

Community Q&A

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[00:00:02] **Krissy Dilger:** So, let's just start a brief introduction we have with us today, Dr. Paula Barreras. Would you like to briefly introduce yourself?

[00:00:13] **Dr. Paula Barreras:** Sure. Well, thank you for inviting me. I'm a neurologist with training in neuroimmunology and a specific interest in myelitis and myelopathies. I trained at Johns Hopkins for the majority of my career where I did also a few years of research in myelitis and neurosarcoidosis and now I have transitioned institutions and I'm currently part of the Cedar Sinai Medical Center team in LA.

[00:00:38] **Krissy Dilger:** And we also have Dr. Hamza Coban. Can you also introduce yourself?

[00:00:43] **Dr. Hamza Coban:** Yes. Again, thanks for the invitation. This is great. I'm currently a neurologist and neuroimmunologist here at the University of Connecticut Health Center in Farmington,, Connecticut. I did my residency training here at UConn and fellowship training at the University of Pennsylvania. I also have special interest in rare autoimmune disorders including transverse myelitis and neuromyelitis optica spectrum disorders. Happy to be here.

[00:01:15] **Krissy Dilger:** Yes, happy to have you both. So, we got a lot of questions. So, I will try and get through as many as we can, but we can also continue this conversation afterwards if we don't get to all of them. But I guess to start off, someone asked, "I would like to ask about relapsing TM medications and diagnostic tests that one needs to continue doing." Is there things that someone with relapsing TM should keep in mind in terms of continuing to get a diagnostic update and ongoing medications that they can take to manage their TM. Dr. Barreras.

[00:02:02] **Dr. Paula Barreras:** Happy to take that first one. The first thing I want to define is what relapsing TM means. That's presumably somebody who had an episode of inflammation of the spinal cord once and then had a second. The most cases of myelitis is where we cannot put a last name to that, meaning they initially tested negative for NMO, MOG or multiple sclerosis or specific disorders are one-time or monophasic events.

[00:02:31] If now you've had two episodes, I think the main thing is to reassess if you now meet criteria for one of those specific inflammatory disorders. So, there should be testing for aquaporin-4 IgG and for MOG IgG to assess if that relapsing disorder is part of NMO or MOG. There should be over time brain MRIs that are repeated to see if lesions have accumulated that may suggest that the relapsing TM is part of a disorder like multiple sclerosis, for example.

[00:03:02] And screening for rheumatological disorders. Sometimes people have relapsing myelitis of unclear cause. We cannot really put a last name to that. And if that's the case, I think once somebody has two severe episodes, usually immunosuppression is started.

[00:03:21] But at that point, because there's no specific last name, usually most people would use something like Rituximab or a piece of depleting therapy which is broad for rheumatological disorders – would cover NMO, would cover partially the possibility of MOG. But I think the most important thing is to make sure that now there is a relapsing disorder that we try to put a last name to it so we can guide therapy.

[00:03:50] **Krissy Dilger:** And Dr. Coban, do you have anything you'd like to add?

[00:03:53] **Dr. Hamza Coban:** No, I agree with Dr. Barreras. I think that the most important thing is making sure what we are really dealing with. I will repeat some of the points made by Dr. Barreras. But I think especially for transverse myelitis, sometimes it can be very difficult to make a definitive diagnosis even though we are getting much better at it.

[00:04:21] A lot of times most of the transverse myelitis that we thought idiopathic transverse myelitis in the past. Now, we are diagnosing those patients with either neuromyelitis optica spectrum disorder, MOG disorder, even with MS or neurosarcoidosis and so forth. So, I think we have to think much harder if someone had a transverse myelitis at some point and had another episode now.

[00:04:50] Again, either in the spinal cord, we need to think harder. Could this be one of those conditions or are we missing something else? But one of the important points is that sometimes transverse myelitis can be missed or misinterpreted. It may not be the myelitis like that implies inflammation but sometimes we see a lot of vascular problems like we call them under a number of myelopathies.

[00:05:20] Sometimes there is an interruption in the blood flow; it can cause some recurrent symptoms or worsening progressive symptoms over time. So, those things have to be reconsidered. In terms of medications at the end of the day, sometimes we may not pinpoint one particular disease but at least we should be able to rule out those vascular problems or other structural problems such as spondylosis, for example another one.

[00:05:52] And after those things are ruled out and if you still end up with transverse myelitis, but recurrent relapsing transverse myelitis, then we turn to the off-label medications. Unfortunately, there is not a specific FDA-approved treatment for transverse myelitis because it's rare and it's hard to study at the same time.

[00:06:16] And because of that so we turn to off label treatments as Dr. Barreras pointed out, B cell depleting therapies such as Rituximab could be one of them. Sometimes the intravenous immunoglobulin can be tried depending on the risk perception and patient preferences.

[00:06:38] **Krissy Dilger:** Thank you for that great explanation. So, we got a lot of questions about recovery after TM and what that looks like. So, Dr. Coban, do you mind talking about what recovery quote unquote might mean for transverse myelitis? Someone says, "I'm three years in, am I still healing? I have scar tissue where the inflammation was. Will that ever heal? Is it correct that the scar tissue keeps the cells from regenerating?"

[00:07:14] **Dr. Hamza Coban:** Yeah, it's a good and important question. I try to avoid making a broad conclusion or generalized conclusions because every patient is different, and everyone has their own disease. Some patients may have a better course, better outcome as opposed to others may have less favorable or worse outcome. And it also depends on the underlying etiology.

[00:07:47] Transverse myelitis can be due to a variety of reasons. Sometimes we see post-infectious or para-infectious transverse myelitis. A lot of times they do better. They improve quite a bit after the initial attack after the initial symptom is treated properly. Sometimes we don't have underlying etiology. We don't know what really caused it. They may have mixed outcomes.

[00:08:21] I think that as a general rule though in a general sense usually we see the most recovery, most improvement in the first couple of months up to three to six months or so, assuming there is no other attack or there is no ongoing insult. After that point on, it's I think in my opinion recovery still continues but maybe a much slower pace and at some point, it may plateau.

[00:08:54] There is that. The other thing and though we still encourage our patients to keep continuing their therapies, physical therapy, occupational therapy and regular exercises to retrain their nervous system in a way and rewire their nervous system in a way. One of the important aspects of it, the opposite could happen. Some even though rare, some of our patients may have a progressive course that we may not be able to explain that well.

[00:09:33] Speaking of the scar tissue, it's true a lot of times, there's a scar after the initial inflammation. That scar tissue can just stay. It may not cause any problem, or it can be a part of the problem and part of the progression. Sometimes it can cause chronic irritation in a way for the spinal cord and those patients may have a somewhat progressive course. Yeah, that's my take on this issue.

[00:10:09] **Krissy Dilger:** Great, thank you. And Dr. Barreras do you have anything to add or?

[00:10:13] **Dr. Paula Barreras:** Yeah, so, in my experience it's true that most of the fast recovery occurs probably in the first six months. But I do think recovery continues in that first year, year and a half. After that point, most people plateau and they may be left with some symptoms.

[00:10:33] I think weakness is one of the things that has more potential for recovery with physical therapy, specifically. From what I've seen, things like neuropathic pain and numbness recover a little bit less and that may be left over long term. There is a scar so often when we do the MRIs, we see the initial lesion and it is initially inflamed, taking up that contrast telling us that things are on fire.

[00:11:03] Later down the road, we repeat the MRI things are no longer on fire, but we still see the shadow of what happened that the lesion is still there. So, you can think about it as a scar tissue. And what's nice about the spinal cord and the brain is that it's very adaptable. So, your body adapts to put signals around that scar and symptoms can get better but often not completely. And often if the person has something decompensating them like an infection or something else, those old symptoms may come back.

[00:11:33] I think it's important to continue to be active and do physical therapy, even if you're beyond that year and a half point because that builds that rewiring and compensation ability around the scar that is left over. So, although that scar is not going to go away, you can build pathways around and overall continue to improve if you build your, what we call the neurological reserve.

[00:11:58] **Krissy Dilger:** Awesome. Thank you so much. So, this is something that's been kind of a topic that's come up recently a bit more. Someone asks, is there such a thing as transverse myelopathy? Dr. Barreras, do you want to?

[00:12:18] **Dr. Paula Barreras:** Yeah, so I have strong feelings about that one. So, I think the terminology has been historically a little bit confusing. So, transverse myelitis is an old term that the transverse just came from the description of a sensory level like across the body from which down there's deficits. And myelitis just means inflammation of the spinal cord.

[00:12:43] So, really when we say transverse myelitis, we just say there's an episode of inflammation of the spinal cord that left somebody with a level of deficits from there down. That doesn't really mean that much

by itself diagnostically. And the preferred terminology these days is myelopathy, which is just a spinal cord problem and we're avoiding putting the label of "itis" of myelitis prematurely. I advocate to remove the word transverse because that transverse doesn't really mean that much for us. We know that people can have spinal cord disorders, an inflammation without a sensory level or with incomplete sensory levels. Although you may or not have that transverse part, you may still have a myelitis. Myelopathies meaning lesions in the spinal cord can be from inflammation or from other things like vitamin deficiencies, infections, sometimes tumors, or things like that.

[00:13:45] By saying myelopathy, we are reminding ourselves to look for those other possibilities before we say, "Okay, there was an inflammatory problem or an autoimmune problem." At the end, if we see evidence of inflammation objectively in MRI, on the spinal fluid, in your blood work, then the label may be correctly put as myelitis. Myelopathy would be the starting point and then from there on, we try to put the disorder in categories, one of which would be myelitis.

[00:14:18] So, transverse myelopathy wouldn't be a term that I would use because I would drop the transverse completely. But somebody can have a myelopathy of let's say vascular causes, spinal cord stroke and have a sensory level from their down. So, there can be transverse in noninflammatory causes of myelopathy.

[00:14:39] **Krissy Dilger:** And Dr. Coban, do you have anything to add?

[00:14:42] **Dr. Hamza Coban:** Yeah, I completely agree with Dr. Barreras on this one. It can be confusing for our patients at the same time for health care providers too. And it may even result in some unwanted consequences. When we use the term transverse myelitis, it implies an inflammation of the spinal cord. But as Dr. Barreras pointed out there are a lot of other reasons that can cause similar symptoms, similar problems.

[00:15:18] And it may cause a bias in a sense and especially from healthcare provider aspect if they just focus on the myelitis part, the inflammation part, the other possible explanation, other possible theologies can be missed which is not a good thing. So, that's why I also prefer myelopathy as a starting term and then try to define afterwards based on the work up and based on what we find on physical examination and imaging and work up results. Yeah, I agree with her on that one.

[00:16:02] **Krissy Dilger:** Okay, great. Thank you both. So, we have some questions about symptom management. So, to start off, can you talk a little bit about neuropathic pain and different management strategies? Dr. Coban.

[00:16:18] **Dr. Hamza Coban:** Absolutely, neuropathic pain unfortunately one of the most common and can be very disabling symptom. Even though the exact mechanism is still not that clear, technically the neuropathic pain usually a problem of the peripheral nerves. But we see quite often with transverse myelitis or other disorders of central nervous system affecting spinal cord.

[00:16:50] So, that regardless it's quite common and can be disabling and we try to treat with symptomatic treatment, symptomatic medications. The one important thing to point out here, I think even if we have an underlying etiology for the transverse myelitis, let's say, at the end of the day we diagnosed them with neuromyelitis optica spectrum disorder maybe the transverse myelitis was because of that.

[00:17:23] Treating that particular condition may not necessarily translate into treating the symptoms. Symptoms still may persist. Most of them will persist and we try to tackle them separately with symptom management. Sometimes our patients may be, it can be under the impression that treating that particular condition with disease modifying therapies will treat their symptoms and they may be discouraged from the treatment.

[00:17:57] They are not designed for that. Unfortunately, they don't work for that. For symptomatic treatment again, it's kind of a trial and say trial and fail basis a lot of times. There are certain medications we use as a first line. And if one medication doesn't work or has side effects, try another one. There are medications like gabapentin or pregabalin, probably most of our patients are familiar with.

[00:18:36] And there's another group of medications we utilize tricyclic antidepressant medications they can be used. Another group called SNRI or again, and another group of antidepressant medication, but we use them for their neuropathic pain properties. And we start with them and change therapy plans as we go on depending on the response and side effect profile.

[00:19:08] One other important thing that I want to point out though, even though it's very common in transverse myelitis to have neuropathic pain, it's okay for our patients to have more than one problem. So, that can be an important aspect of the problem of the symptom. Sometimes they may have a lumbar spine or lower back problems in addition to transverse myelitis.

[00:19:36] Maybe that's the main reason for their neuropathic pain. So, I always encourage my trainees and when we talk about this issue with our colleagues, we stress this possibility to always look out for other possible explanations and not to miss if someone has, for example, a disc herniation or radiculopathy and do appropriate testing for them including imaging or nerve conduction studies.

[00:20:08] And another important thing is again, common things are common, and it can be expected in our patients too. Such as the more common reasons for neuropathic pain, diabetes or certain vitamin deficiencies or certain metabolic infectious problems. We'll be looking out for those other alternative explanations too to tackle this problem.

[00:20:39] **Krissy Dilger:** Great. Thank you. That was a great thorough explanation. So, I appreciate it. Dr. Barreras do you have anything you'd like to add?

[00:20:49] **Dr. Paula Barreras:** Well, I mean, I agree, that just to emphasize that there's multiple medication options in different medication families that may work for that pain. That is essentially the nerves, well, the spinal cord cells firing either being hyper excitable or misfiring when they're not supposed to. So, most of these medications, let's say, quiet down that signal abnormality and antidepressants or anticonvulsants and other medications can be tried.

[00:21:22] And if somebody fails one medication that doesn't mean that they're going to fail the rest. So, just know that there are options out there and don't be that discouraged. The other thing I want to say is that they take time to build up in your system. So, I find that gabapentin, for example, is a common medication that we used, and a lot of patients just try it as needed. Take it once or twice in the week and they decide that it doesn't work, and they conclude that they abandon the medication.

[00:21:52] These medications are usually required to be taken multiple times a day for several weeks before we actually see effects. So, that's another point. And a lot of people ask about non-medication pain strategies, pain management strategies, which I think is important because not everybody wants to take medications. I think medications are important for this type of pain. And it tends to be a refractory for the initial interventions but things like actually exercise can help manage the pain.

[00:22:24] There is support by psychology and therapy to help yourself with strategies to cope with the pain. Acupuncture has been studied for chronic pain and it is a benefit for some people and it's in general a safe

strategy. And tense machines are sometimes beneficial too although the evidence to use them is a little bit of less qualities of small studies, but there's a suggestion that that can help as well.

[00:22:56] **Krissy Dilger:** Great, thank you. And so, the next symptom that someone has asked about is fatigue. Is what are your recommendations for someone struggling with fatigue? Dr. Barreras, do you want to start us off?

[00:23:10] **Dr. Paula Barreras:** Yeah, so, the first thing is not to necessarily blame the fatigue automatically on the myelitis. Fatigue is something that a lot of people with and without myelitis deal with. And the first thing is to try to understand if there is a factor that is fixable that we can intervene on. Is the person sleeping, okay? Are they waking up in the middle of the night because they have bladder problems. And is the bladder issue what we need to fix rather than just put medication for fatigue or for sleep on board.

[00:23:42] Things like thyroid function, vitamin deficiencies, hormonal problems like testosterone deficiency or [inaudible] deficiency. There are some disorders that can manifest with myelitis that can also affect the pituitary gland, for example, neurosarcoidosis can lead to fatigue. So, the first thing is just to assess causes of fatigue. And if we see any, intervene on that underlying cause.

[00:24:11] At the end myelitis itself can lead to fatigue. And the reason or part of the reason is you're moving now, costs you more energy, more calories because walking may not be normal, you know, if you're able to walk but you're left with some weakness or with spasticity that's taking more energy. And if you're not able to walk and you're using a wheelchair, it's a lot of extra energy to move and just do your activities. So, it's common and understandable. So, if we don't find a reason that we can fix, there are again, a combination of support strategies with psychology, there are courses on fatigue.

[00:25:02] That there's one that is a good one offered by the National MS Society, that one is targeting people with multiple sclerosis, but it doesn't necessarily only apply to people with multiple sclerosis. I think that that's something that we can all just benefit from and there are medications that can be used that are stimulants, things like modafinil for example. I don't like to jump there initially because most commonly this is something that can be managed by other strategies.

[00:25:37] **Krissy Dilger:** Great. Thank you. And Dr. Coban, do you have anything you'd like to add?

[00:25:42] **Dr. Hamza Coban:** Yeah, I agree with Dr. Barreras. I think it's when we are first dealing with fatigue, looking into other possible explanations. Not just is that only problem but some things can coexist again, and they can contribute and trying to treat them. This could be a sleep problem. This could be a mood problem or other medical problems. Trying to treat them in addition to treating fatigue or in addition to treating myelitis is the important first step.

[00:26:23] At the end of the day, a lot of times, even after fixing all those potential underlying problems, our patients may still have some degree of fatigue or not much improvement in terms of fatigue. Then we have to turn into some other interventions. There are some non-pharmacological interventions Dr. Barreras pointed out and some pharmacological interventions.

[00:26:51] In my practice, in my experience, I usually, again, as a general rule for these symptomatic treatments. These are symptoms and we are using symptom treatments. Again, try and see. Not every medication works for everyone. And I a lot of times plan a timeline to try one particular medication for symptom management.

Some medications may require a longer trial. Some medications you can see the benefit if there is any within a couple of days or a couple of weeks.

[00:27:32] I usually, if I'm at that point needing to try a pharmacological intervention, I start with amantadine first. If there is no benefit to it and then I move on to other stimulants, controlled substances. And unfortunately, we don't have great guidance. These drugs have been studied several times in different settings in MS or in other medical conditions.

[00:28:05] And there are mixed results but still we try them and if one medication works for our patients, that's great and we stick with that one. One other important thing though, especially with the stimulating medications, things like Modafinil, Adderall, Modafinil, things like that. It's important for me and for our patients to decide on a plan, on a timeline because a lot of times we inherit patients, or they have been on these drugs for a long time.

[00:28:44] It can be not very clear if they're really beneficial, but the problem will be if you were to stop those medications or switch to some something else, it's going to be a big problem because they will have some withdrawal symptoms and it can be harder to differentiate at that point which medication is working, which one is not working. So, that's another important thing to keep in mind.

[00:29:12] **Krissy Dilger:** Thank you. And another person asked about bowel dysfunction. Dr. Coban can you talk about some bowel dysfunction management strategies?

[00:29:26] **Dr. Hamza Coban:** The bowel dysfunction, there are different types of bowel dysfunction. First of all, we need to figure that part out. Definitely, even though we are quite experienced a lot of times I refer them to a urologist as well at the same time. So, we co-manage. One type of bowel problem comes with urgency, frequency and incontinence. The other type would be the kind of opposite, unable to pee or when they go to the bathroom the flow is weaker or it takes a while for them to get started or at the end, they may not be able to empty their bladder completely.

[00:30:21] So, that's different. It depends on the level of spinal cord is affected for the most part and the treatment can be different especially in the beginning. And also, again, I have to point out that there can be other contributing factors such as pelvic floor, muscle weaknesses or stress incontinence could be another one. We need to look out for those too to make a right, more appropriate treatment approach.

[00:30:56] Then I work with a urologist, depending on which type of bladder dysfunction they have. If they have more like a hesitancy and retention, we use medications things like Tamsulosin to relax the sphincter muscle a little bit. It can be helpful. If they have more urgency, frequency we use other anticholinergic medications. There's a new group of medication with less cognitive side effects, beta-agonists, like Myrbetriq or Gemtesa .

[00:31:42] But sometimes they may not be sufficient or there can be side effects. At that point I mostly defer to urologists, and they can try Botox injections sometimes and they may try stimulating devices. There are many options nowadays and with good results a lot of times.

[00:32:13] **Krissy Dilger:** And Dr. Barreras, do you have anything to add?

[00:32:16] **Dr. Paula Barreras:** So, I'll say that, just echoing a little bit what was just said. Bowel function and bladder function are affected very commonly in myelitis and myopathies. And it's an important cause of quality-

of-life disruption. And so, we should talk about it and address it. And for bowel specifically, I think the most common type of dysfunction is constipation and retention and difficulty having a regular bowel movement.

[00:32:45] For that I think that there are tiers of what we should do. The first one I think is diet management and being constipated the most common, I think adequate hydration, just drink plenty of water. Dietary modifications with increasing the amount of fiber in the diet. People can actually have added fiber to the diet always with water. And that's sort of what the first layer of what we recommend.

[00:33:19] Then after that point, if that's not enough then people can use laxatives of different kinds, commonly used things are MiraLAX that is over the counter or milk of magnesia that you know the side effect of it is diarrhea. But I like that because magnesium can actually help with cramps for example. So, it's like a two for one intervention and it's not uncommon that people need multiple interventions at the same time and that's what we call a bowel regimen.

[00:33:54] In addition to water, fiber, and perhaps using regularly Senna or Bisacodyl as laxatives, sometimes people need to use suppositories. Not necessarily every day but there are different types of suppositories, some of which are stimulants and in the moment promote the release of stool. So, we can use that in combination.

[00:34:18] The first levels of that management are often done by the neurologist. But often the people that are most allocated on that are either the PM&R physical medicine and rehabilitation, doctors that are a great tool, especially if they have some expertise in spinal cord disorders and there are specialized centers of rehabilitation that offer that and GI doctors.

[00:34:49] Urologist can I think are part of the medical team that should be involved in patients with myelitis. And they can help us understand if the bladder issues are a hyperreactive bladder or a floppy flaccid bladder because the medications that we can use are different.

[00:35:10] **Krissy Dilger:** Thank you so much. So, we got a few different questions about aging with TM. So, can you talk about what managing symptoms can look like for people with TM for say 20 years or even 40 years down the line? And how does TM impact aging? Dr. Barreras.

[00:35:37] **Dr. Paula Barreras:** So, I think this is a very important question and I'll start by disclosing that we're still learning about this. I think this is an active area where we need to do more research. We know from other disorders like multiple sclerosis that there is a component of progression of disability that seems more than expected for age and in that specific disorder that may be driven by inflammation and other factors. But there's a big component that is not explained by inflammation.

[00:36:05] And I think that's probably what I like to think as accelerated aging. So, that sounds horrible but let me explain. So, as we age, we all lose a little bit of the spinal cord volume and some neurons in the spinal cord and in the brain, that's just what happens. With or without myelitis people in older age walk a little slower, they may be a little bit less strong. And so that happens to all of us.

[00:36:36] What happens is that once you've had myelitis or an injury to the spinal cord, you start at the lower level of that reserve, you have less neurons there. And so, if you lose the normal amount that you were going to lose with aging, you may feel that more or earlier than somebody without myelitis would have felt that.

[00:36:59] So, I do see in my practice that as people get older, they sometimes start noticing worsening function 20, 30 years later after the original event and we repeat the MRIs and often everything is stable. It is just aging on top of less neurons to lose or that's how I understand it, but I think we're still learning about this.

[00:37:23] So, what that looks like is that people may start losing a little bit of walking ability a little bit sooner than folks the same age that didn't have myelitis or the spasticity may get a little worse and things like that. I think the key there is to build up that reserve, build up those neurons that are still there with exercise, staying active as much as we can.

[00:37:52] Even if it's 10, 20 years down the road, I think regular exercise is important and sometimes if there is the conditioning that happens because that happens to all of us, there's a season in your life where you were, I don't know, depressed or less mobile for whatever reason and couldn't get to the gym, people lose function and then a short stay at a rehab place or intense physical therapy for a little bit can regain rescue that function to the prior levels. So, I think it's some symptom management and focusing on building that reserve.

[00:38:29] **Krissy Dilger:** Great, thank you. And Dr. Coban do you have anything to add?

[00:38:34] **Dr. Hamza Coban:** Yeah, I agree that it's very important to understand aging and transverse myelitis or similar disorders. Again, it's hard to tell if there is a direct correlation or if there is an accelerated aging or if the aging is amplifying some symptoms. But at the same time there are other things comes with aging for all of us.

[00:39:05] And those things can be misinterpreted as transverse myelitis related and maybe they can be their own problems. For example, as we get older, we tend to have more medical problems. We start having arthritis. There are heart diseases more common, high blood pressure, diabetes or cholesterol. Those things become part of life for everyone not just for transverse myelitis patients.

[00:39:40] And everything coming together can amplify the symptoms and can symptoms can be felt worse and can just easily attributed to transverse myelitis. But in fact, maybe there are other things other explanation. The other part I think especially with aging in addition to these conditions, there is a high risk of cancer for example. Where it's more common in, in older individuals. Always looking out for those kinds of things and making sure general health screenings are up to date for all of our patients.

[00:40:21] I always encourage them to have a primary care provider first of all to start with and making sure they're screened for age-appropriate cancer regularly and making sure for the blood pressure management, diabetes management if there is any or screening for cholesterol or other possible health problems and being proactive and preventing those problems before they become more of a major issue.

[00:41:01] **Krissy Dilger:** Okay, thank you. And so, we got a few different questions regarding what is in the pipeline right now in terms of research specifically stem cell research or nerve and axon regeneration, that type of thing. Dr. Coban, can you speak to any of that or?

[00:41:33] **Dr. Hamza Coban:** Sure, I think for research in general when we try to do the research for practical purposes or technical purposes, we need to have a more homogeneous or more well-defined problem, medical problem. And then try to address that problem with research. And the other thing is the rarity of the condition.

[00:42:09] What I'm trying to get to most of this research are primarily focused on multiple sclerosis for example, because it's a little better defined and there are specific diagnostic criteria and it's more common and there are more resources available. But it doesn't mean that it's not going to apply for transverse myelitis that's one thing.

[00:42:34] The other thing, there are research ongoing for transverse myelitis specifically to understand better. As I mentioned earlier, we now know some of our transverse myelitis patients are diagnosed with a

different condition now. Maybe neuromyelitis optica spectrum disorder or something else. So, that's also an important thing to point out.

[00:43:02] In terms of those stem cell therapies we get this question a lot rightfully so because they sound promising, and they're advertised as promising. In terms of stem cell, there are different types of stem cell treatments first of all. There is one type especially nowadays has been studied for MS particularly it's called autologous hematopoietic, a bone marrow transplant or stem cell therapy.

[00:43:41] It's basically, how it works is the treatment in that therapy is not the stem cell therapy itself but the chemotherapy part of the stem cell because they're using a very high dose chemotherapy agents and wiping out the whole immune system in a sense and then giving the stem cells back so the immune system can regenerate. Most of the time the chemotherapy portion of the treatment is the treatment for multiple sclerosis for example.

[00:44:16] That one seems promising in some sense, especially for very active MS. But the other ones especially for our patient's interest and maybe one unmet need. Is there any possibility of stem cell treatments that can promote regeneration or repair or remyelination? There have been studies with mesenchymal stem cells. These mesenchymal stem cells can be isolated from our own body from patients from adipose tissue.

[00:44:54] Or sometimes they can use an outside source. Different ways to administer that I know some of them administering through blood IV, some of them try it intrathecal through spinal tap. So, far to my knowledge there is not much promising results yet. At least some of the studies shown to be safe enough to move forward to do larger studies with a larger group of patients and we will see how they will turn out. But so far, I didn't see very promising, very good results with those.

[00:45:43] Another important aspect here is the stem cell tourism. We know and we come across a to lot of times and some of our patients are also interested and even I had done going other countries like in South America or in Europe or Eastern Europe or other places that we know, there are centers doing this kind of therapies. A couple of problems with them a lot of times they don't share their exact protocol and it's hard to speak to what kind of treatments they're using and what protocols they're using.

[00:46:30] And they're overall again mixed results, but that's not something we recommend because we don't have good evidence in terms of safety and efficacy, but it's also a fact that they're available, they're there and some patients, some of our patients prefer to go that route. Luckily, my patients at least they didn't have any major complication or side effects, but they didn't have any significant benefit either.

[00:47:10] **Krissy Dilger:** Thank you. And Dr. Barreras, do you have anything to add?

[00:47:15] **Dr. Paula Barreras:** Yeah, just to emphasize that this is at the moment still experimental, meaning it's not proven to be safe or effective. A lot of shady perhaps not evidence-based interventions being offered under the label of stem cells. And you know that so called stem cell tourism clinics in other countries that are not necessarily offering therapies that are safe or with the standards that we would want.

[00:47:46] So, just cautioning people against that. Now there are trials that are in the context of trying to find out more about the potential of stem cells that are serious studies done by reputable centers and investigators in the US that have been done very preliminary results in the past and there's a trial called BEAT-MS in the context of multiple sclerosis that is still recruiting people but that's not for patients with idiopathic myelitis.

[00:48:25] There is a study I think it's still recruiting based at UT Southwestern led by Dr. Greenberg that's looking into the safety of transplantation of progenitor cells in the spinal cord of people with transverse myelitis, which is a single lesion in the past 10 years I believe. That study is just looking at the safety. So, that's the stage where this is just trying the intervention and see if it's safe. From there on if it's safe, then we would have to do a larger study to see if it helps because it's a big deal, right?

[00:49:06] This implies a surgical procedure, it's invasive. So, if people are interested and, in the area, near to UT Southwestern, they could look at that to see if they would be eligible and contact the study team. But outside that I don't know of any study that is being done in Myelitis with stem cells.

[00:49:31] **Krissy Dilger:** Great, thank you. And I'll just quickly add that anyone interested in that study at UT Southwestern can find information on the SRNA website wearesrna.org under our research tab. So, we've got just a little bit of time left. So, I'll try and get at least one more question in. So, someone asked, "My gait has worsened over the last two years." Is there anything that this person can do to correct or improve it?" Dr. Barreras.

[00:50:12] **Dr. Paula Barreras:** Yeah, but we need an evaluation to understand why the gait is worsening. So, we cannot really give advice blindly let's say. Gait can worsen because of aging; gait can worsen because there is stenosis and degenerative disc disease that can affect people with or without myelitis in the past. So, a new set of MRIs making sure there's no new lesions, taking a look to see if there's stenosis, seeing if the gait problem is because the person is now maybe deconditioned and what is needed is more physical therapy.

[00:50:53] See, like Dr. Coban said earlier, make sure there's no other process like a new medical condition, cancer somewhere that may be stressing the system and leading to worsening symptoms of the old myelitis. If you know all that evaluation comes back with no alternative explanation then the intervention, we do is physical therapy and rehabilitation.

[00:51:21] **Krissy Dilger:** Dr. Coban, anything to add?

[00:51:25] **Dr. Hamza Coban:** Yeah, I agree with Dr. Barreras. A lot of times in my experience also the most common reason is the insufficient symptom management for the most part. But certainly, we need to make sure there is no other thing is contributing either structural disease or herniation or another medical condition. And one other important symptom that can worsen is spasticity which is very common.

[00:52:01] And if spasticity is not well addressed, the gait will be reversed and it's going to continue to get worse. I think that's another important thing to address properly. Sometimes to address that we use systemic medications and sometimes we use local injections like Botox and a lot of times after optimizing those symptoms, the gait also improves.

[00:52:31] Sometimes there can be some mild issues. To boost the walking speed for example I sometimes just order off label Dalfampridine which is technically indicated FDA approved for multiple sclerosis, but we can utilize for these conditions too to see if there's going to be any additional benefit. Those are the main things and at the end if everything is addressed properly and on repeat scan there's nothing new, we sometimes say that too that and we can't explain that well, but we do our best to make it better with therapies or otherwise.

[00:53:25] **Krissy Dilger:** Great, so, we only have a few more minutes left. So, I don't think we'll have time for a full question, but I just wanted to open the floor and kind of ask if there is anything you want to close out

the session with or anything you want listeners to know about, you know, any hope you can give or anything you'd like to add Dr. Coban if you'd like to and obviously, I'm putting you on the spot. So, no worries.

[00:53:58] **Dr. Hamza Coban:** Of course, I think I'm grateful that we came a long way as a community to addressing these rare neuroimmunologic conditions. And now we are making more accurate and more timely diagnosis and a lot of times we are able to prevent significant disability. But we have to be aware that we have to acknowledge that we still have some limitations.

[00:54:32] There are still a lot of unknowns and as a community I know we are working hard; everyone is working hard. I think there's a lot of hope that I think we will keep learning about this condition and we will have better treatments, better approaches and hopefully better outcomes.

[00:54:57] **Krissy Dilger:** A great sentiment and I completely agree. Dr. Barreras anything you'd like to close this up with?

[00:55:05] **Dr. Paula Barreras:** Yeah, I mean, I'm an advocate as you know of the terminology changing and the criteria for diagnosis changing. So, I'll say that anybody who was diagnosed as idiopathic transverse myelitis especially over 10 years ago or maybe even like over eight years ago was probably diagnosed at a time where we didn't have the standard test that we use today to screen for neuromyelitis optica, for MOG and for some other causes of autoimmune myelitis.

[00:55:38] So, it's always good to circle back with your neurologist and ask if that has been ever checked and confirmed that you got the full evaluation the first time around and the diagnosis is actually idiopathic myelitis and not something else because that may have implications for the risk of relapse in the future. If things are still idiopathic myelitis just know as a hopeful thing that most of these are one-time events.

[00:56:10] And although what happened and it may be that you are left with a lot of symptoms, chances are this won't happen again, and that recovery will continue, and that people can have full happy lives after myelitis.

[00:56:25] **Krissy Dilger:** Right, yeah. I love that sentiment because it is so true. Well, thank you both. We're out of time and thank you for everyone who joined us today. We appreciate all the questions that were submitted, and I do apologize we didn't get to all of them, but hopefully we can answer some more in a podcast coming up or in another format, but I hope you all have a great rest of your day.

[00:56:52] **Dr. Hamza Coban:** Thank you. Thanks for having us. It was great.

[00:56:56] **Dr. Paula Barreras:** Thanks for having us.