

Understanding Myelitis

Efforts to Update Diagnostic Criteria

You can watch the video of this podcast at: youtu.be/AisPcfLkAz8

[00:00:02] **Dr. GG deFiebre:** Hello, and welcome to the SRNA "Ask the Expert" podcast series. This episode is titled, "Understanding Myelitis: Efforts to Update Diagnostic Criteria." My name is GG deFiebre and I moderated this episode. SRNA is a nonprofit focused on support, education, and research of rare neuroimmune disorders. You can learn more about us on our website at wearesrna.org.

[00:00:26] "Ask the Expert" is sponsored in part by Amgen; Alexion, AstraZeneca Rare Disease; Genentech; and UCB. For this episode, I was joined by Dr. Benjamin Greenberg and Dr. Kyle Blackburn of UT Southwestern Dallas. You can view their full bios in the podcast description.

[00:00:48] Thank you so much for joining me today, Dr. Blackburn and Dr. Greenberg, to talk about myelitis and potentially new diagnostic criteria. So, to start can you just talk about what we're talking about today and kind of why does it matter? Dr. Blackburn?

[00:01:06] **Dr. Kyle Blackburn:** Sure. So, kind of to give an overview of why we're meeting today. Over the past few years, a group of neurologists has been starting to meet and we're starting to conceptualize what a new terminology for inflammatory myelopathy, what we're now calling myelitis, what that would look like.

[00:01:28] And also doing some updates to the approach that a neurologist would take to arrive at an accurate diagnosis for a myelitis case. So that's kind of an overview of what we're doing and really the reason that it's important. Well, for one of the reasons is the terminology really has not been updated in several years.

[00:01:52] So the last time that the definitions of transverse myelitis, as it's currently referred to, were updated was in 2002. And to kind of give a parallel diagnosis of multiple sclerosis has been updated about three times over that same timeline. So, it is something that's probably been really something that's really needed is an update to these criteria.

[00:02:19] And it matters for a few reasons and we'll certainly delve into these a little bit deeper, but there are pretty significant impacts to how we discuss myopathies--and we'll get a little bit into the transverse versus kind of dropping it down to myelitis--it really ties to the clinical discussions, how we would like those to go going forward. And then there are also really important implications for some of the research that can be done on myelitis based on these recommendations.

[00:02:56] **Dr. GG deFiebre:** Got it. And so why are this podcast and this kind of discussion more broadly important for people who have been told that they have transverse myelitis. Dr. Greenberg?

[00:03:07] **Dr. Benjamin Greenberg:** Yeah, it's a great question and, as Dr. Blackburn mentioned it's been over 20 years since there was a criterion out. And just to put that in perspective, we didn't have an aquaporin-4

antibody test for neuromyelitis optica. We didn't have an anti-MOG antibody test for anti-MOG associated disorder.

[00:03:26] We didn't have diagnostic criteria for either of those. We had not had our first outbreak of acute flaccid myelitis in the world. A lot's changed since 2002 and what we've struggled with and frankly, what our community and patients and families have struggled with, is a lot of confusion over the use of terminology.

[00:03:47] Patients come to me all the time saying, well, I was told I have transverse myelitis and acute flaccid myelitis or transverse myelitis and multiple sclerosis or neuromyelitis optica. And when we as a community of practitioners got together, we realized that we have not been doing anyone any favors by utilizing an approach to not just diagnosis

[00:04:11] but to a nosology, a descriptive approach of cases by using 20-year-old pathways. So, if I'm an individual who's been told I have transverse myelitis, there's still a lot of confusion over which literature applies to me. Different articles, different podcasts. How should I be categorized so I get the best information that is appropriate to my situation.

[00:04:38] So the point of this exercise is to help clarify for both practitioners and patients who are currently faced with a diagnosis of inflammation in their spinal cord, or the sequelae from inflammation of their spinal cord. And very importantly, to the patients who are yet to come. Those individuals who are gonna join our community

[00:04:58] over the next several years. It is important for us to help add these clarifications so that people can get the best access to information and care that we can provide.

[00:05:09] **Dr. GG deFiebre:** Got it. And so, let's go back, all the way back to 2002 where, when the original diagnostic criteria were developed. So, what were they, what were the diagnostic or what are, you know, what are they? They're still the criteria now for transverse myelitis. Dr. Greenberg?

[00:05:28] **Dr. Benjamin Greenberg:** So, it started in the exact same place that we're gonna start in 2025, and it's the most important place for practitioners and patients. And that is taking a history and doing a physical and having a patient telehealth care provider. There's something wrong. And for that description to trigger

[00:05:49] in the mind of the practitioner, this could be related to the spinal cord. So, we all start at the same place, a sign or a symptom that a person's spinal cord isn't working. Now, in 2002, based on everything that was known, the first step was to rule out compression of the cord. Is there a bleeding or an abscess or a tumor or a disc from a spinal cord pushing on the cord?

[00:06:15] And to do that the criteria recommended getting an MRI. And separating out people who had structural issues or compressive issues from those who had intrinsic spinal cord pathology. And then from there the criteria asked practitioners to look for signs of inflammation. And they gave specific checklist of what would qualify for inflammation or not, based on the MRI and spinal fluid.

[00:06:46] And then it went on to say, if you have myelitis, you should look for evidence of multiple sclerosis. Or back then neuromyelitis optica based on a clinical history. And that was it. And it was very limited in its understanding of the multitude of pathologies that could present with myelitis and the different patterns that could be looked for to help a clinician get an accurate category.

[00:07:17] And it was limited in its list of what we call red flags. The list of warnings to practitioners to highly consider a diagnosis other than myelitis. And so, it left us for the last 20 years as a great starting point, a spectacular starting point to get the community organized. It gave us a framework to get organized and now we're due to give it a new version, a new polish, if you will, based on everything we've learned.

[00:07:46] **Dr. GG deFiebre:** And then what did transverse myelitis mean? So, the, \ you know, word transverse as part of the diagnosis and how was it used? Or is it still being currently used by doctors? Dr. Blackburn?

[00:07:59] **Dr. Kyle Blackburn:** Yeah. And, you know, none of us were around at the inception of the word transverse. Or the use of transverse myelitis is kind of the colloquial term, but, and I've heard two stories around this.

[00:08:11] One is that it was described on autopsy data that. The initial reports whenever people looked at what was going on in the spinal cord after someone had passed at autopsy, saw inflammation that looked like it was across the entire, what we call transverse plane, which is basically an anatomic plane where if we kind of take a slice

[00:08:33] of an individual on an image and they have an upper half and the lower half. If you look at the spinal cord that way you can see inflammation all across it. So, they called it transverse for that reason. The other story that I've heard about this is actually that it was the sensory level that patients would experience.

[00:08:50] So the level at which they would lose sensory loss was usually across the plane of the body like this very neatly, so they would call that a transverse myelitis. So that has been--so transverse myelitis has been the really accepted term for spinal cord inflammation for really well over a hundred years.

[00:09:12] The issue with how it's been applied really more recently, and really probably even since the get go, is transverse myelitis is it's best to think of it as a syndrome. And a syndrome is really just a clustering of symptoms that tend to go together and can have many causes. So, if we take chest pain as an example. If someone's experiencing chest pain, it could be due to the thing we, most of us, know of is a heart attack.

[00:09:39] But there are actually many, many causes for chest pain when you actually look at the list. So, chest pain would have a syndrome attached to it, and that's probably how we should think of a term like transverse myelitis. Unfortunately, it has also become the shorthand for when many clinicians are talking about idiopathic transverse myelitis.

[00:10:00] And so it has also become used as a diagnosis. And that's when we get to a specific cause for let's say that chest pain or a specific cause for that inflammation of the spinal cord. So, it's been a little bit co-opted in both situations and that can obviously be very confusing for patients to navigate.

[00:10:19] It's also very challenging for us to not navigate on the clinical side, especially on the research side. I wanna highlight that because patients--whenever definitions of transverse myelitis and what that actually means differ, we start getting a lot of heterogeneity and a lot of mixed pictures in different studies.

[00:10:42] So one study may highlight use different criteria than another, and they would naturally arrive at different conclusions because of that. So, it creates a lot of uncertainty in the quality of the scientific publications around that. So those are the two instances where I've kind of seen this term used in a way that may not be optimal for clinical care or research.

[00:11:09] **Dr. GG deFiebre:** Got it. What has really changed in our understanding of spinal cord inflammation since 2002? I know we talked a little bit about some of the changes, but Dr. Greenberg, is there anything else you wanna highlight that we've learned since then? Relevant to kind of the potentially new diagnostic criteria.

[00:11:28] **Dr. Benjamin Greenberg:** So, I think there's a variety of things that have changed, and part of it has been in, as we've identified more reliably what are called secondary causes of myelitis. The best example is anti-MOG associated disorder in our viral-associated acute flaccid myelitis or aquaporin-4 associated neuromyelitis optica.

[00:11:50] These conditions can have overlapping and sometimes confusing phenotypes. But once we had a blood-based test or an epidemiologic study to prove viral association, we were much better at sorting out the parameters of typical features and atypical features of these different conditions.

[00:12:14] I'll give one of the best examples. So, for the longest time, neuromyelitis optica as a clinical diagnosis was defined by the length of the lesion in the spinal cord. So, if you had a really long lesion, we would say before we had the blood test, this is consistent with neuromyelitis optica.

[00:12:30] Now, thanks to the blood tests, we know two things. Number one is there are other things that can cause longitudinally extensive lesions. Anti-MOG associated myelitis can be long. And secondly, some people with an anti-aquaporin-4 antibody can start off with a short. lesion, and they may go on to have a long one, but they start as a short.

[00:12:49] And so one of the things we've learned now is it's pretty standard for everybody with myelitis in the beginning, regardless of their pattern, to get a test for the aquaporin-4 antibody or the MOG antibody because it helps us in a much more rapid fashion get people into the right category. And so, we've always been worried about circular logic.

[00:13:10] You start with a group, you identify a biomarker, and then you redefine the group. But in the case of aquaporin-4 antibody associated disease, it's helped us tremendously in terms of the clinics. So, when I started and I'm now officially old. When I started in this, we diagnosed a lot of patients as idiopathic transverse myelitis because we couldn't find a cause.

[00:13:37] That number has dropped dramatically compared to where we started. For the number of people we get--whether it's MOG, aquaporin-4, flaccid myelitis category--the rate of idiopathic myelitis has just plummeted, and that's good. It's good for everybody. And it also helps us chip away now at the population that's left where we haven't figured out the antibody.

[00:14:05] We're getting to a smaller and smaller number, which will be easier and easier to tackle scientifically as we pair them off and separate out background noise versus not. So, there's a lot in the patterns that have emerged that have changed the way we practice. And has really led to us tailoring therapy in a much better way.

[00:14:26] **Dr. GG deFiebre:** And so, Dr. Blackburn, you talked a little bit about some of the issues that come with using the term transverse myelitis, like the heterogeneity and research. So, beyond that, what are some other reasons or the key reasons behind retiring the term transverse myelitis for just myelitis.

[00:14:46] **Dr. Kyle Blackburn:** Yeah. I think there's a few different reasons for that, for that kind of direction. So, the term transverse myelitis, because it has that anatomical description in it technically doesn't capture the full breadth of the disorder. So, as Dr. Greenberg was talking about you know, we can see longitudinally extensive myelitis, which is certainly a hallmark for NMO and several other diseases.

[00:15:13] We can see myelitis that on the imaging is not taking up the entire transverse claim. We see a lot of different patterns, so it is technically an inaccurate term at that point. The other reason for retiring it is really to kind of have a fresh start in how we approach these disorders alongside the new clinical approaches and the clinical guidelines that are being proposed, that will be proposed once they get to the final versions.

[00:15:43] So the idea is by retiring a term that has been used both as that syndrome we talked about and as a diagnosis, we will have a little better communication with patients. We will kind of adopt this new term, the just myelitis, which really is meant to serve as a description of a syndrome and then encourage clinicians to kind of work from there to figure out the exact cause before labeling it as idiopathic, considering the multitude of causes that have come up in the 21st century. So those are really two of the big reasons that we retire.

[00:16:22] **Dr. GG deFiebre:** And so, what does the term myelitis now mean and how is it different from transverse myelitis in practice. Dr. Blackburn?

[00:16:30] **Dr. Kyle Blackburn:** Sure. So, I will say the term myelitis really is how we envision it being used is in place of what transverse myelitis is probably intended to be. It's meant to describe the syndrome that is caused by many specific causes of spinal cord inflammation. And the hope is that by basically, just co-opting a new term, we're starting a new conversation at the bedside, and physicians will walk in and say you know, you have myelitis. We are still on this search for what that specific cause is.

[00:17:07] There are a small group of patients who after our best approach will not have a known cause, but we are looking for known causes of spinal cord inflammation, which could have implications for your treatment going forward. That's really the conversation that we hope to see evolve from this.

[00:17:27] **Dr. GG deFiebre:** Will this change someone's diagnosis or treatment plan? Dr. Greenberg?

[00:17:34] **Dr. Benjamin Greenberg:** Yeah, I think there's two ways to think about it. In its root, the answer is no. I think it's really more about clarifying. And so, you know, before we had certain testing, people were miscategorized, and so people were told, you have idiopathic myelitis, idiopathic transverse myelitis, and then we got an aquaporin-4 antibody, and I had to come back into the room two years later and say, just kidding. You have neuromyelitis optica. And as science and medicine advance, it is not unusual for us to have to go back to our patients and say, listen, we've gotten smarter, and we've gotten better about this.

[00:18:16] And so the language is changing. And I agree completely with what Dr. Blackburn said in terms of the nomenclature. Myelitis is a better, accurate term for inflammation in the spinal cord. The word transverse doesn't add anything. And in fact, it only confuses the situation. And so, while we are changing the nomenclature, what we hope to do is help people in their journey and frankly help clinicians and researchers partner up with individuals in that journey.

[00:18:51] So, am I gonna go back into a room in the coming years and say to a patient who has lived under the title transverse myelitis for years and say, listen, you have the same thing you always had. I'm gonna start referring to it as just idiopathic myelitis. And the answer is yes that is gonna happen, and all it does is provide a benefit to individuals to get into a clearly identifiable group.

[00:19:21] That allows clinicians and researchers to apply the best standard of care and science for discovery moving forward. This can be an emotional event. I've been through this a couple times. I completely understand that a lot of our personal identity and community gets tied by the labels we apply to things. In the end, in my opinion, the label is less important than the accuracy of what we're describing. That's what we're trying to do here. Labels are gonna change for some folks. It'll be an adjustment, but I think it's a step in the right direction.

[00:20:04] **Dr. GG deFiebre:** Got it. And then how will this impact those with idiopathic myelitis in particular. So, you've talked about there's a MOG associated myelitis or aquaporin-4 associated myelitis. How will this have an impact on those with just idiopathic myelitis? Dr. Blackburn?

[00:20:23] **Dr. Kyle Blackburn:** Sure. Well, of course, as Dr. Greenberg alluded to a diagnosis like this becomes part of your story and, you know, the words around it changing can feel very kind of uneasy and can feel like things are shifting and then that's totally understandable.

[00:20:41] But from the pragmatic standpoint of clinical care for those that are truly fit the criteria and are identified as idiopathic myelitis, the impact to their clinical care probably would not change much at all, I would think. Really not at all. For the treatments that are offered to them, to an individual, are gonna be the same.

[00:21:01] The rehabilitation plans are gonna be similar and are gonna be based on the clinical struggles the individual is having. And I think those, I really don't foresee any significant impact to the clinical care for an individual who has had a small label change in their diagnosis.

[00:21:20] **Dr. GG deFiebre:** Got it. And then, you know, obviously this has an impact on the patient journey and experiences with other physicians or insurance companies. So, how might this affect communication with other doctors or insurance companies moving forward, Dr. Greenberg?

[00:21:40] **Dr. Benjamin Greenberg:** So, you know, we think that the modifications we're making in general shouldn't restrict access to care, shouldn't change people's ability to access medications or therapies or clinical care in any way, shape or form.

[00:21:58] We definitely think the biggest benefit, if I'm being totally transparent and blunt with our community is gonna be the future patients. I think what we're gonna be doing for the community is making it easier for next year's myelitis patients to get high quality, efficient care, and an accurate diagnosis and avoid a misdiagnosis in a significant way. Relative to our existing patient population,

[00:22:35] I actually think this is gonna be helpful to some folks because there are still individuals who I think are misdiagnosed. And so, if I'm a neurologist and I don't see, even if I do see, a lot of patients with this or perhaps I don't, this type of contribution always gives people the chance to read, sit, and reflect, and to sit back and say, you know, I do have a patient where this red flag was

[00:23:03] present. Maybe I should revisit this. And so, one of the hopes for individuals who currently carry a transverse myelitis diagnosis who may have had an alternate cause: a blood flow issue, a dural AV fistula, anti-MOG antibody. Putting this into the ether of the scientific literature and into the community may hopefully help individuals move from an inaccurate to an accurate diagnosis.

[00:23:30] I think the biggest return will be for our future patients, but I don't think it's gonna hurt and potentially could help individuals who are dealing with these conditions today.

[00:23:40] **Dr. GG deFiebre:** What does this new framework mean for research and new treatments moving forward? So, we talked about kind of the impact on the clinical aspect of things with patients, but in terms of research and potentially new treatment.

[00:23:55] **Dr. Benjamin Greenberg:** Yeah, if I could jump in. I love this question, and Kyle, I'd love to hear your comments as well. Just an interesting historical note on this. So, when the acute flaccid myelitis outbreaks

were being recognized in their truest sense in 2014, in the summer of 2014. Thereafter, the outbreak in Denver, that got recognized by our colleagues at the University of Colorado.

[00:24:24] A call went out and a call was put together with over 30 centers from North America, getting on the phone line to compare notes on what we were seeing. Because everyone was seeing a couple cases, but we didn't have the full scale of what was going on nationwide. It was on that call we made the point if you look through the historical literature and you search for case reports of children who fit this pattern that we now call acute flaccid myelitis, there were over 25 different names in the literature being applied, going back a hundred years, being applied to the exact same clinical scenario or what seemed to be the exact same clinical scenario.

[00:25:05] On that call, we made the proposal. We suggest we all use the term acute flaccid myelitis to define this cohort so we can communicate with each other. So much of research is around communication and if I call Dr. Blackburn at five o'clock on a Friday and I say, I have a myelitis patient, we know what we're talking about. And now if we use the term acute flaccid myelitis, we know what we're talking about.

[00:25:40] The literature is replete with just lots of different ways to refer to patients who've had inflammation in the spinal cord. And part of the point from a research perspective is to get us all using the same nomenclature in a systematic, clear way so that we can compare results. I can pull a paper published

[00:26:01] from colleagues in Italy a year from now. And when they say myelitis using these criteria, I know exactly what they included and didn't include in that category. So, part of this is just in the sharing of data. I'll ask Dr. Blackburn to comment on the design of research or the conduct of research, but for me, just a lot of it is speaking the same language with our colleagues from diverse populations around the world.

[00:26:26] **Dr. Kyle Blackburn:** I mean that, and that's really the primary reason or one of the big reasons is it's really important that you have kind of the same set of rules that you're applying in terms of name for a disorder and the timing of the disorder, like the length of time that we would consider this disorder,

[00:26:47] knowing that some of the mimics of myelitis can present like really, really rapidly, like the spinal cord infarction or can drag on for several months, like some metabolic conditions. And we know myelitis is kind of in a little bit of an in-between time window. So, standardizing those time windows. Standardizing the workup that should be done. All of that serves so that when people are conducting research, if these criteria are well adopted, we'll have more uniform pictures in the literature about cohorts of myelitis patients.

[00:27:22] And that, that's nice because it, with a rare disease, one of the best ways to really compile information and learn something very substantial from it is to do what's called a meta-analysis. So that's where you would take multiple papers about a topic and kind of try to combine them together, and this is the central message that we're learning from this, from all of these patients that have been studied.

[00:27:48] That's very challenging to do right now with the literature, as Dr. Greenberg described. It's kind of heterogeneous. You really can't interpret what one criterion means versus the other. If we have one accepted degree of criteria, you can compile those together much better and feel much more confident that what you're getting is, for example, the true proportion of patients that are idiopathic.

[00:28:12] Up to this point, it's probably very hard to define in the modern realm. And we would need a study like that. As far as treatments, of course, knowing the proportion of patients that are idiopathic on the clinical side has huge treatment implications.

[00:28:28] If we're better diagnosing the mimics of myelitis, people aren't going to be --if you have a spinal cord infarction, we identify that early. You may not necessarily need chronic immunotherapy. Right. Like a patient with neuromyelitis optica would. So we are, you know, by helping get to the best diagnosis early, we're kind of tailoring treatment to that. And by having better definitions, it may promote treatment trials on other forms of spinal cord inflammation That's definitely possible down the road.

[00:28:58] **Dr. GG deFiebre:** And then how can patients kind of advocate for themselves during this transition in terminology, and where can they go for more information or to ask questions about what's going on?

[00:29:11] **Dr. Benjamin Greenberg:** Well, this is my chance for the ever and ongoing shameless plug for the SRNA, which obviously has been at the forefront for advocating for myelitis patients now for well over 25 years. And I actually view this as a partnership. I am hoping that this will be supportive and useful for patients, but I'm actually also hopeful patients will help spread the word.

[00:29:39] Because often people receive care from clinicians where you may be the only myelitis patient that your practitioner is seeing. And you can be an ambassador and an educator. And so, when the new guidelines get published, they'll be posted on the SRNA website and available to folks for download and consideration.

[00:30:04] I'm sure we'll do some more podcasts and discussions about it and would encourage members of our community to reach out to the SRNA with questions where that we can address for everyone as an educational opportunity. But really, it's gonna be through that online medium and both the guidelines and a patient guide that we'll put out with it in terms of how this may apply to you.

[00:30:31] But we encourage people to then talk to their healthcare providers and say, "Listen, these new criteria came out. I'm curious, based on my case where would you put me?" And it's a great opportunity to have a clinician partner up with you and go through the checklist and say, "Yeah, I think you're idiopathic myelitis," or, "you know what, looking at this, we really should consider test X, Y, or Z." And I think it's gonna not just be hopefully helpful to you, the individual, but you can be helpful to the community as we raise awareness.

[00:31:04] **Dr. GG deFiebre:** Definitely, and we've learned as well, you know, we started as the Transverse Myelitis Association and are not now the Myelitis Association, but you know, also have learned over time, over the past 30 years.

[00:31:17] So anything else you want to add before we end this podcast? I'm sure we'll have additional conversations as you talked about Dr. Greenberg, but just kind of wanted to open it up as a, with any last thoughts.

[00:31:30] **Dr. Benjamin Greenberg:** You know, you raised a great point GG, as we're talking about name changes being emotional events, you actually highlight probably one of the biggest name changes in our community over these decades.

[00:31:40] And that was the transformation from the Transverse Myelitis Association to the Siegel Rare Neuroimmune Association. Honoring our founders, Pauline and Sandy. And I remember with the board there being very emotional conversations about the impact of changing the name. And I really don't want to come across as glib or insensitive to the impact of name changes.

[00:32:11] Just thinking back to that, it was a big deal to change the name. But there have been growth opportunities with it and advantages and benefits to our community through that name change. So, like

anything else, there are growing pains and adjustment periods, but in the end, as long as there has been a thoughtful contemplation about what that changes too.

[00:32:37] I give credit to the colleagues around the world and Dr. Blackburn for coming together and having very thoughtful exchanges around what does this mean? Not just to the community, but to the individual. I really think in the end this is a more of a, a benefit than anything that it could cause from an obstacle or challenge perspective. So, I'm excited to see the update and hopefully everyone will get something out of it.

[00:33:06] **Dr. GG deFiebre:** Dr. Blackburn, anything to add?

[00:33:09] **Dr. Kyle Blackburn:** Absolutely. And you know, we don't take undertakings like changing a term that's been around for over a century lightly. But I do think that there are a lot of advantages to making this change to patients going forward and even current patients dealing with this condition.

[00:33:27] And I think we're really hoping that this just kind of facilitates a lot of growth in this space as we go forward. So, I'm actually looking forward to seeing how these are adopted as we go. As we, as they publish.

[00:33:41] **Dr. GG deFiebre:** Great. Thank you both so much. Really appreciate it.

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