody's first manifestation of MS could be "transverse myelitis." And then we either find at that time that they have other evidence to suggest that they actually have MS or later on as you talked about later on, it may become more apparent as they develop a second attack, which is characteristic of MS. And then of course, we may initially have someone come to the hospital with transverse myelitis with inflammation in

their spinal cord. And at that point, we may say this is your diagnosis and this is where people get confused and this process, it's an iterative process. It is a feedback loop.

[00:18:44] You come into a hospital with this episode of transverse myelitis, or you come to a specialty center with that diagnosis and your doctors are supposed to say, let's look at all the causes and figure out what's going on here. Eventually, that label may be changed. So, I always tell people, as you alluded to you can have this transverse myelitis secondary to MS or MMO or MOG, but at that point, it is no longer idiopathic. So, I wouldn't label you with that "diagnosis of transverse myelitis" when we actually mean idiopathic myelitis. So many, it's just that umbrella and TM can be a symptom of all of those diseases. But whenever somebody says it is their diagnosis, they usually mean idiopathic. So, I really don't think those two can co-occur.

[00:19:42] **Krissy Dilger:** Thank you so much for trying your best to answer that question. I mean, complicated.

[00:19:47] **Dr. Kyle Blackburn:** I think we need figures for that one. Like here's the breakdown.

[00:19:51] **Krissy Dilger:** Moving on to symptom management. What treatments are available to address numbness, nerve pain, and spasticity? Dr. Blackburn if you want to start us off?

[00:20:03] **Dr. Kyle Blackburn:** Sure. So pretty big topic. But maybe the first thing I'll say is for numbness. Unfortunately, I don't think I can say that there's a primary medical or surgical treatment that's going to fix numbness, especially numbness due to spinal cord injuries like myelitis. So, I sometimes see people that are miscommunicated with their doctors and their doctors think they're having nerve pain but they're actually just having numbness and that medications like gabapentin and duloxetine aren't going to help that. So unfortunately, that's the only thing that we have that will let that is time and potentially your body's own process, recovering it. But for the uncomfortable things like nerve pain and spasticity, we definitely have treatments.

[00:20:52] So for nerve pain, we often start with medical therapy if it's bothersome. And I always tell people with these symptoms, this is really trying to treat -- what this is trying to treat your symptoms and any discomfort or effect on your quality of life they're having. There are some people that have minor nerve pain that really doesn't seem to be the biggest driver of their disability or the biggest driver of their quality of life. And I don't tend to treat that, unless it's really needed, but we have a number of medications and things like gabapentin and duloxetine and some seizure medications can often be helpful for nerve pain. And some of those can also help with spasticity. But in the spasticity realm, you may hear about medications like baclofen or tizanidine being fairly common.

[00:21:42] For specificity, specifically, I'll also add stretching is critical. I think no matter the degree of your specificity getting a stretching regimen is good for all of us. So, it's just good advice anyway. But specifically, if you have some specificity that's giving you trouble doing stretching is a good line to limber things up and keep it moving. In addition, beyond medical therapy, we can get into some interventions. So, there are certain units that are called neuro modulators like a tens unit that can be used in some cases for neuropathic pain. And sometimes people use that because they don't tolerate medications or are on medications and still aren't getting the results they need. And then we can -- actually in more severe cases or cases where the pain is really a big driver and medications have failed, sometimes we can do things like even stimulators. I think that's really probably a lower percentage for most people, but it is certainly an option for spasticity.

[00:22:48] Certainly the management can get more aggressive as well. Probably the next step for medical therapies for most people is doing things like Botox injections. So not just for cosmetic reasons. we can do Botox to help loosen those muscles up and help things like medications and spasticity and stretching be

more effective. And then in the extreme example, somebody who has really severe spasticity that's really impacting their life, they can do things like pumps, they can have actual baclofen pumped into around the spinal cord and that can actually help loosen things up without causing as many side effects. Dr. Galli, did I miss anything?

[00:23:28] **Dr. Jonathan Galli:** No, that was like perfect. I wish I had recorded it for my residence. And I think the only thing I would add to that is when I'm working with my patients on symptomatic treatment, whether it's neuropathic pain, spasticity, all these things, the general rule is like a lot of these medications will "work," but they do have side effects that make them hard to either get to a dose that is adequate, with gabapentin, a lot where people, by the time they get up to a dose that's like working, they're like, but now I'm a zombie. So, in those cases, like the treatment's worse than the actual symptom. And so, it is something that just being upfront, takes time to really dial in sometimes and it takes creativity with you and your honest feedback and your providers saying like, okay, like this option didn't work. So, let's try something new because the side effects were too much or things like that. So that's my approach. But I think that was a beautifully comprehensive review.

[00:24:46] **Dr. Kyle Blackburn:** Thank you.

[00:24:48] **Krissy Dilger:** Well, this is being recorded. So, if you do want to preference in the future, I'll make sure to send you a link. Thank you both. And moving on to our next question. This person has had TM for 16 years. Their neurologist says, the MRI shows, no changes, but there are no reasons for why their mobility is getting worse. Does this mean that there's something going on? Like what would your opinion be in this situation from what little we know? And then this person also wants to know why spasticity progresses over time. Dr. Galli if you want to.

[00:25:27] **Dr. Jonathan Galli:** Yeah, sorry. This is a great question and it's one that I get from my patients where their symptoms do seem to progress. And even though they're fluctuating do seem to worsen in time and it can be ambulatory issues, walking, balance, it can be spasticity, it can be their neuropathic pain. And I've actually just as a slight aside, I'm not sure why this is the case, but I have patients with transverse myelitis who have relatively small, like lesions and like certainly less lesion burden in some of my MS patients. And I don't know why. But those four patients are still like way symptomatic in comparison to some of my MS patients who you think would be more but they're not. Maybe one day I'll be able to answer that question.

[00:26:20] So we certainly see disease like symptom progression in the setting of image stability. So, this story is not one that I would say is different than what I oftentimes see. Reasons why mobility are getting worse could be one of several. Certainly, we see spasticity worsening over time. It can be a little bit more refractory at treatment. It just may need more aggressive treatment. And if things get severe enough, you can actually develop more contractures that can really be -- it's called to treat. If I see somebody who's having worsening mobility, despite a very stable lesion, I typically will ask myself maybe not necessarily what else is going on from a diagnostic standpoint because I still believe it's idiopathic transverse myelitis. But I tend to also ask myself like, what else could be going on? Have you developed over time an underlying polyneuropathy that's gone into the balance issues?

[00:27:29] Certainly if patients have what we call proprioceptive issues or issues of position sense with their walking, if that's not aggressively worked with physical therapy, that's something that can decline over time. So, it is something that we do see despite normal imaging, and it really is just staying up and staying aggressive with ongoing treatment with physical therapy and things like that. One thing I know I run into with my patients across the board that I'm sure that many of you all have probably run into is we -- the number one thing we do with mobility issues is send to physical therapy and physical therapy will work with you

for a while, get you better, they'll say go home and do your exercises, which is easier said than done. But oftentimes once PT is up, I will see my patients decline again.

[00:28:26] And unfortunately, with reimbursement, physical therapy, they're reimbursed based on like improvement in outcomes. So, once you're improved, they discharge you. If there was a way to keep you in physical therapy, every week forever, that's probably the ideal situation. It doesn't happen. But I generally, if I have somebody who's declined again within a year or so, I'll just send them back to physical therapy.

[00:28:53] **Krissy Dilger:** Dr. Blackburn, do you have anything you'd like to add?

[00:28:56] **Dr. Kyle Blackburn:** No, I absolutely agree. And it's obviously hard to give specific advice in a specific situation. But I actually encountered a situation like this yesterday where somebody had it, it didn't actually end up being transverse myelitis. They had another type of myelopathy, another type of spinal cord injury, but they had experienced some progressive decline. And we actually identified just a couple of things that were happening and one of them was they've been very medically ill in addition to that and had not been mobile as much as they have been. And I agree with Dr. Galli. Where I see this the most is often people who haven't been able to effectively -- who haven't been able to carry out a physical therapy plan or continue a home exercise plan.

[00:29:43] So I always emphasize to everyone and I'm happy to do it to this audience today is we are not really immune from doing exercise. It's needed for our health status and physical therapy is just a very regimented type of exercise if you really get down to it, and in some ways. So, I really encourage people to keep up their home exercise program. It's just good for your general health anyway. But for you, it's really critical to maintain function and ideally continue to push the boundaries that you've achieved over time. So, I really encourage people to keep working at therapy, at least some degree of home exercise program every day and I think the patients that I've had that have been successful at that have really maintained their function. So, I strongly emphasize that.

[00:30:35] **Krissy Dilger:** Thank you. Our next question is I believe always a hot topic about stem cells. So, is there a near future for the use of stem cells or other injectables to address chronic pain? And this person was particularly interested in the sacral region. Dr. Blackburn, do you want to start us off?

[00:31:03] **Dr. Kyle Blackburn:** Sure. This is certainly a hot-button issue, and we talk about it a lot in the clinic. So, stem cell therapy for recovery of function, whether it be pain, mobility, improving spasticity, numbness, really just the general recovery of symptoms from a spinal cord injury, still very investigational. The trials that are ongoing are mostly looking at -- I mean, they're still trying to figure out what's the best way to deliver a treatment like this. What's the best way -- is that even safe to do it, is where we are and that's going to take a while to overcome? So, we're still a ways away from being able to say, inject a stem cell into a spinal cord and have a heal. But it is an area of interest. It is certainly something that's being explored and hopefully one day we'll have better answers. Along those lines, as you see, I'm talking about this very cautiously and talking about how this is a safe and investigational treatment. So really if someone is offering you stem cells at this point for a fee, usually for injection, I often find that those probably aren't using adequate evidence-based techniques. So, I advise a lot of caution to people who are seeing stem cells advertised as a cure-all for something. At this point that we're still investigating these and determining their safety profile.

[00:32:38] **Dr. Jonathan Galli:** I have the same feelings and such. I think the only other thing that you all may read about or hear about is the use of stem cell transplant with autoimmune conditions. And this is also something that's very early in investigation. And there is some MS literature that it's an effective treatment and really aggressive patients, but it's got potential for quite a bit of adverse, things because they're essentially



resetting your immune system. So, I think within our field, there's a lot of hope that the use of stem cells either for treatment of the actual relapsing condition or to use it to regenerate, nerves or help with chronic pain and things like that. I think there's a lot of hope, but I think we're still very early within that.

[00:33:43] **Krissy Dilger:** Thank you. Thanks for that explanation. So, this person wanted to know, are there any resources for long-term care for TM patients and/or resources for caregivers? What advice do you have for long term TM patients and their medical professionals, families, and caregivers? Dr. Galli?

[00:34:08] **Dr. Jonathan Galli:** Yeah. I mean, when I have a patient with transverse myelitis, actually one of the things that I do is actually loop them in with the SRNA for this very reason because I think, obviously this -- I'm biased because I'm part of this whole thing. But I think this is incredible like a patient, education, and advocacy group. So, I actually point them here because I think there's a lot of more of the logistical things that we as a group are able to offer even more so than me in clinic. Advice for long-term transverse myelitis patients in general, I think having a care team that you're comfortable with is really key to just good long-term outcomes and not just like from a neurological status, but just a quality-of-life status. I think establishing yourself a with a really good neurologist is really important and one that listens to you and understands your condition and is willing to participate in your care and help you through, the symptoms and the residual problems that came from the initial injury.

[00:35:22] I'm really lucky at my clinic nurse, Tracy Schafer is an incredible resource for me that she's able to reach out and just check in on my patients, especially if they're like going through a rough patch with whatever, if they're symptom symptomatically not doing well or like, even if they're having a rough patch in life for some other totally different reason. But I think with that like sometimes social work can be really helpful, especially just providing other resources from like a caregiver burnout standpoint and things along those lines. So, I really utilize these other resources as well. And then I always put a plug in if you will for a good primary care doctor, which again, my bias is showing my wife's a family medicine doctor. But I have the best outcomes in my patients that have a good primary care doctor because they're able to take care of all the other things and let me focus in on your transverse myelitis and managing those symptoms. And so, I have a really -- at least at the University of Utah, like we have awesome primary care doctors who I share patients with and they're able to manage like, things like blood pressure and like cancer screening and things that I wouldn't be able to tell you about right anymore. So, I think those are all really important things to consider.

[00:36:57] **Dr. Kyle Blackburn:** Again, I think you did a beautiful job summarizing that. So, there's just so much -- there's just so many different ways that this disease can impact someone's life that it really spans what we would consider medicine in a way. Where we think about focusing on identifying a disease and treating the symptoms, but it just impacts so much more than that. And I think the SRNA is a great job of plugging you into the things that we're not thinking of in our immediate radar. And I think that's really critical, and I do think it's a really good thing to keep caregivers in mind. I think everything you said is perfect. We often utilize social work, good primary care to make sure that everybody's getting the care that they need and getting the equipment and everything that they need at home.

[00:37:55] **Krissy Dilger:** Thank you. This next question is specific, but I guess we can also expand it to generally speaking. So, this person needs knee replacement. They just want to know is there anything they should know about how this might affect their TM or any considerations. But in general, are there any considerations for surgery and having TM?

[00:38:24] **Dr. Kyle Blackburn:** It's a good question. So, whenever somebody needs like an orthopedic surgery like this, I think it's one if all the other typical interventions have failed, like getting pain relief, physical therapy,



all the typical things we're supposed to do before a knee replacement. If it's truly gotten to that point, I think it's perfectly safe from the standpoint of not exacerbating your myelitis to proceed. Again, we talked about this is a low risk of relapse. So, if somebody needs a knee replacement, I feel totally comfortable with them doing that. Knee replacements, I always counsel people and I did my orthopedic surgery rotation. Knee and hip replacements are not minor surgeries, and they need a lot of rehab. So, you're going to -- you may have a different rehab regimen than the average patient that has a knee replacement. But obviously, we talked about the importance of rehab and regular exercise anyway. So, I totally support it. I don't know that I have any other specific things about surgeries necessarily as far as aging with TM. And I don't know that I have any specific guidance there, either. Dr. Galli, do you have anything?

[00:39:48] **Dr. Jonathan Galli:** No. I mean, I think that when I'm counseling my patients and again as we age, potentially, you need more joint replacements and things like that. The discussions always risk benefit, like what you're alluding to, and the rehab may be more difficult than if you didn't have transverse myelitis, especially if you already have baseline mobility issues, balance issues, walking issues. But one thing I do discuss with my patients and it's very individual and case by case is that could this surgery actually make your mobility better in the long run if we can get you through the rehab. Because if you have a bad knee on top of balance issues and a little bit of plasticity that bad knee is going to make it harder. I've certainly had patients that for orthopedic reasons are at a higher fall risk and they get them taken care of and they actually do that. So again, I usually encourage them to talk to their orthopedist and get the idea of what the rehab will entail and things like that. But that's my approach to things as well.

[00:41:03] **Krissy Dilger:** Thank you all. So, this person says they're getting constant feelings of vibration from the waist down which is uncomfortable and affecting sleep. Is there any way this can be managed or general tips about sleeping with some of these issues?

[00:41:23] **Dr. Jonathan Galli:** Yeah. It's not uncommon. So classically, I think that the teaching for neuropathic pain is like burning or electrical pain, but this vibration sensation is not atypical. And it's certainly one that I see in my patients. Transverse myelitis affects the cord, I certainly see in my EMS population, my patients with cord lesions are not just more symptomatic from like a mobility standpoint, but from a pain standpoint, spine lesions just really are painful like they just are. And my guess is that this vibration sensation is just more of an atypical neuropathic symptom. So, in my patients that have this sensation or perhaps it's more of that lance electrical line, I typically will treat them with neuropathic pain medications.

[00:42:28] And certainly if it's something that's affecting sleep, my approach is to try to kill two birds, one stone and find -- we have certain medications that are actually -- they're quite helpful for nerve pain and the big side effect is they make you super tired. So, we utilize that and say we're going to use this as a sleep med. It'll help hopefully with your nerve pain and maybe it'll knock your headaches out too. So that's my approach. Sometimes you also just have to use a sleeping medication along with neuropathic pain meds. But that would be my approach if you were my patient.

[00:43:04] **Dr. Kyle Blackburn:** I absolutely agree. This vibrating sensation is something that we hear about a lot. I don't think it's been probably acknowledged enough in medical literature that this is a valid thing that happens. But we certainly hear it enough to suggest that it is, and we take the exact same approach, try neuropathic pain meds or sleep aids to see if it'll help.

[00:43:28] **Krissy Dilger:** Well, thank you both. This next person is asking why can getting overheated trigger symptoms. What do we know about why and how symptoms can change over the course of a long pseudo-flare? Dr. Blackburn if you want to start us off?

[00:43:49] **Dr. Kyle Blackburn:** Sure. I think it's a really good question why getting overheated can cause that worsening of symptoms I was talking about earlier. And I don't know how well it's been studied, but I think that the general thought process has been that the heat tends to cause the conduction through the nervous system, through those nerves, to be even further impacted. So, you already have an injury to these, it's impacting conduction and then the heat compounds that we actually can see that on some of our muscle and nerve tests that temperature -- if you're actually too cold on those tests, we can actually see that the peripheral nerves don't fire as well as they should, and we try to get you up to temperature. So, it works both ways.

[00:44:39] So what do we know about why they change over the course of a long flair? And it sounds like somebody may be alluding to the fact that their symptoms worsened after something like that. Again, I don't know that I could -- I'm trying to interpret what they're asking about, but I will say one thing that I've noticed is some people we always talk about these symptoms completely resolving after the stressor is removed, for example, cooling off. But I have had some people who felt that their pain -- even after a relapse, they felt that their pain exacerbated in the weeks after that relapse. And I think things like that are -- I always tell people sometimes the healing process or the inflammation going away, that part of the process sometimes unfortunately brings on some unpleasant things and that's where spasticity or the pain can actually increase. So, I think that's what I would counsel in that situation.

[00:45:40] **Dr. Jonathan Galli:** I think that's spot on and one thing I also will discuss with patients is, you have a nervous system injury, and your brain is incredible and can overcome a lot of that, but your brain is essentially working overtime constantly trying to make things work. And so, any little insult to that system, whether it just be, I have been sleeping well, I'm sick even if it's like a mild cold, what have you like that adds stress into the system and just pulls away the brain's ability to compensate for what is that injury. So, it's very common and I get this question a lot of like why in the world, like when I'm stressed and not sleeping well, does everything pick up and you're not having new inflammation, but you're just not compensating as well for it. So that's just the way I think about it if you're having one of these unmasking episodes if you will, even if it's not heat-related. So that's just one other thing that I wanted to add in.

[00:46:50] **Krissy Dilger:** Thank you both. This person wants to know how often they should have an MRI done after being diagnosed with TM. And they also want to know is the long-term use of IVIG recommended as a treatment for recurrent TM. Dr. Galli?

[00:47:10] **Dr. Jonathan Galli:** I was going to say, I think that one's fine. The simple answer for your first question is it depends; I typically will do closer repeat imaging in my patients that I presume are idiopathic transverse myelitis. I will typically do at least annual imaging for a little while a couple of years, both brain and spinal cord. Again, that's more just making sure there's not MS or something like that sneaking about. But again, it's very patient-dependent, and like what my level of concern of clear idiopathic transverse myelitis or could there be something else going on. I will tell you that like my NMO patients, I don't typically do annual imaging because you wouldn't unless they have new symptoms, I should say just because you wouldn't expect things to go on in the background.

[00:48:11] MS typically tends to have more annual imaging because MS tends to have more clinically silent lesions if you will, where you can accrue them in the brain and you just don't notice that's typically where I'll see them. So that's the way I think about it. It just depends on my level of concern that could you be having developing something else in the background. But again, with transverse myelitis being monophasic, it's not necessarily something that you have to do annual imaging forever, again, unless symptoms change. Part of that is patient dependent. If I have a patient who's really worried and they want to do annual imaging, I don't say no. I think it's pretty harmless. And then the question about long-term use of IVIG and recurrent TM gets

back to what we were saying earlier. If somebody has recurrent transverse myelitis. I'm going back to the drawing board to say what is causing this because that is going to drive my treatment.

[00:49:10] I will tell you right now, the -- Dr. Blackburn, I don't know if you guys are on the IVIG train for your MOG patients. But right now, I can tell you our group is pretty heavy on using IVIG first line for MOG that may change in six months, everybody. So, I'm just going to put that out there as well. But it really depends -- and that's where finding the reason for the relapsing is important because if somebody's having relapsing, transverse myelitis and we're missing like a sarcoidosis, that's something that I'm going to treat completely differently than I would MOG, which I'm going to treat completely different than MS, which I'm going to treat completely different from NMO. So, I hope that answers the question. So, if I saw someone with a current transverse myelitis, I'd really be wondering why to help guide what treatment to use.

[00:50:03] **Dr. Kyle Blackburn:** And I absolutely agree. The MRI frequency after a diagnosis of TM is really determined by, is there a risk of relapse or has somebody come to us with already three or four MRIs that suggest stability, for example. So, in those cases, if I'm very suspicious for MS, Dr. Kyle was talking about absolutely, we would be doing interval imaging to look for those silent lesions he was talking about. For other causes, it may be a little less frequent and only if symptoms recur as he was talking about. And then with the IVIG question, yeah, we are on the IVIG train from MOGAD.

[00:50:43] So we will commonly use that but as far as a first-line treatment, let's say that we're catching somebody with an acute recurrence and we're talking about what are we going to treat with them within the hospital, the evidence on these things is limited. But IVIG I think is a perfectly reasonable thing to try for an acute exacerbation of transverse myelitis if we don't feel that we know the cause. Oftentimes you'll see steroids used in these cases. And I would strongly advocate for that as well. But IVIG if somebody were to say, I'm in the hospital for an acute exacerbation and I have myelitis if they had received IVIG, I would think that's a reasonable thing to do in general.

[00:51:30] **Krissy Dilger:** Thank you. The next question is about cognitive issues. So, what is the best support for cognitive issues, Dr. Blackburn?

[00:51:42] **Dr. Kyle Blackburn:** Well, that's a really good question and not something I expected to see on the transverse myelitis discussion, but we're here. So cognitive issues can really have a lot of different causes. And so, the first thing I want to add is in many cases, this is not the -- for many people that have had transverse myelitis, they're having cognitive issues. It's often not necessarily a sign that they're having Alzheimer's disease, let's say, for example, we see cognitive issues due to a variety of things. So, when somebody comes to me and says, I have a cognitive symptom, we obviously want to do some testing to figure out why that is. I will counsel you that some of the best testing takes several hours to administer it. And it makes everybody feel dumb at the end of it to be frank. So don't walk away from it feeling like that you failed in a way. There's really is no way to fail it.

[00:52:36] But cognitive, that's usually the first thing is to get a better understanding. And those are administered by a medical professional type called a neuropsychologist who can often give us a lot of great information. They're trained in both assessing the mood disorders in addition to cognitive disorders in many cases, and they're often able to provide us some insights. Common things that I see our patients struggling with if they get testing or just in general from a cognitive standpoint, one of them is their energy levels. We know that fatigue is very common in these disorders and a manifestation of fatigue that sometimes people will feel is just as they exert themselves, they'll notice that they either feel more tired, a physical sensation that they want to go to sleep, or they feel that they cognitively just cannot do more complex tasks. And that can be

managed. Fatigue management is a very tailored approach. But if we think that the source of a lot of these cognitive issues is fatigue, we can treat that.

[00:53:44] Another aspect that I think is underappreciated are the mood disorders and sleep and how those can impact your cognition. So oftentimes when somebody is saying that they're reporting some issues with their cognition, I'll often ask them about sleep. If somebody's been on a bunch of steroids for a while, we worry about things like sleep apnea if there's been weight gain. So, we want to certainly assess for that, but also just making sure that their sleep patterns haven't been affected by being in a hospital or something of that nature. Because certainly, I think we've all experienced this, if you're not sleeping well, you're thinking, and memory processes just aren't going to work well. And then mood disorders can have a profound impact on your ability to process information effectively. So, we also tend to focus on that. Those are just some of the general things. Obviously, this gets a little more specific if we're talking about inflammation that's impacted the brain and has caused injury to the memory circuits. At which point, we may recommend interventions like rehabilitation or speech therapy to help. But in general, for these disorders, I think those are where I tend to find the cognitive issues arriving from.

[00:55:01] **Dr. Jonathan Galli:** I totally agree with all that. I think for me, it's really optimizing everything that can contribute to cognitive issues is really a mainstay in this and the neuropsychic testing can really help see what's underlying it. And I think also offer reassurance, oftentimes in patients to be able to say based on this, you definitely don't have Alzheimer's disease. I think that's usually our biggest concern.

[00:55:32] **Krissy Dilger:** That's great. Well, thank you. I think we probably have time for about one more. So, we just have a few minutes left. So, let's see which ones we have left. Let's go with this one. Back to diagnosis and diagnosis changing. This person has received several different diagnoses, recurring TM, MS, maybe neuropsychic diagnosis. But this person wants to know if it's worth taking medication. They're obviously feeling frustrated because their diagnosis keeps changing and their disability is progressing.

[00:56:13] **Dr. Jonathan Galli:** Yeah. And I don't want to say it's not uncommon because usually once somebody is diagnosed with MS, that's a correct diagnosis. But actually, as an example, inherited a patient who carried an MS diagnosis for five years, we'll say, and they actually kept having recurrent optic neuritis despite being otherwise adequately treated. Now, they weren't on the E20 therapy, but they were just not behaving like MS should if you will. And so, in that case, we actually went back to the drawing board, I evaluated him and actually ended up saying I think this may be more likely to be neurosarcoid, switched his treatment, and has been much more stable. So, this does happen.

[00:57:06] And I will tell you neurosarcoid in general is something that you always have to have in the back of your mind as a provider, especially when things aren't responding to treatment as well. I would love to have a crystal ball where I could just nail a diagnosis every time, get on the right treatment, but we don't. So, in this case, I certainly think it's worth taking the medication that you're being recommended with the knowledge that sometimes it takes us time to get to the bottom of your diagnosis. And really, that's to hopefully allow for you to improve from a functional standpoint, but also to prevent further disease progression.

[00:57:56] **Dr. Kyle Blackburn:** I absolutely agree. And one of the frustrating things that we're dealing with is that we don't have that crystal ball and maybe that's where we need to invest the rest of our time and resources is getting that because sometimes while we're getting better and better, this process can be frustrating, it can be really hard to nail it the first time. And if somebody is experiencing worsening, then I absolutely think that would indicate, especially if providers are pointing out that they're seeing new evidence on MRI scans that there is something inflammatory that seems to be taking bites out of the spinal cord in this case.

[00:54:23] And I would absolutely advocate for doing some treatment even if your doctors are saying that this is something that we're going to try empirically and try to figure out as we go along. I think it's good that they're being honest with you and telling you these are the things that we're thinking about, but that they're not 100% certain yet themselves. You really want doctors that will be transparent about that. So absolutely, if somebody is progressing like this, I think taking treatment is reasonable.

[00:59:07] **Krissy Dilger:** Great. Thank you both so much. Unfortunately, we're at the end of our time, but I think this is a great discussion and hopefully, we can continue this conversation in the future and possibly answer a few of the questions we didn't get to in a podcast if you would be interested, not to nail you down. But thank you both. And for everyone attending, thank you for submitting questions and participating.