

In-Person Breakout Session III:

TM and AFM

You can view this presentation at: youtu.be/yCOWJfnLNjo

[00:00:04] **Dr. Benjamin Greenberg:** Welcome, everyone, to the breakout session. So, just to make sure you're in the right place, this session is going to be focused on transverse myelitis and acute flaccid myelitis. If you thought you were in the MOGAD/ADEM session, you're wrong, but it's your lucky day. This one's going to be way better than anything that happens over there. The breakout sessions end in a tug-or-broke competition between the sessions, and team TM/AFM is going to win, I have no doubt.

[00:00:29] So, I'm joined today by colleagues Leslie Benson and Carlos Pardo, who are coming to be below the Mason-Dixon line and all the way south from their respective homes in Boston and Baltimore. We really wanted to make this, obviously, educational but somewhat informal and conversational. There are a lot of topics that we could talk about when it comes to myelitis, whether it's the classic transverse myelitis or the acute flaccid myelitis.

[00:01:00] We didn't want to presume that the topics that we would put at the top of the list were the ones that were most important to you. So, I'd be curious. I don't know if either you want to start with a few comments at all about your perspective, but pretty soon, I'd like to hear from you just in a sense of what the biggest questions or topics are that you deal with. And there's a lot that we can address. Carlos or Leslie, are there any comments you want to make?

[00:01:28] **Dr. Leslie Benson:** Just a little background, because I'm not sure we've given it yet: I'm a pediatric neuroimmunologist, so I see kids and can offer the perspective for the younger patient population, the questions that impact that population.

[00:01:46] **Dr. Carlos A. Pardo:** But Leslie is not afraid of pathoneurology. So, you can ask also questions related to the above. I think that, as Ben has stated very well, we are not going to show any magic slide. So, forget about this, but we don't want to show you a slide, we don't want to give a lot of information the value's gone next day. What we like that we do is, we establish a very good conversation in which you are going to basically ask questions that you would like to clarify, and we will try to do our best.

[00:02:23] So, we are dealing with two major group of disorders -- not two disorders, group of disorders -- in which we are still learning. But we like that you ask the question is those things that are always in your

mind: Why I got this? or What is going on? But I think that the most important part is, let's start with a good conversation. I call that what's going to be a roundtable but it looks like people are far away, but if you want to come here, you're welcome. Go ahead, Ben.

[00:02:57] **Dr. Benjamin Greenberg:** All right, you all. I'll open things up, and actually, at certain times, I may ask just by a show of hands. You do not have to self-disclose anything. There's no pressure here. But just to get a sense, in terms of who's in the room, for either patients or caregivers or family members or friends of individuals affected, how many people here are coming to this conversation concerned about their transverse myelitis diagnosis and anything related to that?

[00:03:21] And then, is there anyone in the room coming from the perspective of acute flaccid myelitis, in that categorization? Okay, so some. So, a bit of a split, but that's exactly what we're open for, both. I'll start by just asking if anyone is willing to share: as you sit here today, what is your top concern?

[00:03:40] So, if there was a question either about symptoms or something you've been managing, please share. And I forgot to put one caveat in this, and that is for all of us: there may be some questions that get to be very specific in terms of your management at a medical level. We cannot give specific dictated advice of, "Oh, I would take this drug at 300 milligrams a day." We can talk in generalities.

[00:04:12] And what you'll hear us say over and over again is: we're happy to work with individual practitioners that you're working with and offer more concrete advice. So, if there's a very specific question of, "Hey, should I have my gallbladder out?" we're probably not able to answer that for you, but we'll do our best, based on the topics you ask, to put it in general commentary. So, with that as a caveat, I'll open up the floor. Yes, sir. Oh, and there's a microphone, and this is being recorded. The audio is being recorded, so we'll ask that you have the microphone for the question purely so that we can keep track of things.

[00:04:51] **Audience Member:** Hi, I have TM for 15 years. I've been taking 2700 milligrams of gabapentin every day since then. My issue is fatigue, and I've heard that gabapentin has that kind of effect on people. I'm just wondering -- I know you prescribed something else -- but is there anything I could do in terms of the fatigue I feel on a daily basis where I just don't have any? I have it in my mind all the things I want to do, but my body just doesn't want to work with me.

[00:05:47] **Dr. Benjamin Greenberg:** Jeff, thank you for the question. It's a spectacular question. I'm going to repeat it just to make sure everyone in the back was hearing. If I say anything incorrectly, Jeff, throw something at me. So, Jeff shared a story of being diagnosed with transverse myelitis over a decade ago and has been on a drug, gabapentin, sometimes called Neurontin, taking it multiple times a day. I didn't ask: what was the reason for the gabapentin? Is it for pain management?

[00:06:16] **Audience Member:** Pain management.

[00:06:17] **Dr. Benjamin Greenberg:** Pain management reasons, but is also struggling with what's described as fatigue. So, I want to do this with my day, but my body won't do what I want it to do from an energy perspective. Then, what are the options for managing this? That's the summary of the question. It's a great question. It's something we deal with, I would say, every clinic in our myelitis center, and this is something that crosses over pediatric and adult.

[00:06:41] Leslie, I'll start with you. When somebody's coming in on any medication, and so, whether it's gabapentin or anything else, and the chief complaint, the reason for sitting with you, is fatigue with a background of a myelopathy -- a myelitis diagnosis -- what's your general approach to the situation?

[00:07:00] **Dr. Leslie Benson:** Yeah, I think it's a balance, right? So, you're trying to figure out: how do I optimize my pain management and minimize my fatigue? And so, finding the sweetest spot you can with your gabapentin is one option. I imagine that's probably been the game you've been playing. Not working.

[00:07:21] Okay. But then, I think that the next question in my mind, if I hit a point where I couldn't manage the pain without fatigue that the patient wasn't happy with is: let me think about what other medications are there. Are there other medicines that maybe would be better tolerated? Sometimes, patients who don't tolerate a sufficient dose of gabapentin, it's kind of cousin Lyrica is one of the medicines that gets used.

[00:07:47] There's a class of medications called tricyclic antidepressants that we use in some of our kids. So, I think there are other meds, but they come with their own host of side effects. And so, there's not a one-size-fits-all medicine for the problem. And then, when you find the best medicine that you can, walking that balance beam, then I think we start to talk about how do you manage fatigue as well.

[00:08:13] And we talk about fatigue a ton in our MS population and our myelitis population. I think some of the concepts of fatigue management are applicable to a multitude of conditions. Most of the -- I'd say the crux -- of fatigue management is lifestyle, which isn't always easy to hear because it's not fun to change your lifestyle necessarily. But things like making sure you are optimizing sleep at night and working on the quality of your sleep at night to make sure you're waking refreshed is one thing that we can work on.

[00:08:58] For some people, exercise during the day can actually be quite energizing. And so, for some of my patients, good exercise, consistent exercise can then help with both the quality of sleep at night and the daytime fatigue. So, for some patients that's helpful. Again, if you have myelitis your ability to exercise and what exercises work are going to vary. And then, we sometimes do things like an enzyme, Co Q-10 has some data in MS for helping with fatigue, and it's a pretty safe thing to take.

[00:09:28] Some patients do a trial of that and see if it helps with their energy levels. It's a complex problem, and then even to the point that sometimes we use medications for fatigue to help wake people up during the day. It's a big topic, and the nuances of where each patient is at with their fatigue varies. That was a long-winded answer. What do you want to add?

[00:09:53] **Dr. Benjamin Greenberg:** Well, but there's a lot there, and I'll just maybe put the same data in a slightly different construct. But just for fun -- so, if you are, again, if you want to self-disclose, if you are someone affected by one of these conditions, of you in the room, how many of you have fatigue?

[00:10:09] All right, so hands down. If you're not affected by one of these conditions, how many of you have fatigue? All right, we've got a few. So, it's important to know fatigue, and I think we're at 95% of the room is fatigue, and it's after lunch, and we're talking. So, back to the siesta.

[01:10:23] **Dr. Leslie Benson:** Because adding mine with it, yeah.

[00:10:25] **Dr. Benjamin Greenberg:** There you go. So, one of the concepts in our clinic and in rehabilitation medicine -- we have Dr. Sinn here, I may have her pinch it a little bit -- is the notion of energy conservation. Here's the way I describe the fatigue to individuals in my clinic: it's all about a household budget. So, we all have to figure out how to live within our financial means.

[00:10:55] And there is an income and an expenditure. And if you spend more than you make, you're going into debt. And it's the same thing for the energy you use in a day. You make a certain amount of energy in the day -- you have an income, and you have expenditures. If you expend more than you made, you go into

debt, and fatigue sets in, and it's the brick wall that you hit at 10:00 AM or 2:00 PM or 3:00 PM, and your day is done because you have spent your entire budget by whatever time occurs.

[00:11:24] And so, really the options -- I mean, politics aside, Congress hasn't figured out balancing a budget -- but you have to balance your energy budget every day. And so, you really have two options: increase income or decrease expenditures. Those are the two things. So, the first thing you do in a household is you create a budget. Where are you spending money?

[00:11:44] I'm paying with teenagers for a lot of streaming services that I never look at, but there's money going out the door for every type of streaming service, and that affects our budget. One of the things to remember, regardless of your diagnosis: once your spinal cord has been affected, whether you fell off a motorcycle, or had an immune system event, or an infection affect your spinal cord, every step you take costs more money than it used to.

[00:12:13] So, imagine all of a sudden, the utility company said, "Hey, we know we're charging you 10¢ per kilowatt hour for your house. We got to change. It's going to be 50¢ per kilowatt hour." Your lights are on for the exact same amount of time in a day, but you're spending five times your budget on electricity than you used to. That's essentially what happens after a spinal cord event.

[00:12:33] You are spending more money on every step. So, the simplest thing, getting up and getting dressed in the morning. That is what? You can do it, but you have spent a huge amount of energy that you used to use for other things in your day, and now you can't. And so, when we're approaching fatigue in our clinic, I break it down into this notion of income and expenditure. And everything that Leslie said, I agree with a 1000%.

[00:12:58] There are things that can increase your income. Sleeping a complete eight uninterrupted hours a night is one of the biggest ways to build an income. So, one of the top priorities on our clinic when somebody says, "I'm fatigued," the very first thing, before we get to medications, is to say, "Are you sleeping at night?" I have fixed more fatigue in my clinic by treating bladders than anything else.

[00:13:22] If I can get somebody not to get up at night and go to the bathroom, I salvage energy during the day because they're sleeping. So, sleep is in the income category. Exercise is in the income category. Nutrition is in the income category. Hydration is in the income category. Lots of things we do -- Co Q-10. Lots of things that may increase your income, but then, we get to the expenditures. And this is, in my world, the real tricky part.

[00:13:50] Leslie's polite and talks about lifestyle choices. Sometimes it's lifestyle, and sometimes it's mechanics. So, if you have altered walking mechanics -- so, we're supposed to walk left, right, left, right. Our heel is supposed to strike the ground before the toes. And if you have that little bit of weakness on your right side, and you're swinging your leg and you're not lifting the leg, you are spending more energy walking than you should be.

[00:14:18] So, we refer people to folks like Dr. Sinn to get fitted with an AFO brace. Not because you look better walking that way, but you actually end up saving energy. So, there are some approaches in rehabilitation medicine, bracing and other things, that aren't just meant for structural but are actually meant to help with the fatigue side of things. And so, getting better mechanics can go a longer way, but it's a little bit of all these pieces. And medications, you're right, play a huge role in this.

[00:14:51] And, unfortunately, in my experience, it's trial and error to see, "Can we find a medicine for a person that takes away pain but isn't adding to the expenditure by fatiguing the patient?" I can't guess which patient will respond to which drug yet, even after all these years, and so it's trial and error. So, if drug X isn't the

right balance for a person, we try drug Y, drug Z, but in the background, we try all these other approaches to manage that.

[00:15:19] I don't want to put you on the spot, Clarice, but I don't know if you have a comment about this from the rehabilitation perspective on energy conservation or the fatigue aspect. And would you introduce yourself for everyone, I kind of just called you out.

[00:15:32] **Dr. Clarice Sinn:** Clarice Sinn. I do pediatric rehabilitation medicine, but I'm also Board Certified in adult rehab medicine. Used to work with Dr. Greenberg in Dallas. I'm now at University of Kentucky. You, kind of, said everything I would. My biggest talk with my patients is that energy, you know, we're using a lot more because you're not walking in a normal gait pattern that we would consider.

[00:15:54] So, it takes them a lot more. So, sometimes we talk about adaptation. Are there ways that we can adapt what we're doing so we're saving energy? The biggest talk I have with parents is when we go to the wheelchair talk. The biggest concern is, "If I give my kid a wheelchair, they'll never walk again." And that's usually not the case. Same with the adults. My best example is: okay, we're going to go to the playground. But let's say the parking lot is half a mile from the actual playground.

[00:16:23] If you park your car and your kid wastes all of their energy walking to the playground, now they can't play at the playground. What was the point? What if we use the wheelchair to get to the playground, and then, once we're at the playground, they can get off, get up, and play. So, that's usually the example I use for the kids. Save that energy for something fun or, in the adult world, something you have to do -- may not be fun.

[00:16:47] But also, let's say standing up and doing laundry is exhausting. It wears you out. So, we can talk about, okay, somebody brings you the laundry, but I can sit down and fold the laundry. So, there's a lot of different ways, and it's very patient-dependent. Like, what are your goals? What do you want to get out of this? And so, we kind of focus on that.

[00:17:07] Are there ways we can do it to make it easier, either through equipment like bracing, adaptive devices, or just make it easier for you to do it. So, when I do my consultations, I always say, "My goal is to get you back to doing what's fun," -- for kids. In the adult, it may not be fun, but what you have to do as an adult.

[00:17:26] **Dr. Benjamin Greenberg:** Well, so, I've stolen part of that in the clinic, and I break all steps. Every step you take today, I put it in one of four categories: it is a necessary step, it is a fun step, it's an investment step, or an unnecessary, unfun, noninvestment step. So, the necessary steps are things that you have to do: to get up to go to the bathroom, for example. That's a necessary step; you need to go do it.

[00:17:50] A fun step: you want to go out to dinner with friends, or you want to go to the playground as a child, but you should be able to do that. Then, there are the investment steps: that's exercise. So, sometimes, you have to do an investment and expend some energy to build a savings account that ultimately gives you interest payments that you get to live off of later.

[00:18:08] So, exercise, even though it's an expenditure, can actually increase your budget over time. And then, there's the fourth, which is what you're talking about: the unnecessary, unfun, un-investment steps. Walking to the playground -- we're at ground zero for most unnecessary steps in the world: airports.

[00:18:27] You can get from security to your gate 50 different ways. I don't know why any of us walk from security to the gate. That is the worthless ways to set. So, I had this conversation with a patient of mine, and I used some of your examples. And she came back to clinic six months later, and she was doing very

well. She had gone from hitting her wall at 2:00 PM in the day to hitting her wall at 5:00 PM in the day -- three hours, which was huge for her.

[00:18:50] This was a big deal. So, some people, they hear that are like, "Well, that's not a big deal." This was life-changing for her. She did it by looking for every unnecessary step, and she showed me a picture of her kitchen -- I'll never forget this -- and she said to me, "You know, I thought about how many steps I waste making dinner." I said, "Well, tell me about this." She says, "Well, the easiest dinner to make is spaghetti."

[00:19:14] "There's a box of spaghetti. You boil the water. I don't even do a homemade sauce, it's a jar of Ragu. But I counted all the steps in my kitchen to go from the pantry to where the bowls are to where the this is. I walked my kitchen four times to make spaghetti. So, I decided to rearrange." Now, she puts away all of her groceries next to the pots or pans that would be used for those groceries.

[00:19:36] So, you open her cabinet, but it looks like she has dementia, because in the colander is pasta and sauce and anything you would use a colander with, and in this pot are boxes of macaroni, and in this pot is soup. And she said, "Family members came over and thought I needed a psychiatrist." She says, "I walked to one cabinet, and everything I need for dinner is in that cabinet, and I cut out the steps."

[00:19:58] And she did more things and just go bonkers with her kitchen, but she got three hours out of the day. No medication changes, no exercise routine, just changing her routine in her house and her setup. So, those unnecessary steps, they're everywhere, but they can make a big difference for fatigue. I mean, Carlos, I don't know if there are other approaches, either on the medicine side or the life side.

[00:20:24] **Dr. Carlos A. Pardo:** I think that the three of you actually touched the critical aspects. I will add a little bit about the issue of the medications and fatigue because that is a major, major practical problem for patients and for us. Is, as much medication you take for calming down the pain, you are going to get fatigue. The majority of those medications produce those side effects.

[00:20:50] So, as Leslie stated before, it's extremely important that you discuss with your physician if there are other strategies or other medications. Unfortunately, gabapentin and Lyrica are extremely famous to produce a lot of fatigue and increase the amount of fatigue. So, it's a good conversation with your health care provider and see if that's the best option, particularly if you have been already 12 years with that medication.

[00:21:16] There is a second element that Leslie and Ben mentioned, but I will overemphasize: your sleep. How many of you have naps during the day? Almost half of the group. How many of you have naps for more than 30 minutes? Okay, all right. So, I encourage you to have a nap during this meeting, but don't be serious about it.

[00:21:52] The reason is, one of the most frequent problems that we have with the sleep disorders is something that we call sleep hygiene. We don't have a good sleep hygiene in general. Number one: we don't go to bed on the right time. Number two: we keep watching TV, and got sleepy, and then we believe that we are sleeping and the TV is on, or we have all the practices that basically are disrupting the sleep.

[00:22:21] For example -- right, exactly -- so, TikTok and all the media that you go and go to bed and just keep doing that. That is disrupting your sleep. You don't imagine how much light is coming from your iPhone, okay, and you are putting that in your retina. And guess what? You are inhibiting, basically, the retinal-pineal gland network. So, it's keeping, basically, your brain active. So, you need to develop a strategy to sleep better. Why sleeping better is good thing? Because when we sleep, our brain and spinal cord are detoxified. So, one

thing in the past 10 years in neurology is, we are learning more and more about the basic size of sleep and the way that the brain recovers.

[00:23:19] We use our sleep to recover the brain, and the brain uses that period to detoxify from a lot of metabolic things that we generate during the day. During that period, actually, we are going to clean up our brain. So, if you don't sleep well, if you sleep only three hours, four hours, you don't have enough time to detoxify your brain. And guess what? Next morning, next day, you are going to be with brain foginess, and you are going to be somewhat disoriented.

[00:23:56] Think about your sleep routine. Think about if you have a good hygiene with your sleep. Go to bed on time. Don't get distracted, TV, radio, or cell phone, and they will feel extremely important. Don't eat too much before going to sleep, because if you have meals, like, one hour before, two hours before, three hours before, actually, that has very important metabolic impact on the brain. Your sleep is not going to be really relaxing.

[00:24:32] So, one of the messages that I want to emphasize is: pay attention to your sleep. If you think that your sleep is not normal, talk with your health care provider, get a consultation with a sleep specialist. Last thing: how many of you recognize that you are a snoring person? Okay, all right. Be careful with that, because you may have a condition: sleep apnea disorder.

[00:25:00] Sleep apnea disorder is very frequent when we exceed our weight, and that is one of the major factors for sleep abnormality. You believe that you are sleeping -- no, you are snoring all the time. Then, next day, you are going to be tired and exhausted. You need to fix that, and you need to talk with your health care provider to get a very good assessment for sleep disorders and make sure that you take care of that risk factor.

[00:25:27] **Dr. Benjamin Greenberg:** Yeah, I couldn't agree more, and I'll add one just creepy experiment if you want to do. So, if you get a Nest Camera or one of those cameras you can have, have somebody go into a dark room where you have the Nest camera. How many people's phones have facial recognition, that's how you unlock your screen? Oh, well, camera. Have somebody stand in front of the camera in a dark room with the phone in front of them. It's infrared light, and it's a strobe light flashing at your face.

[00:25:53] The entire time you're looking at your screen, it is flashing at you. And, as Carlos said, for very unfortunate reasons, it's the exact wavelength of light that tells your brain you should be awake. And so, every time you're looking at one of these screens, you are getting a completely invisible stimulus -- that you can see with night vision from a Nest Camera -- of this strobe light flashing at you. And it's really resetting our clocks in very creepy ways. So, I just throw that out there just to really upset everybody. So, yeah.

[00:26:31] **Audience Member:** I have an issue with my (inaudible) and I took it for 3 years, but then my brain seemed like it took me a while to finish my sentences. And so, I got moved to dantrolene. I was on that for eight months, and I had every side effect that just (inaudible). The last medication was duloxetine (inaudible) had an issue with that and (inaudible).

[00:27:56] **Dr. Benjamin Greenberg:** Yeah, so if it's okay, I'm going to broaden the question just topic-wise to: multiple trials of medications for symptoms, either muscle tightness or pain, and either with growing used to it -- what we call tachyphylaxis -- the medicine isn't working anymore, or side effects, or concerns about side effects that are having you decide, "I know this is recommended, but I'm going to avoid medicine X, Y, or Z."

[00:28:22] So, this is a common question around in the world of symptomatic management. When we're using medicines, what should we be aware of? What should the approach be in general? And this could be

broad -- about pain or spasticity -- just the general approach of how we prescribe, judge if there is an effect, judge if there is a side effect, and make decisions about switching versus not.

[00:28:46] Before you answer, I'll just put in a plug. I'm pretty sure every medication's label, at some point, says 'risk of death.' And so, it's one of those ones where we see it. It's always really about, "Well, how big a risk of death are we talking about here?" And so, never let that one dissuade you, but it gets to the fundamental. Leslie's laughing at me, but it gets to the fundamental thing, which is what you're going to say: talk to your health care provider about it relative to the individual.

[00:29:17] How do you approach it? So, you're prescribing a medicine for an individual. How do you counsel them in terms of declaring success, failure, need to change, those types of things?

[00:29:28] **Dr. Leslie Benson:** I think I would reword the 'never pay attention to the death side effect.' Like, if it's 50%, maybe do pay attention.

[00:29:36] **Dr. Benjamin Greenberg:** I mean, listen, this is like the Dumb and Dumber: "Is there a chance to come out with me?" "One in a million." "So, you're saying there's a chance." You know? I mean, it's always a matter of how much in, to be fair, to be zeroed out. One in a million may be too high a risk for you for the indication that you're being recommended the medicine. So, you may say, "Thanks, but no thanks." If it's one in two, that's probably a risk we're all like, "Yeah. I don't think so." But, yes, it does matter. The number does matter.

[00:30:03] **Dr. Leslie Benson:** But do you think that's a great kind of segue to: it's really up to the patient? So, when we're talking about acute management or long-term prevention of attacks, I tend to feel pretty strongly, like, I want to make sure people understand the risks of not treating. Whereas, when we're talking about symptomatic treatment, it's a very different construct. Like, I'm there to support you in fighting and helping you be the best you -- live the best life you can.

[00:30:29] And so, ultimately, the patient is the person who knows how bad the symptom is and what risks they're willing to take to treat that symptom. And so, if that death risk is deterrent from the symptom and they'd rather just deal with the symptom, I'm going to respect that. And so, it really is an individualized and patient-driven decision when it comes to what we classify as symptomatic management.

[00:30:57] We're not treating the underlying disease. We're not treating the chance of a relapse happening. We're treating the current symptoms that are impairing function -- whether fatigue, pain, spasticity, headaches. It's really the patient's experience that drives how hard do we push to treat the symptom. I mean, that's kind of broad view.

[00:31:22] **Dr. Benjamin Greenberg:** But in a granular way, you write the prescription for drug X. So, for a lot of drugs, we start at a low dose and we go higher. Sometimes there are early side effects, sometimes late. You have general words of advice both in terms of what to expect, what your approach is, or when you want to hear from your patients in terms of their experience.

[00:31:45] **Dr. Leslie Benson:** It's also super individualized, right, Ben? Because some drugs will work within hours, other drugs take two months before you can assess whether they're beneficial. So, it depends on the medication that we're using and what we expect that medication to do. And so, Ben alluded to trial and error earlier, but really, a lot of symptom management is, "Here's a medication that might help your symptom. Try this low dose. If it's not enough, here's your up-titration plan."

[00:32:11] “Please check in with me at X time, when I think you might be seeing side effects or an effect, and then we can regroup on whether, if you’re well-controlled, stay there. If you’re having side effects, maybe we need to take a step back.” It really depends on how you’re tolerating it, how much benefit you’re seeing, and what our goals are of using the medication before we can make the decisions about how high to push that medication and when to call it a failure.

[00:32:41] **Dr. Benjamin Greenberg:** Carlos, do you have nonprescription approaches to either pain or spasticity that can take the place of a prescription?

[00:32:49] **Dr. Carlos A. Pardo:** The answer is, yes. Actually, I learned this after being a soccer coach for my kids. You always need to have plan A, plan B, plan C. Let’s take symptom by symptom. So, we already talk about pain, but let’s talk about the spasticity. This is the major question that you have. Medication for spasticity have the same type of side effects that we deal with pain.

[00:33:16] A lot of brain fogginess, tiredness, fatigue, and a lot of side effects. So, guess what? The first thing that I do when I have patient that is spastic, I need to assess what is the magnitude of spasticity, because the first line of assessment that I do and management is talk with my colleagues in rehab. So, in other words, if a patient come to us, basically, we examine them, we evaluate the magnitude of spasticity.

[00:33:46] There are a lot of strategies from therapy rehabilitation point of view that are very good and very free of side effects, right? So, that’s one of the first low-hanging fruit that we approach is: let’s make a plan with physical therapy rehabilitation. Make sure that it’s a good plan for managing spasticity. Let’s go to the management with medication.

[00:34:10] Again, here is plan A, plan B, plan C. You can introduce medication that is quite strong, like baclofen, or you can introduce another medication, like tizanidine, or you may introduce other medication, but this is a trial-and-error approach. Now every patient metabolizes these medication in a unique manner.

[00:34:34] Basically, they develop different type of metabolic pathways where the patient develop a lot of side effects. So, you need to try and see if that patient is able to tolerate the medication well without too much side effects. If that fails, you need to establish the temporal use of that medication. You say, “Okay, I will try baclofen for two months, three months, four months. We will increase the dose.”

[00:34:59] It’s a very frequent mistake to add to one antispastic medication a second antispastic medication and a third antispastic medication. That’s a mistake. Frequently, what we recommend is just let’s start with a titration regimen, and then optimize the dose and titrate the dose to reach an optimal dose. If we are not able to achieve that, that is when we need to move to plan B.

[00:35:25] And plan B may be a different medication or a combination of physical therapy rehabilitation with medication. So, that basically, in summary, what the norm prescription approach for spasticity. Probably, you can help us later to understand how you manage that from your point of view. But the other thing is, one of the medications that you mentioned, duloxetine, is also called Cymbalta, okay?

[00:35:55] So, a lot of use of Cymbalta is originally antidepressant medication that we use frequently for many things, including pain. And it’s a very good medication. But again, is the issue of how we are going to titrate and, particularly, what is the main goal of the medication. If the main goal is pain management or the main goal is try to modulate your mood to make sure that you are not depressed or something like that?

[00:36:22] So, it's basically playing different roles and establishing, basically, a good way to evaluate what we call the outcome. So, anytime that we prescribe a medication, we need to set up the timeframe of using the medication, and we need to establish the goal and the outcome measure, meaning how we are going to evaluate that the treatment is successful or not. Do you like to comment about spasticity?

[00:36:54] **Dr. Benjamin Greenberg:** So, Dr. Sinn is coming to the mic, yeah.

[00:36:56] **Dr. Clarice Sinn:** Yeah, for spasticity, if that's your main issue, first line is therapy, stretching, bracing, all of that. But sometimes, in my first consult, the tone could be out of control. So then, I'll go ahead and start a medication on top of those other things. I have a few patients who, no matter what med I give them, get way too sleepy. They just don't like the outcomes or the side effects from it. Where the muscle pain or spasms are pretty focal, meaning, like, it's just my calves or it's my bicep, but it's not just everywhere.

[00:37:29] This sometimes will do injections like Botox, Dysport. That works pretty well because you're not getting those other side effects of the sleepiness and fatigue, and it goes exactly where I want it. So, if I do an injection into your calf muscle, it's going there. Whereas, if you take muscle relaxant, it can be affecting the whole body. So, sometimes that's an option as well just depending on what the issue is.

[00:37:56] **Dr. Benjamin Greenberg:** And last comment, I know we have some more questions. There's a comment Carlos made that I just can't overemphasize: it's cataloguing the different issues. So, I've been guilty of having patients come to me saying, "I'm in pain." I prescribed drug X. They come back and they say, "I'm still in pain." And we do this for two years in a row, and it turns out they had three different aches, and a drug works for one pain, but not the other two.

[00:38:20] So, they were still "in pain," but actually, the first drug was very effective at getting rid of one of the three pains. So, if you're having these symptoms, particularly pain and spasticity, cataloguing and understanding if everywhere you experience it is the same or different, because you may get a benefit in one area with one drug, and you have to break it down for your provider to know what's responding and what's not. So, I know we have a question in the back and then right here. So, in the far back.

[00:38:49] **Audience Member:** Hi, I'm Cathy Salmon. My husband was struck with TM last July. And same, unlike the fish, is relevant because we floundered until I came to the annual meeting last year and literally stood up in front of everyone and begged to get into UT Southwestern. Two weeks later, we had an appointment with Dr. Tardo and are beyond grateful for the team and the care at UT Southwestern, outstanding.

[00:39:17] Now, I have to speak in generalities because that was our instructions, and I absolutely will, but Dr. Tardo told me to ask you this. So, I thought maybe today would be...

[00:39:30] **Dr. Benjamin Greenberg:** That doesn't sound general. Can I get a judge's ruling? Okay.

[00:39:32] **Audience Member:** I thought today might be more relevant than Sunday (inaudible) and hopefully if anybody else is interested, (inaudible).

[00:39:40] **Dr. Carlos A. Pardo:** Your microphone is off, so.

[00:39:43] **Audience Member:** Sorry.

[00:39:43] **Dr. Carlos A. Pardo:** Your microphone is off.

[00:39:45] **Dr. Benjamin Greenberg:** I think it actually may be the receiver. No, it's whether or not the signal's getting to here. Yeah. I'll repeat if people can't hear.

[00:39:52] **Audience Member:** So, question is around (inaudible). It's interesting how we talk to about (inaudible) here. It's a topic that is very (inaudible) and all we hear are only positives, not the negatives. (inaudible) or they don't talk about this (inaudible). So, my question to you all is for those who may someday be interested (inaudible) or is there any source other than clinicaltrials.gov or the National Health Library that summarizes (inaudible).

[00:40:39] **Dr. Benjamin Greenberg:** Okay. So, the question, which is a good one, is around stem cell therapy, and you can go to YouTube, Facebook, online, or talk to friends, and everybody knows somebody who knows somebody who went to a clinic in Panama, and went in a wheelchair, and is now a marathon runner running 4-minute miles. You never hear about the risks or the downsides.

[00:41:00] And the question is, if you're interested in that therapy, beyond clinicaltrials.gov or other resources in the U.S., what are the avenues? And, there will be a talk, an update on the Q-Cell trial, on Sunday, and I'll include there's some inclusion about other stem cell therapies and how we separate them out. I mean, Carlos, we've had this conversation for a very long time. I'll let you take the first swing at this.

[00:41:23] **Dr. Carlos A. Pardo:** I'm going to swing here, but I will allow Ben to complete. So, this is a topic that is not new. When we had the first meeting back in Baltimore, more than 20 years ago, this was one of the topics, particularly because during that time was the explosion of information about stem cell therapy. Everybody was crazy about stem cell therapy. Unfortunately, when we are trying an intervention in human beings, we need to prove that, that intervention is effective, and we need to go in a very long route from testing what we are going to use, meaning the stem cells, making sure that those are safe, and doing trials first in an animal model, and then moving to the human beings.

[00:42:15] In the past 30 years, we have been dealing with obtaining which would be the best stem cell to put in a spinal cord in the brain. We have candidates, and we are using some of those candidates already. So, we already focus in the potentiality of the stem cells. The second that has been done in the past 30 years is, what is the best way to introduce that stem cell in the environment that we like to basically make sure that we are going to obtain a good outcome, meaning regeneration.

[00:42:57] That part of the assessment has been a little bit controversial because the results have been in different ways. We have animal models that have been showing some interesting findings in potential remyelination, potential regeneration, but other tests have been a little bit on the negative side. So, that part is still undecided. We don't know what is the best technique. We don't know yet what is the safer technique to get that stem cell where it should be working, but the most important part is safety.

[00:43:43] Anytime that you intervene in your human body, you open basically the skin, or the skull, or the vertebra, or the spine, you are exposing the body to a major risk -- major risk of infection or maybe a risk of bleeding and other things. One of the problems that we encounter with stem cells is, in some circumstances, we may need to induce some degree of immunological suppression to make sure that, that stem cell is going to engraft in the tissue that should be working. And that imply a risk because that imply a risk of infection, right?

[00:44:23] So, again, the major issue that we have: why we still don't have any stem cell plan of treatment at this moment is because we haven't achieved the assessment of safety and the proof that there is a good outcome. And, for example, Ben is going to clarify that with the work that he is doing, but I think that one of

the beauty things that we have in this country is that we have some guidelines. We have basically, norms to evaluate interventions, medications, and the stem cells.

[00:45:02] I need to give you an anecdote about one of my patients that, unfortunately, went to one of these countries and basically paid because he had capacity for pain. And it was very sad because we advised not to go, because the explanation I'm giving to you. Anyway, so there is no really a good control of these stem cell therapies in these countries. And the quality that is used is really minimal. The surgical procedures or the interventional procedures are really minimal.

[00:45:39] So, this poor patient actually got in bad situation because infection and the reaction to the graft of cells that was given. Again, it's simply because, the use of those stem cells is being offered by people that, yeah, have some idea about the manipulation of stem cells, but in many ways, is a deceiving approach, because it's producing more harm than benefit, because they haven't proven that it's effective or it's safe. Always when I get the question about stem cells, I say, "We are still in the face of testing. We are still in the face of evaluating safety, and we need to be realistic."

[00:46:23] We are not able to jump right away. I mean, Ben is going to explain to you how long we have been taking from going from point A to point B. It has been years. And the reason is, we are not playing with mouse or mice. We are not playing with animals. We are playing with human beings. And we need to be extremely ethical and transparent in what we are doing. And that's exactly the duration in time for achieving the main goal.

[00:46:55] **Dr. Benjamin Greenberg:** When I was at my first symposium, Doug Kerr was asked the question, "When are we going to have a stem cell trial?" He said, "Five years." That was a total off. Fifteen years later is when it really came about. And I agree with everything Carlos said, but I'll just make two comments. The first one may sound a little cynical, but it's not. It's very hard. It is extremely hard to see the perpetual online stories being told of success in different clinics around the world and not sit back and say, "That's got to be true. Why am I not doing it?" That's a very difficult position to be in.

[00:47:37] And there's a couple challenges. So, number one, I've had lots of patients who have travelled overseas for what was advertised as stem cell therapy. And not a single one of my patients who either had a bad event or no help recorded a YouTube video. I keep begging them, and they say, "I feel embarrassed. I gave them \$30,000. I had a GoFundMe page. My family donated money, and I went to Panama. I had these cells. I'm exactly the same. I'm embarrassed." And I say, "I know, but you'd really help me out if you'd record YouTube videos."

[00:48:16] Then we look to the individuals who report a success. In my experience, for at least the patients I've had who have come back, who are functioning better than when they left, I can document that. I know they're functioning better. I ask in detail what happened on those four weeks on the beach in Panama. They said, "Well, they gave me stem cells." I said, "Well, what else happened?" "Well, there were infusions going on." Turns out, five days of high doses of steroids make us all feel pretty good.

[00:48:46] Then, they all, during their weeks of monitoring, worked with the physical therapist every day. I was like, "Well, I've been asking you to work with a physical therapist for two damn years, and it hasn't happened, and you just hit 30 days straight." And over about 90 days, their benefit slowly wanes, and they're told, "You need to come back for another treatment," over and over again. So, if I'm purely cynical, I think this is just charlatan medicine trying to take people's money. That's the pure cynicism.

[00:49:15] And so, I'm fully committed on the science side to having a rigorous process to decide that things are safe and hopefully effective relative to stem cells. I'll just note that one of the biggest pieces of science

that makes me cynical is a lot of these centers overseas will harvest a person's stem cells from your fat tissue or from your blood -- they have different advertisements -- and then infuse them into you. We have tried for 20 years to infuse cells into your vein and get them to the point of your scar, and they don't make it to the scar. Your liver and your lungs, with every blood cycle, clear out these cells.

[00:49:59] So, if I give you a billion cells, 95% of them are gone into the liver and the lung within an hour of circulation. They're just gone. And then, the ones that are there to migrate to where the scar is, is not what we see in any of our models. And so, the science behind the intravenous administration of "stem cells" is just completely lacking. And so, we're working hard to figure out what's the right cell, and what's the right way to get it where you want it, and make sure it doesn't go where you don't want it, and make sure it doesn't turn into something you don't want.

[00:50:38] We really wouldn't benefit from having some liver tissue in our spinal cord. That's not going to be so helpful. And so, that's why the science has been hard and has been long fought. And in general, I'm not a fan of the overseas experience. My final statement of cynicism for the day is: let's all be honest. How lucrative is Big Pharma in America? They're doing pretty well, right? We can all agree. Again, whatever your politics are, they're doing pretty well. If those treatments were working and curing folks, you're telling me Pfizer wouldn't be rolling out clinics left and right in Dallas?

[00:51:17] I mean, just the market forces are a big red flag to me to say that if these aren't being pushed into trials to get proven here in the U.S., people who have even a monetary goal to bring this to the U.S. are looking at the data saying, "Yeah, something's not right there." And so, there are all these red flags to me to say it's slower, but to go the right road. So, the last part of your question was, how do we keep track? And this is where I'll put in the plug, frankly, for SRNA.

[00:51:17] This organization is doing everybody a service by being your watchdog, by taking the meetings with investigators, taking the meetings with companies, reading the scientific journals, looking for new discoveries, having the podcasts, having the webinars, and then posting on their site. I think they do a very balanced job of, even when things are in the early stages, getting the word out there. That's a very safe go-to place to get a balanced review of what the options are.

[00:52:19] **Audience Member:** (inaudible) and go next year for this.

[00:52:23] **Dr. Benjamin Greenberg:** All right, more videos. So, I know there's one in the back, but I believe you were waiting up first. So, if it's okay here and then the back? Here, okay.

[00:52:35] **Audience Member:** My question is, it's been since 2017 since I've seen a neurologist for my TM, and I'm (inaudible).

[00:52:52] **Dr. Benjamin Greenberg:** So, the question is about keeping up with neurologists or physiatrists. Who should be on your care team years after an event? I can say one sentence and let everyone chime in. It depends is the answer. There are certain conditions where a neurologist absolutely has to be involved. So, if somebody has a condition that's at risk for recurrence, anti-MOG associated disorder, neuromyelitis optica, etcetera, a neurologist really should be involved. If somebody's had a single event of myelitis, there are a lot of different clinicians who can play the role of helping manage the long-term aspects of things.

[00:53:34] Depending on where you live, it may be a neurologist or a physiatrist, or both. But in general, I would recommend having at least one or the other because things change. There are new discoveries, new interventions, and primary care physicians are amazing and wonderful, but this is not where their attention is

going to be. So, having an episodic check-in is worthwhile. And we are all aging, second by second by second. Some of the symptomatology we had five years ago may be a little different today as our bodies change.

[00:54:98] And a physiatrist and some neurologists, maybe not all, will be attuned to putting those things together. So, my general recommendation is it's good to have at least one. It doesn't have to be frequent check-ins; even if it's based on your needs once a year or so, having them on your team is not a bad idea. I don't know if you disagree.

[00:54:29] **Dr. Leslie Benson:** No, I mean, I think I very much agree. I think the myelitis and AFM community are the ones who tend to I see less and less over time, and then they come back when a question arises. So, our follow-up to do is space out, but having somebody who has an interest in your condition, and an eye on what's going on, and an eye on you because we don't know what's going to happen over time. And, it's not just the medicine that's changing.

[00:54:58] It's the individual, and you don't know what's going to happen, right? Having somebody who is at least aware in the recent years of your condition, if you do acquire something else, indeed that collaboration between providers can be beneficial as well.

[00:55:16] **Dr. Carlos A. Pardo:** I always use sports as an analogy. So, you need to have a quarterback, okay? So, it's extremely important that you have a team. Managing myelitis and myelopathies in general requires a team. And the reason it's important is because the neurologist alone is not going to be your primary care doctor. There are issues that are going to emerge later after you get transverse myelitis or you get a myelopathy that are important issues -- let's say bladder dysfunction.

[00:55:48] So, you need to have a urologist. At least, identify a neurologist who can help you in the future if there is any bladder dysfunction, serious bladder dysfunction problem. So, in other words, it's a very good idea that you develop the scheme to have a team working with you. That doesn't mean that you need to go every six months to every member of the team. That means is that you are going to identify somebody that you can basically ask or go when you have issue related with the specific problems.

[00:56:23] The neurologist -- and I always emphasize this to the patient that come to our clinic -- the neurologist is not the best primary care doctor. You need to have somebody in internal medicine or general medicine that guide you dealing with different aspects of your health. Is your body scan okay? Is your rehabilitation plan going on in the normal way? Is the person who is taking look of your bladder function and whereabouts what is going on with your symptoms?

[00:56:55] So, you need to develop that plan. Again, every patient is different. There are patients that probably may have visual problems because there is neuromyelitis optica. So, that person need to have on board an ophthalmologist or a neuro-ophthalmologist in that team, right? There is issue of pain management. So sometimes, it's important to have a pain management specialist.

[00:57:20] So, in other words, you need to have a good team with a good quarterback in which the neurologist is one of those players, it's not the only player. The rehabilitation specialist is one of those players, not the main player, but the urologist is the same. But you need to develop that plan. And in that way, probably you are going to have a more comprehensive management of the problem that you have.

[00:57:46] **Dr. Benjamin Greenberg:** Over here.

[00:57:47] **Audience Member:** Hello, This started for me five years ago, but for the first three and a half years I was a medical mystery. Then I got diagnosed with TM a year and a half ago. My question is mainly about the mechanics. For me, it's where my quad muscles have been permanently contracted for the past five years. I thought for a while that I had something progressive because my quad muscles were hard as a rock, right after I was recovering from a virus, which is how this started.

[00:58:23] My quad muscles were hard as a rock, and then my calf muscles became hard as a rock later. Now I would say I think that I was overcompensating for what the quad muscles couldn't do, and that's why the calf muscles became so rock hard. Anyone who feels my legs are just shocked at how hard the entire leg is. Muscle relaxants did not do anything at all for me. I did have Botox injections for a little while.

[00:58:55] I think that what was really hard with Botox injections is that I didn't know that they had to do the EMG each time to know where to put the injection in. And so, when, you know, normally if you're going to have huge needles put in you or something, you try to relax as much as you can. But, of course, you can't relax when your muscles are permanently contracted. So, very, very painful, and I was concerned with the Botox because it loosened the muscle, but then the brain can't communicate because there are times where your muscles need to tighten.

[00:59:30] And so, I really wound up with my legs too loose where I started falling. And so, right now, I'm struggling in the newness of what my diagnosis now is, just in the balance of how much to use the legs, how much to not use the legs. Potentially, is it bad that I'm having to rely on the calf muscles? I'm also finding it very hard, like, I can walk easier than I can stand. I understand now when you walk, you're using your hip flexors, and when you're standing, you have to engage your quad muscles to stand.

[01:00:11] So, I get shakier and shakier, and if I keep pushing it, I will eventually fall. And so, I'm just questioning, like, what is the balance? I don't want to just be sedentary. I don't want to just be in a scooter or a wheelchair all the time, but it's just hard to know what the balance is. I do know about Botox now. I don't know anything about bracing. This is the first time I've ever heard that, to be honest. That will be my next question (inaudible). We have got two.

[01:00:44] **Dr. Benjamin Greenberg:** Yeah. And so, if I can, I know, Clarice, I'm going to want you to comment, but I want to point out two things embedded in your question that are really important beyond the specific of that leg. One is: the recognition that symptoms can evolve over time even after a static injury. So, the spinal cord injury happens. I fell off my motorcycle on Wednesday, I got stabbed on Wednesday, or I had myelitis on Wednesday.

[01:01:11] Whatever the punch to the spinal cord was, can happen. But then, for months or even years after the event, there can be an evolution of symptoms, sometimes through physiology -- and I'll explain what I mean by that -- but sometimes through compensation. So, when a quad is weak, part of the way you stabilize your knee comes from the calf muscle. So, to stabilize the knee, the calf tries to take over, and you can get secondary issues.

[00:01:36] Or, if you're somebody who swings your leg just a little bit every time you walk, my orthopedic colleagues, when watching you, hear the same sound: cha-ching, cha-ching, cha-ching, because you're going to be in their clinic with knee, hip, or low back pain. It's going to happen. And so, people will come in years later and say, "Well, now my back hurts," but it's from the same original injury. So, this evolution of symptoms can get challenging because we have to separate out the primary and the secondary.

[01:02:06] And this is really where physiatrists can be extremely helpful in getting in to that details. But you raised the issue of kind of those recalcitrant symptoms, the symptoms that just don't seem to go away. In your case, it's a quads muscle that is extremely tight. I'll let Clarice comment on specifics around muscle spasticity and advanced interventions, whether it's intrathecal therapy or anything else you're going to mention. I will say stick with it.

[01:02:35] So, people will feel like they're tilting against windmills over and over and over again. I can guarantee one thing: if we don't keep trying to improve it, it will 100% not get better, guaranteed. There is not going to be a day -- I would love for this to happen where you wake up and it's gone by magic -- that's not the path. There are lots of different ways to deal with these very troubling, just annoying, ongoing symptoms -- and I'm not minimizing at all -- life changing symptoms, whether it's a tight muscle, or neuropathic pain, or fatigue. but it can and usually does get better. It's about finding that path. I'll let Clarice talk about specific paths.

[01:03:17] **Dr. Clarice Sinn:** Yeah, and I would say, it is very common when you're dealing with tone for a spinal cord injury. Sometimes you're using that tone to walk, you know? So, it is a very fine line. If I take away too much of your tone, now my kid can't walk. And parents will say, "Well, you made my kid weak." And it's like, "Well, no, they were always weak. They had tone. I took away that tone. I did not make them weak. They were always that way." So, sometimes it's explaining that.

[01:03:45] There's different options, the Botox. You do not have to do EMG guided Botox. I don't. It comes down to how you're trained. Some people, they're creature of habits. This is the way I was taught, it's the way I'm always going to do it. I was lucky. I was trained under people who did anatomical, meaning that's the quad muscle. I'm just going to go in it. There's EMG guided, and then there can also be electrical stim. I use electrical stim when it's a really small muscle, and I don't know if I'm hitting it.

[01:04:12] EMG, you are correct. If your whole entire muscle is tight, it's going to sound angry. So, I don't need EMG to tell me that. And for EMG to work, you have to be able to isolate that muscle. I do kids, and getting a kid to isolate a muscle movement while you're sticking a needle in them is never going to happen. I have partners who swear by it, that EMG works. And I'm like, "I don't know how that works."

[01:04:39] For me, the quad muscle is huge. I'm not going to miss it. I'm not worried about missing it. I mean, it's the whole freaking muscle here. I just do it. I may do in a bigger person four different sites, making sure I hit it. But yeah, I don't think you need the EMG, but it could just be that's how they've always done it, and that's the way they're going to do it, but you could find somebody else.

[01:04:59] **Audience Member:** (Inaudible)

[01:05:01] **Dr. Clarice Sinn:** Okay.

[01:05:02] **Dr. Benjamin Greenberg:** Well, 49 more, and she'll be ready.

[01:05:06] **Dr. Clarice Sinn:** Yeah, the only time I use EMG is if I'm not getting the results I like, and I'm like, "Well, maybe I need to be in a better part of the muscle." But I mean, it's very rare that I do the EMG route. The other thought: so you could do intrathecal baclofen. They do pumps, but I've had a lot of patients who they do that and it takes away all their tone, and now they're not happy because they can't walk. Some kids do great with that or adults, same thing. You can do trials with a neurosurgeon.

[01:05:31] What they do is before actually putting the pump in you, they do it's like a lumbar puncture. They inject it, and then they're going to monitor you for a couple hours in post op and say, "Oh, wow, we really like

that. Is this something we proceed with?" Or you're like, "Gosh, it took away all of my tone. I can't stand up. That's horrible. No, we're not doing that." But a pump is a big commitment because it has to be refilled. It's lots of appointments. You're going. You're putting something foreign into the body. There's a risk of infection.

[01:06:00] Only your physiatrist understands the baclofen pump. Every time you show up in the ER with whatever, the ER docs are going to be like, "We don't know what that is." They're calling physiatry and assuming it's the pump. The pump has to be the issue. It usually isn't, but there's just a lot that goes along with it. The other thought you were talking about, it throws off your mechanics. The other muscles can become tight, bracing.

[01:06:24] So, whether it's like an AFO. Sometimes, people with hip weakness, you have to go above the knee, so then it becomes a KAFO. So, AFO just stands for ankle foot orthosis or a brace. KAFO is knee ankle foot orthosis. So, it's not, but you'll just hear KAFO. A lot of my patients with spinal cord injuries, spina bifida, you'll have to use KAFO. Kind of thinking of the old Forrest Gump movies. However, the higher up you go, the harder it is to wear because you have to wear over clothes, under clothes.

[01:06:58] If you gain the slightest bit of weight, lose the slightest bit of weight, it may not fit. So, we use KFOs in little kids. However, it comes time to a point that it's just not functional and they say, "I don't want this anymore," or sometimes they lock at the knee. Well, that's great but now you want to sit down, you know, so you can't sit down or I need to go to the bathroom and I can't. So, there's a lot of different options, but you can definitely try. AFOs can help with quad weakness. It helps give you the support. So, I'd probably start with that, getting a brace. What type of doctor did the injections? Was it a physiatrist or -- Neurologist. Okay.

[01:07:37] **Dr. Benjamin Greenberg:** Damn, I was hoping she was going to say physiatrist.

[01:07:39] **Dr. Clarice Sinn:** I was going to say because a physiatrist should have done the brace route as well, but I don't know where you live, but I would look into seeing a physiatrist for possible bracing and then potential trying injections again.

[11 01:07:52] **Audience Member:** And some of that we're seeing a lot of success to people with (inaudible).

[01:08:00] **Dr. Clarice Sinn:** Yeah, so we're also seeing a lot of success too in the clinic with some of the robotic bracing so that you get a little bit of either a combination of E-Stim or passive or just passive support. So, where you initiate and then it helps pull things through, so you get a smoother gait. So, say a little bit more with dynamic bracing as well.

[01:08:25] **Dr. Benjamin Greenberg:** And I'll just throw out two things to add to the list. One is: needle for pain and spasticity. But for spasticity, I have a certain percent of my population that responds to acupuncture as a way to manage some of these symptoms. And so, it's a routine referral that we make in our clinic for management of some of these chronic symptoms. The second is, if there are just things that aren't with this type of symptom management going well, it's one of the indications to do a visit at a place like Kennedy Krieger, where they do a comprehensive evaluation and maybe you're there for a week.

[01:08:54] And it's really a combination of what's going to be the orthotic approach, the rehab approach. Because, usually, it isn't just one thing. Usually, more than one, and investing that time with a very experienced rehab team who can then reach out to your own rehab team and coordinate is not an unreasonable use of time. So, I think you were waiting.

[01:09:15] **Audience Member:** Hi, I'm a program manager in a research lab. If you think it's appropriate, I'll talk a little bit about my research. But if it's not, that's totally fine.

[01:09:23] **Dr. Benjamin Greenberg:** Depends on what the research is. If it's abducting neurologists in a garage, no, I prefer not. Go ahead.

[01:09:31] **Audience Member:** Thankfully, it's non-invasive stimulation to try to treat -- we have one study that's looking at neuropathic pain, one study that's looking at reducing hyperexcitability in the spinal reflexes, which we hope will reduce spasticity. So, if you're interested in that, please come talk to me. But more than that, SRNA has a lovely page that has all of the research that they've approved and looked at and has been passed by the IRB, so it's designated safe.

[01:10:01] I just highly recommend you look into that and see what studies might interest you. Like, if you came to do a study with us, I couldn't guarantee that we would reduce your pain or even reduce your spasticity, but it really helps the future. It helps move research along to hopefully find future solutions to these problems.

[01:10:25] **Dr. Benjamin Greenberg:** Thank you. And so, again, keeping up with those options on the SRNA website, there's a great clearinghouse for all those studies that are going on, not just disease modifying, not just stem cell, but on the rehabilitation or interventional page. So, I think it's one two. I think he was first and then, okay, we'll go here first. Arm wrestle. You two, duke it out.

[01:10:47] **Audience Member:** Hello, I was diagnosed in 2013 and found that they had a conference in 2013. So, I came here and I was lucky enough to be diagnosed with TM within 24 hours, but they were like, "Okay, great, bye. We'll see you later." I didn't have much information. So, when I came to the second patient education, I suddenly found out about spasticity, but it was something that this place told me about. Not my neurologist, not my primary care because I didn't know what it was.

[01:11:26] It was just like, "Oh, my legs are tired. I already have plantar fasciitis. But, hey with TM, I don't feel it. So, that's a good thing." But now, 10 years later, I am getting more feeling back in the leg. I felt like two leg casts were on my legs, and I was just dragging around this extra feeling. But now it's coming back, and now I'm feeling the plantar fasciitis, darn it.

[01:11:54] What I wanted to know is, what other options are there for spasticity? Right now, I'm doing PT with -- again, they're not really into that where I'm at. So, I go to a massage therapist who does deep leg works up, and we do it until I cry and just getting out the knots and getting out the muscles because, like you mentioned, is the outer thighs and the calves. She's like, "I've never felt anyone this rock hard."

[01:12:29] **Dr. Benjamin Greenberg:** Although we should have a "who's leg is harder" competition at the end. I think we all kind of want to feel our needs about that.

[01:12:37] **Dr. Clarice Sinn:** PTs and occupational therapists, they all specialize like we do. So, you want to look to see PTs who deal with neurological disorders because if you're going to a sports med physical therapist, yeah, they don't deal with that. They're dealing with back injury, knee injury from usually a healthy person or an elderly person with bad arthritis. So, I always look at the web page or ask, "What are the types of stuff you deal with? Stroke, brain injury, transverse myelitis?"

[01:13:05] Because a neuro PT should know exactly what spasticity is and how to deal with it. So, I always tell my parents you need to do the research because not all PTs, they may have got it in training, but they may have chosen sports medicine route. So, I would look into that because, yes, the PT should know it, but maybe you're at a sports place who mainly deals with that or an orthopedic place for osteoarthritis. They're not used to the neurological issues.

[01:13:31] **Dr. Benjamin Greenberg:** So, two things, and correct me if I'm wrong. I want to quote you and I want to quote you exactly. It's been 10 years since it, and sensation is coming back now.

[01:13:42] **Audience Member:** Yes.

[01:13:43] **Dr. Benjamin Greenberg:** So, everybody in the room and anyone listening to the audio recording remembers, if you've ever been told, "Whatever you get at a year is all you're going to get," that is not correct. You can speak to this nice lady upfront and know, there is not a window that closes on your nervous system change. It is folklore. I know it's not the point of your comment, but I really want to make sure people hear it.

[01:14:11] There is not an artificial door in how things change. And then I will put in a plug. Carlos will be emceeding this afternoon. I don't know if you know that, but you are. From 3:45 to 4:15, Christina Sadowski, her entire talk is spasticity management. So, I actually think we're going to get a lot of this answered as we get to 3:45. So, definitely be front and center for that.

[01:14:39] **Audience Member:** Hi, my name is Greg, partner to Rose here, who had her first index episode of TM in April, so pretty fresh. I have a few questions, if you would indulge. Of course, we're interested in recovery, but we're also interested in root cause, in the pursuit of recovering as well as possible, but also treating properly and preventing any potential recurrence. So, first of all, the fact that TM already is sort of a catch-all, right? It's kind of a diagnosis of exclusion to an extent. We don't have specific antibodies like some of these other conditions do.

[01:15:24] First of all, we want to confirm if it actually is myelitis. As Dr. Parry, you mentioned earlier today, 20-30% of them is not, it's something different. And so, I guess, I mean, how does one go about finding that out? Another thing is, speaking of root cause, is anyone doing work in finding common threads in between patients that can help point towards a root cause? For example, from my understanding TM is more common in females.

[01:16:03] Is there some kind of hormonal thread to pull on there? Are there genetic variations, etcetera? Are we finding out information about what could be sort of the deeper root cause of that that could then inform therapies? And then lastly, in this section, I have two rather small ones after this. Lastly, do you often find that patients with TM have other seemingly, decidedly, unrelated medical conditions. Okay and that's a lot.

[01:16:33] **Dr. Benjamin Greenberg:** No problem. So, confirming diagnosis, root cause, and other things that could be going on in the three topics. So, I'll go in order. Carlos first, in terms of if somebody has been told they have myelitis, but they want to confirm the diagnosis. Then I'll ask Leslie to talk about root causes and how we go up around those studies.

[01:16:57] **Dr. Carlos A. Pardo:** The answer to your question, 'What is the root cause of transverse myelitis,' is extremely complex and has a lot of political implications for me. He knows that. The reason is I have been fighting in the past several years about the term 'transverse myelitis' because I believe it's a misnomer. I do prefer to use the term 'myelitis' alone. Forget about the transverse. When we identify myelitis, that is technically an inflammation in the spinal cord, there is a wide spectrum of causes of that problem.

[01:17:36] You can have a viral infection that may cause myelitis, you may have an autoimmune disorder, you may have a rheumatological disorder that may trigger that reaction, or you may have an infection that few days later, few weeks later, trigger an inflammation. So, there are different routes for that. One thing that I always encourage people is to think about giving the 'last name' to the myelitis. It is an autoimmune

myelitis, or it is myelitis triggered by an infection that we call post-infectious myelitis, or it's an infection that is really triggering myelitis, like, happening in polio, or AFM, or something like that.

[01:18:18] So, that is where we go. Now, as it was discussed extensively this morning, actually, the causes of myelitis actually have been very I mean, there are a lot of people have pay a lot of attention to that in the past 20 years. The good news is all of these markers that emerge like AMOG and NMO markers have been very helpful for us to categorize the last name of the myelitis. So, to simplify my answer in your particular situation is, you may need to discuss with your neurologist and say, "Okay."

[01:18:56] "All right, did we test the autoimmune potential here? Did we test the role of infection or rheumatological problem?" That is basically the best approach that you can use. Now our colleagues in pediatric neurology actually are sometimes in more difficult situation because kids that have myelitis, they are not able to express themselves what they experience. So, for that reason, I'm passing the microphone to Leslie.

[01:19:28] **Dr. Benjamin Greenberg:** Go ahead.

[00:01:28] **Dr. Leslie Benson:** Just to kind of dovetail on what he's saying, I think that we as researchers need to understand the underlying cause of myelitis better so that we can get better at understanding why is there such a spectrum of outcomes as well, right? Some patients recover beautifully. Some are left with just bladder-bowel problems. Some, we don't get an inkling of improvement, and we don't know why. So, there's a lot of work still to be done on what is causing this and how do we do a better job of treating those who aren't going to have a beautiful outcome.

[01:20:08] The SRNA is funding one of my fellows right now so that we can look at kids with first attack of myelitis and try to see how many are left in that bin of idiopathic myelitis because we can't always figure out and give an exact biomarker name to the disease. And so, definitely, there's work to be done. I don't know that we're going to have an answer for you in the next two years at these symposia. Maybe you do. I don't know.

[01:20:37] **Dr. Carlos A. Pardo:** No, you got to answer.

[01:20:42] **Dr. Leslie Benson:** But to answer your, "Do I need more workup? Do I need a second opinion?" I think that depends. If you feel you have a neurologist or a team that knows the disease, and has done a thorough workup, and is super confident in your diagnosis, and has a good ongoing plan that they know whether you need additional monitoring for recurrence or that sort of thing, then maybe you don't need a second opinion. But if there's an inkling in the back of your mind of, "I need somebody else to tell me I'm on the right track," it's never wrong to follow that inkling and be comfortable with your diagnosis and who's treating you.

[01:21:20] **Dr. Benjamin Greenberg:** I would break this down into three steps. Carlos, I was expecting something in your answer, and I didn't get it. So, I'm going to fill in what I expected. And that is: step one, was the syndrome I have inflammation of the spinal cord? Myelitis means inflammation of the spinal cord, versus, if I may, what Carlos was referring to earlier today, that 20 to 30% number was around people who have blood flow issues to the spinal cord. And they can look indistinguishable to a lot of clinicians. And so, the first step is, did I actually have myelitis?

[01:21:55] If that's in question, going to a specialty center and having that conversation, "Look at my history, listen to me, what I experienced," and that's the most important thing. "Look at my scans and look at my test. You agree it was myelitis -- yes/no -- is not a waste of time in any way, shape, or form. Once you're in the myelitis category, everything Carlos and Leslie said in terms of have I had the complete workup for

underlying conditions that would cause it? Yes or no? Those are kind of the steps in making sure you're on the right journey.

[01:22:29] Relative to your comment about data and research and causation and pulling on the threads, I've got good news and bad news. The good news is we've made tremendous progress on that side between the testing for AQP-4 disease, anti-MOG associated disorder, better testing for neurosarcoidosis as a cause of myelitis. We are way better at this than we were when I started in this field. Massively better. That's the good news. The bad news is every paper you read about myelitis prior to 2015 around causation is wrong.

[01:23:03] It is because we didn't know we should look for the anti-MOG antibody before 2015. So, there will be a table there where it says we looked at 50 people with myelitis. Some of them had anti-MOG as a cause, and that explains it. So, the amount of people who are winding up in the category of idiopathic myelitis. Does everyone know the definition of idiopathic? The doctor's an idiot. The patient's pathetic. Like, we can't figure it out. I don't mean it. What we mean is the doctor is an idiot. It means we try our best. We do the full workup, and we can't find the cause.

[01:23:35] So, idiopathic means you have the full workup. You can't find the cause. That bucket is getting smaller and smaller every year, but it means we have to redo the studies on causation with just those people using the most up-to-date science we have because the old buckets were mixed in terms of causation. It's a challenge for the field from an epidemiologic perspective. But is it fair, Carlos? I don't want to put words in your mouth that we start with. Is it myelitis, yes or no?

[01:24:02] **Dr. Carlos A. Pardo:** Right, exactly. And, again, I think that as it has been mentioned several times is we need to put the pieces of the puzzle together. The pieces of the puzzle together are basically the clinical interview. All the information that you are giving to the neurologist or the clinician taking a look at your case is extremely valuable. It's very valuable. Let me give you an example. I have one patient recently say, "I got paralyzed in 30 minutes, after exercising in the gym in the morning." I say, "Okay." And the patient say, "Well and then I went to the ER, and I was not able to urinate."

[01:24:46] I said, "Okay, I know what you had," right? So, just without MRI, I was able to say, you may have had a stroke because you were exercising, and you put basically some vascular stress in your spinal cord and this evolved quickly. As compared with a patient that say, "Oh, in the past three or four weeks, I have developed this numbness and tingling has been going on for several days." I know that that patient probably likely had an inflammation that is evolving in a super acute way, and I need to look for demyelinating disease probably.

[01:25:20] So, it's putting the pieces together, and the main elements of that puzzle is the clinical description of what happened at the beginning and before. A good neurological exam, your clinician, your health care provider needs to examine you. They don't need to take a look at the MRI first. They need to examine you.

[01:25:45] The third one after clinical assessment, clinical neurological assessment is obviously to take care and take a look of the blood testing that need to be done, take a look of the MRI, take a look of the spinal fluid, and with those at least five elements, the clinician can generate the differential diagnosis. And so, sometimes it's not going to take one hour. It's going to take probably few days or even weeks to achieve that diagnosis.

[01:26:19] **Audience Member:** Yeah, that's why I decided to do it (inaudible).

[01:26:30] **Dr. Benjamin Greenberg:** So, what we're going to do is last question because we're overtime, and I want to make sure everybody gets their break as you're getting the mic. 3:15 downstairs will be the next

presentation. So, after this question, we'll adjourn, and we're happy to talk to you throughout the weekend but, yes, last question.

[01:26:46] **Audience Member:** My question (inaudible) has there been changes in the last week (inaudible).

[01:27:08] **Dr. Benjamin Greenberg:** So, the question is around anti-MOG testing, and is it possible to test negative initially, but on a subsequent test, find out you're positive. The short answer is: yes, that's possible. We have had situations where the initial test is negative and a subsequent test is positive. There are individual circumstances around the time of testing and how it was tested that can help us decide what are the chances that's happening, but it's not unusual for me, at least, after I have a negative, to at some point potentially retest if I had a high probability of suspicion for anti-MOG disorder. If I have a very low level of suspicion, it's a different situation. So, it's not unusual to retest, and that's true for AQP-4 as well. Sometimes we retest if there's an initial negative.

[01:27:53] **Dr. Leslie Benson:** Just from the pediatric perspective, I'd say the literature and the experience are a little different. We typically trust the MOG test, if it was sent to Mayo or someplace that we know is doing the latest cell-based assay, and it's done before treatment in the acute period. If it's drawn after you've started treatment, you're always down, then we will be a little bit more obsessive about retesting.

[01:28:18] The problem is those later tests, if they're negative, they don't really tell us that we had gotten an ideal sample that would have been negative. But in pediatrics, it's different than adult with Aquaporin-4. We have seen patients seroconvert to positives in a way that the Mayo literature would not support.

[01:28:37] **Dr. Carlos A. Pardo:** All right, can I add? Actually, the other thing is important is in neurological test may be negative at the beginning, but if the clinician is convinced that the neurological problem is either associated with MOG or Aquaporin-4 should retest that months later because it's a very frequent problem in autoimmune disorders and neuroimmunology.

[01:29:02] **Dr. Benjamin Greenberg:** All right. So, I want to thank Carlos and Leslie most importantly, I want to thank all of you for sharing and asking great questions. Hopefully, you have a good symposium and visit.