

# Transverse Myelitis

## Diagnosis and Treatment Guidelines

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**Krissy Dilger:** [00:00:00] Hello, everyone and welcome to the SRNA Ask the Expert podcast series. Today's podcast is entitled "Transverse Myelitis: Diagnosis and Treatment Guidelines." My name is Krissy Dilger, and I will be moderating this podcast. SRNA is a nonprofit focused on support, education, and research of rare neuroimmune disorders.

[00:00:22] You can learn more about us on our website at, [wearesrna.org](http://wearesrna.org). This podcast is being recorded and will be made available on the SRNA website and for download via iTunes. During the call, if you have any additional questions, you can send a message through the chat option available with Zoom.

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[00:01:44] Horizon is focused on the discovery, development, and commercialization of medicines that address critical needs for people impacted by rare autoimmune and severe inflammatory diseases. They apply a scientific expertise, encouraged to bring clinically meaningful therapies to patients. Horizon believes science and compassion must work together to transform lives.

[00:02:07] For today's podcast, we are pleased to be joined by Dr. Elena Grebenciucova and Dr. Ram Narayan.

[00:02:15] Dr. Grebenciucova completed neurology residency at the University of Chicago in Chicago, Illinois. Dr. Grebenciucova has been interested in autoimmune disorders of the central nervous system, including rare neuroimmune disorders, since medical school. After residency, she completed a neuroimmunology Fellowship under the mentorship of Dr. Brenda Banwell and Joseph Berger at the Perelman School of Medicine of The University of Pennsylvania.

[00:02:44] Currently, she's an assistant professor of Neurology of MS or Neuroimmunology and neurological infections at Northwestern University in Chicago, Illinois. Dr. Grebenciucova sees patients with rare autoimmune conditions, including NMO, MOG, antibody disease, transverse myelitis, and autoimmune encephalitis.

[00:03:06] Dr. Narayan is an Assistant Professor of Neurology in the Division of Neuroimmunology at the Barrow Neurological Institute in Phoenix, Arizona. He also co-directs the Demyelinating Disorders Clinic at the Phoenix Children's Hospital, which offers patient care in the areas of multiple sclerosis and related neuroimmune disorders to children in the Southwest region.

[00:03:28] Dr. Narayan received his medical degree at PSG Institute of Medical Sciences and Research in Coimbatore, India, and completed a neurology residency at the University of Texas Southwestern Medical Center in Dallas, Texas, and a multi-institution neuroimmunology fellowship at UT Southwestern and The Johns Hopkins University.

[00:03:52] Welcome, and thank you both for joining us today.

**Dr. Elena Grebenciucova:** [00:03:55] Thank you for having me.

**Krissy Dilger:** [00:03:56] Great, so, to get started, can you just give us a brief overview of what transverse myelitis is, Dr. Narayan?

**Dr. Ram Narayan:** [00:04:05] So, transverse myelitis can be defined as an inflammation of the spinal cord. And this particular word transverse myelitis has numerous implications.

[00:04:17] So, in general, any condition, any disease process, any abnormality involving the spinal cord can just be called myelopathy. And, when that myelopathy is from an inflammation, this is because of any inflammatory cause, maybe an infection, any autoimmune cause, it would be called myelitis.

[00:04:39] And as a subcategory of myelitis... So, let's say you get myelitis from a virus. You could get myelitis, you know, because of an autoimmune phenomenon. So, when you get myelitis, and we presume that the likely cause is an immune-mediated cause, then we would call it transverse myelitis.

[00:04:59] But, but conventionally, transverse myelitis was, when it was described earlier, it was described as inflammation that involves the entire cross section of the spinal cord. But we don't see that in actual practice, we see different shades of transverse myelitis, so to say,

**Krissy Dilger:** [00:05:16] Okay, thank you for that overview. And, Dr. G, what are the signs and symptoms of transverse myelitis in the acute stage.

**Dr. Elena Grebenciucova:** [00:05:25] Yeah, so, transverse myelitis, because it is inflammation of the spinal cord, it can attack any part of the spinal cord. So, starting with your cervical spinal cord, which is in your neck area, and going down to your thoracic spinal cord, which is where your ribcage and your sort of like upper abdomen is, and terminating in the CONUS, which is the end of the spinal cord, which is a little bit lower in your back.

[00:05:54] So, transverse myelitis, because it can be short segment, so it can affect a tiny, as part of the spinal cord, or it can be a long segment, meaning it can be very long and infecting several levels of the spinal cord, you know, going just in the neck area or sometimes in the thoracic. So, the ribcage upper abdomen type of area, right?

[00:06:19] So, it can be short segment transverse myelitis or a longitudinally extensive transverse myelitis, which is what we typically say when it's something that spends three vertebral segments or longer. So,

essentially what that means is that symptoms can vary based on the region that is affected and the amount, the area of the spinal cord that's affected.

[00:06:44] It can be a very is small area or it can be a very large area. So, each patient is affected very differently. Some people can present with just minor sensory symptoms, such as numbness and tingling in an arm or leg, or both arms or both legs, or some people can have this band-like funny sensation that's wrapping in a band-like distribution around their trunk and it could be in a half a day and on the left or on the right side, or it could be all around.

[00:07:17] And, likewise, people can have numbness, tingling, or sometimes even a burning or painful sensation. Occasionally, people describe these sensations like an electrical current running through or like a sensation of a tight, kind of like a saran wrap, wrapping around the arm or leg. And so, the descriptions are very different, and they are theory individualized based on how the patient perceives them and feels them and, sometimes, pain can be a major component, as well.

[00:07:50] Other cases of transverse myelitis present with weakness and the weakness can be mild or it can be profound and rather severe. So, somebody could present with just mild weakness in the arm or leg, or somebody could present with severe weakness in both arms or both legs, or more so on one side than the other side. And, typically, the symptoms develop, you know, over hours and over days. They're not sudden. Other symptoms, you know, beyond the sensory symptoms, the motor strength symptoms and pain symptoms. Other symptoms include bladder issues. So, many patients with transverse myelitis can experience bladder dysfunction and the amount of dysfunction ranges from, you know, bladder urgency, having to go to the bathroom all the time, to incontinence, in some instances. And so, you know, it's really variable, based on the reaching of the spinal cord affected and based on the extent and the severity of inflammation.

[00:08:54] And, you know, sometimes what we see on the MRI that looks like a large lesion in the spinal cord doesn't necessarily translate into bad symptoms to the patient and, sometimes, a very small lesion, depending on where it's located, can, you know, cause very severe symptoms in a given person.

**Krissy Dilger:** [00:09:16] Great, thank you so much for that descriptive explanation of the signs and symptoms. That's really helpful. Dr. Narayan, can you tell us how transverse myelitis is diagnosed, including what diagnostic tests are used?

**Dr. Ram Narayan:** [00:09:30] So, the most important component for the diagnosis of transverse myelitis is the clinical history and the clinical examination. That is where a heavy emphasis is laid by physicians. So, the history matters, particularly on when this started, how long did it take from the onset of the very first symptoms to the worst? What does the patient look like when the patient is asked at his or her worst, meaning what is the clinical exam like? Are we able to elicit reflexes? Are the reflexes exaggerated, the deep tendon reflexes, I mean? And so many other things. So, it's really the clinical history and the physical exam performed by a well-trained neurologist.

[00:10:13] Now, after this, the MRI of the spinal cord becomes very important. We typically try to get an MRI of the entire spinal cord. So, that means the cervical spinal cord and the thoracic spinal cord. In very rare instances, we may also include the lumbar spine MRI, but it should be remembered that the spinal cord itself ends at the level of the L1 vertebra. So, the spinal cord itself essentially ends above the lumbar vertebra.

[00:10:41] The other thing to remember, so, the other tests that are very vital as part of transverse myelitis is the MRI of the brain as well, because, a lot of times, transverse myelitis can occur at we call quote-unquote

secondary transverse myelitis, which could be an inflammation of the spinal cord as seen in part of other disease conditions like MS, et cetera, where the brain MRI becomes vital.

[00:11:07] The other very common experience that patients that have transverse myelitis undergo is a spinal tap. So, that's another very important diagnostic test. And, of course, the regular labs, you know, the blood labs that we draw. So, besides these tests, depending on the individual case, the clinician may choose to do additional testing.

[00:11:31] You know, particularly once we get the common causes ruled in or ruled out, we may try and look at some rarer causes, if we still don't find answers. And that involves more sophisticated diagnostics.

**Krissy Dilger:** [00:11:46] Okay, thank you. And, Dr. G, are there other disorders that need to be considered or rolled out while making a transverse myelitis diagnosis?

**Dr. Elena Grebenciuova:** [00:11:56] Yeah, absolutely. So, you know, transverse myelitis, of course, is just a descriptive term that tells you this inflammation in the spinal cord. So, it's not really a diagnosis on its own. It's a description of what's happening and, therefore, we really need to understand what's causing this case of transverse myelitis. Is it a part of multiple sclerosis? Is it a part of a disease called neuromyelitis optica? Is it a part of the disease called MOG associated demyelination? And MOG is myelin oligodendrocyte glycoprotein antibody. Or is it a part of the paraneoplastic disorder? And paraneoplastic means that it's an autoimmune neurological condition that's associated with some sort of a cancer that perhaps has not been yet discovered. Or, at times, transverse myelitis can also be infectious.

[00:12:48] So, it can happen due to a number of viruses, including herpes viruses and, you know, chickenpox, zoster viruses, syphilis can cause, again, lesions in the spinal cord. Even HIV can. But those present a little bit differently than a typical acute transverse myelitis. And, you know, looking at themes like a recent infection or, you know, occasionally a recent vaccination. Is there a causality there? Is it a post-infectious transverse myelitis, which is very rare? Is it post-vaccination transverse myelitis? So, when we do these workups, we basically look at the symptoms and look at what this transverse myelitis looks like on MRI, and that allows us to understand, is it more likely to be as part of possible multiple sclerosis? Is it more typical like neuromyelitis optica or MOG associated demyelination?

[00:13:45] And so, what we typically will send out is we will send out highly sensitive tests in the blood for the NMO antibody, which is anti-aquaporin-4 antibody. So, it's being sent out in blood via a cell-based assay that is highly sensitive. There are some assays that are not highly sensitive. So, one has to be very careful with which test was actually sent out. We also send out MOG antibody, which is likewise a cell-based assay that's sent out in the blood and that's another antibody that could be the cause of transverse myelitis.

[00:14:20] And, of course, you know, within the context, we send other workup, you know, occasionally depending on the age and risk factors. We do think about paraneoplastic or potential cancer associated transverse myelitis cases. In some instances, depending on what the sampled spinal fluid looked like. In fact, we may be very matched considering an infection and different types of infections can cause transverse myelitis. Even Lyme disease, very occasionally, very rarely, it's actually exquisitely rare, but it can be the cause of acute transverse myelitis, among many other infections, including many other viruses. So, the workup is really quite extensive, but it is tailored to the specific clinical scenario to you know, what the MRI looks like and, most importantly, what does the cerebral spinal fluid look like.

[00:15:13] And one of the cautionary tales that I will tell you is that, in the workup of transverse myelitis, we have to be very humble about how sensitive some of these tests are, like how good are they at picking up

the answer, right? And so, some of our tests are not a hundred percent sensitive, meaning that they miss a small percentage of cases.

[00:15:36] And so, in those instances, it's always good to retest it in about three to six months or if new symptoms arise. One of those examples is neuromyelitis optica antibody anti-aquaporin-4. Occasionally, in the disease, initially it can be negative. And that's why, if it's negative initially, but the suspicion is high, we've always retested in about six months. Particularly, the caveat is if a patient already received steroids or are they on a suppressive treatment or, say, plasma exchange or IVIG, you know, and the antibody was sent afterwards, that can diminish the chance of picking it up. And, therefore, it definitely needs to be repeated and kind of reviewed at a later point to make sure that it wasn't missed.

**Krissy Dilger:** [00:16:26] Okay, great. Thank you so much for that overview and, Dr. Narayan, this question came in from one of our community members. If no lesions appear on MRI, can a person still have TM and do lesions ever appear on a follow-up MRI done further out from onset that if somebody got their MRI originally at the start of their symptom onset, could it be possible that lesions would appear later?

**Dr. Ram Narayan:** [00:16:52] Yeah, thanks. This is a very frustrating situation, both for the patient and for the provider, when this happens. So, first of all, first thing, it is exceedingly rare for you to have a diagnosis of transverse myelitis when the MRI of the spinal cord is normal. Now, that comes with a lot of caveats.

[00:17:14] Can there be a situation when you can have a normal MRI of the cord with the clinical presentation of transverse myelitis? The answer is yes, but it's very rare. So, let's look at some data here. So, first of all, it's important to remember that spinal cord imaging itself, the MRI of the spinal cord itself, is a technically challenging test. So, know, the MRI tends to perform poorly when there is a lot of bones around the structure that you're trying to image and, as you know, the spinal guard is only surrounded by bones, the vertebral column. And so, by virtue of the anatomy, it's a place which is technically challenging to image.

[00:17:59] Second, it is important now, when the radiologist is reading the spinal cord MRI, he or she may not be always aware of the clinical findings on the patient. So, it's important for the neurologist also to take a look at the images himself for herself and, in addition, we would want to make sure that the patient does not move when the MRA is being obtained. So, sometimes, when we get an MRI of the spinal cord, we see various reports like, you know, the imaging was limited, the interpretation was limited because of movement artifacts, et cetera. So, in those cases, we actually don't hesitate to repeat the entire MRI under anesthesia, for example, because getting a good quality MRI is very important.

[00:18:45] Now, when you take the technicality off the table, then there may be a few conditions where, for example, the initial MRI can be negative. This has something to do with the evolution of the disease process. For example, there may be some diseases that start off at a sub-radiological level, meaning they start off with clinical symptomatology, but the signal has not yet begun on the MRI.

[00:19:14] And then the signal shows up on the MRI and rarely the signal may go off at a later time when the MRI is being done. So, in other words, for example, there is a condition called spinal artery stroke. So, in that particular condition, if an MRI is obtained very early in the course of the disease, sometimes the cord MRI can be normal, whereas a patient may have a classic presentation of transverse myelitis, number one. Number two, well, in that case the diagnosis is not transverse myelitis, but, you know, it's spinal artery stroke.

[00:19:48] The second instance, so, the Mayo Clinic published a case series of about 77 patients, if I'm not wrong, on patients with MOG associated myelitis. Okay, so, MOG antibody related transverse myelitis. So, in this particular condition, they found that about, I think, if I'm right, eight patients or so that had a normal

spinal cord MRI at the beginning, but the majority of them, at a later point of time when the imaging was repeated, they showed the signal.

[00:20:21] So, in summary, it's important to remember a few things. Number one, it's very rare to have transverse myelitis with a normal MRI. And that should typically make the, the clinician consider other possibilities. Number two, there are some possibilities where the MRI can be normal, even in transverse myelitis, albeit these circumstances are rare.

**Krissy Dilger:** [00:20:47] Thank you so much for explaining that. That's really helpful. Dr. G, a question actually came in. This person's son's diagnosis has gone back and forth between transverse myelitis and spinal stroke. So, the question is does the area on a spinal cord determine the diagnosis for existence of damage ranging between C level and T level? Does that signify more towards TM, or does it not really matter?

**Dr. Elena Grebenciucova:** [00:21:15] So, lower thoracic spinal cord regions particularly supply, but the anterior spinal artery are slightly sort of more common to see spinal cord stroke there, but it is true that, occasionally, we see this in the cervical spinal cord, as well. Those are very rare.

[00:21:35] So, it would be very difficult to base the diagnosis purely on the MRI imaging. I would rely more heavily on the onset of the symptoms, how quickly they occurred, because typical inflammatory transverse myelitis takes many hours and sometimes days from the beginning to, you know, the most, sort of, worst symptoms. Whereas a spinal artery stroke, and that's the cause of myelopathy, the onset is much quicker. It's actually very fast, often evolving over, you know, minutes to a near hour or several hours. Whereas, again, inflammatory conditions typically take much longer and are much slower to advance. Yes, there are, you know, if the history's poor and confusing, then the exam can be very helpful to see if there is a dissociation in motor and sensory symptoms, to try and understand if this was more of an anterior spinal circulation or a posterior spinal circulation that was affected. So, it's, you know, it's not just the location, and it's not just the MRI. It's really the combination of the examination findings and a very thorough history that is most, sort of, reassuring, you know, against the spinal cord stroke.

**Krissy Dilger:** [00:23:02] Okay, thank you so much. And, Dr. Narayan, we also got a few questions in just now about lesions that appear on MRI originally. Is it possible for them to disappear on follow-up MRI, following that initial MRI? Or once you have a lesion, will it always be there?

**Dr. Ram Narayan:** [00:23:23] So, first of all, that depends on the underlying condition, whatever caused transverse myelitis. Now, let me presume that we're talking about the more common form of transverse myelitis, which is called idiopathic transverse myelitis. At least, we think that's the most common form of transverse myelitis now. And when I say idiopathic transverse myelitis, I mean the kind of transverse myelitis that is thought to be immune-mediated. Typically, it's a one-time event and typically does not recur. And when I say secondary transverse myelitis or transverse myelitis, that happens as part of other conditions, like MS, NMO, MOG antibody disease, et cetera, or even conditions which are actually not transverse myelitis, but other causes of myelopathy, like a spinal artery stroke. Now, all of these can get lumped under transverse myelitis in general. But, to answer this question, if we're talking about the garden variety of transverse myelitis, which is a one-time immune mediated event, that is about two thirds of chance that lesions tend to get better with time.

[00:24:25] So, either you will have a decreased length of the lesion, or you would see decreased and, you know, decreased intensity on the MRI. And, typically, if the patient has enhancement, meaning if the lesion lighted up with contrast at the onset, on follow-up imaging we would expect that the enhancement resolves.

[00:24:44] In about one third of the patients, so probably less than that, the lesion tends to be constant, and it may not go away. That said, it is also important to recognize practice patterns amongst neurologists. So, the majority of us, if we are convinced that this is a one-time event of the spinal cord, and if we're convinced that this is idiopathic transverse myelitis, we may not follow up imaging on these patients unless patients come back with new symptoms.

[00:25:14] And so, because follow up itself may not be a pain on every single patient, the data on this is not very robust. There are a few papers published, but there is not a lot of data on it. And from what we know, about two thirds of lesions tend to get better or sometimes resolve. And about one third of the times, lesions tend to stay, you know, very rarely.

[00:25:37] But there are also experts that would say one third of the times, the lesions completely go away, one third of the times you're looking at some kind of an improvement in the lesion, and one third of the time the lesion may degenerate into axonal damage, permanent damage.

**Krissy Dilger:** [00:25:53] Okay, great. Thank you so much for that. So, acute treatments. In the acute phase of transverse myelitis, what are the typical treatments used?

**Dr. Elena Grebenciucova:** [00:26:04] Yes, of course. So, once infection has been ruled out, which is very important, and once we think that transverse myelitis is truly caused by inflammation that is ordering you in nature, typically the first thing that we do is administer high dose IV steroids. Many patients will actually improve pretty rapidly after IV steroids, but it depends on what is the cause of transverse myelitis. So, for example, in multiple sclerosis, quite often, patients who present with transverse myelitis have a very nice response to steroids with marked improvement, and sometimes within days, sometimes it takes longer.

[00:26:49] In patients with neuromyelitis optica spectrum disorder, response is often or less robust. And when we see less than complete improvement or very slow improvement, and the patient has severe symptoms, such as severe weakness, the next step is to ask a question, is this likely to be neuromyelitis optica spectrum disorder or MOG associated demyelination, or perhaps something else?

[00:27:17] And if the patient has not improved after steroids, we typically go to plasma exchange, which is a filtration of your blood through a catheter inserted into a vein. So, we filter the blood, usually every other day for about three to five sessions, to try and get rid of an antibody that could be causing that transverse myelitis.

[00:27:41] And that's when we have a high suspicion that what we are dealing with is NMO spectrum disorder or something else. In some instances, people can also try IVIG. Although the evidence in NMO spectrum disorder all stands for plasma exchange, with plasma exchange being superior to IVIG. So, there is a question of NMO spectrum disorder and the differential diagnosis, which is often the case.

[00:28:07] Plasma exchange is the next step. I think that giving IVIG is always a possibility, but it's best to do so after plasma exchange because otherwise it wouldn't make sense. So, if you give IVIG first and then you do plasma exchange, then you are basically washing out the IVIG out of the blood. So, it makes no sense to do that.

[00:28:26] So, typically we start with steroids and, depending on the response and depending on the completeness of that response, we go next to a plasma exchange and, in some cases, IVIG can be considered.

**Krissy Dilger:** [00:28:38] Okay, great. Thank you. And, Dr. Narayan, is cyclophosphamide used ever for acute transverse myelitis and in what situations?

**Dr. Ram Narayan:** [00:28:49] So, at some instances, I would say in a small number of instances, we may have to use medications like cyclophosphamide, et cetera, to treat the acute phase of transverse myelitis. Now, as Dr. G mentioned, we typically start with steroids. We would typically follow that up with plasma exchange and/or IVIG, only depending on the response of the patient. Now, let's say we have somebody with transverse myelitis. They've gotten steroids and they've gotten plasma exchange and maybe even IVIG, and they have not shown any sign of improvement. At that instance, we first want to reconsider a diagnosis, make sure we're not dealing with and non-immune mediated process, at that point of time, for example, a spinal artery stroke or a tumor of the cord, et cetera, those kinds of conditions, which may not at all respond to any immune treatment.

[00:29:42] So, that's something to always keep in mind. But, if we are still thinking about an immune mediated condition, the patient is, you know, definitely showing some improvement, but it's not all the, you know, all where we want it to be, then we could potentially consider heavy duty medication, what we call chemotherapy.

[00:30:00] So, an example of that would be cyclophosphamide. Now, cyclophosphamide, the evidence, one of the good sources for evidence for cyclophosphamide in transverse myelitis comes from my mentor's study, Dr. Greenberg, when he was at Hopkins, and this probably is in 2007. So, they studied cyclophosphamide in the acute phase of somebody presenting with transverse myelitis and they found, no, this was a retrospective study, meaning this was not designed in the form of a clinical trial, but they just reviewed, they just did an audit of charts of patients who had transverse myelitis that were treated with cyclophosphamide, when they came in acutely into the hospital.

[00:30:40] They found that there might've been a benefit for adding cyclophosphamide in acute cases of transverse myelitis, when the severity at the time of presentation was pretty bad. So, when the severity was to the point of total paralysis, which may not happen in the majority of patients with transverse myelitis. In that subset, maybe there might have been a benefit. Now, as far as I know, since that point, I don't think there has been any prospective study or a clinical trial studying the use of cyclophosphamide in the acute phase of transverse myelitis. And so, at this point of time, it's largely left to the judgment of the clinician in question.

**Krissy Dilger:** [00:31:24] Great, thank you so much for that explanation. And then, Dr. G are there side effects or concerns with any of the acute treatments or any reason you wouldn't use one of these acute treatments for a specific patient?

**Dr. Elena Grebenciucova:** [00:31:40] Yes, absolutely. Well, so I think that, when we are dealing with something very severe, that treatment is necessary, right? So, if somebody comes in, particularly with severe weakness, you know, we have to treat. Occasionally, in patients who actually have multiple sclerosis, when they present with very minor sensory symptoms, high dose steroids is not always necessary because, at least in cases of myelitis due to multiple sclerosis, steroids can speed up the improvement, but they don't necessarily change the outcome.

[00:32:15] But for true initial cases of transverse myelitis, where the person has a lot of symptoms, yes, we use steroids. So, some of the side effects of steroids include water retention, increased risk of infections, but the increased risk of infections is typically more so pronounced with chronic use of steroids. Typically, three to five days of steroids, you know, doesn't amount to really high risk. But it's really important to screen the patient for any signs of infection, you know, test them for COVID, you know, make sure they don't have a UTI, before giving them IV steroids.

[00:32:49] You know, many of these steroids can also make somebody anxious, can make somebody a little depressed. So, people have a history of bipolar disease, if they have to have steroids, this is a tough situation.



It needs to be done under the supervision of an inpatient physician because this could exacerbate, you know, mania or bring on mania or cause depression. Occasionally, people who are naive to steroids may develop severe psychiatric symptoms due to steroids, acutely, like acute psychosis. It's very rare, but that's why we usually exercise caution and not administer IV steroids on outpatient basis, but do so on the inpatient basis.

[00:33:30] So, some people, when they get IV steroids, can get a little bit of increased heart rate, can have a little bit of flushing, but these are rare and minor symptoms. Steroids generally are pretty well tolerated. Now, IVIG, intravenous immunoglobulin. So, intravenous immunoglobulin, what that is, it's basically pooled proteins from other humans these little proteins from the blood, they basically downregulate inflammation. So, that's intravenous immunoglobulins.

[00:34:01] And intravenous immunoglobulins because these are proteins, right, they increase the thickness in your blood, right? So, imagine if you're somebody who maybe has some heart disease, like blood vessel disease, coronary heart disease, or maybe they are somebody who is in their sixties or seventies, who's had some heart attacks and they have high cholesterol and their blood vessels in the heart maybe a little narrow because of the cholesterol plaques. Occasionally, IVIG can increase the risk of basically blocking one of these little narrow arteries and, therefore, increasing the risk of a heart attack. That's exceedingly rare and it's really more so in patients who are high risk for heart disease.

[00:34:49] Same goes for kidney disease. So, very occasionally, IVIG can cause kidney damage. Luckily, it's very rare and most people recover, but, occasionally, people can even need transient dialysis to recover from kidney failure. But the people who seem to be at risk for that are people who are of older age, people who have chronic kidney disease, and people who have advanced diabetes. So, an average young person, you know, with transverse myelitis, you know, is pretty safe when they are getting IVIG. But then, if it's somebody with multiple chronic conditions, like diabetes, heart disease, kidney disease, this is where we have to be a little bit more careful and investigate the risk versus benefit.

[00:35:36] Plasma exchange. So, plasma exchange, you know, because we are filtering your blood through a machine that's connected to a tube, we're shifting volumes of your blood, right? We are doing it slowly, but some people can develop a little bit of low blood pressure during this episode. And so, again, those people who have advanced atherosclerosis, meaning they have advanced cholesterol plaque buildup in their blood vessels in the neck, or maybe in the heart, they can be slightly higher risk for when you drop their blood pressure, right? So, if you drop the blood pressure and you have a very narrow blood vessel that's supplying your heart, and that narrow blood vessels suddenly can propel the blood to the heart. Well, somebody can have a little, you know, a heart attack. Or, you know, if that blood vessel happens to be the blood vessel that's feeding the brain, like the carotid artery on the outside of the brain, and you drop the blood pressure and that blood vessel was really dependent on the good blood pressure, because it's so narrow, to push the blood to the brain, while there is a very tiny risk of having a stroke.

[00:36:48] Fortunately, these are exceedingly rare, exceedingly rare occurrences. And the people who are at risk are truly people who are, you know, have known heart disease, high cholesterol, long-term, you know, carotid disease - a narrowing of their carotids -, people who are elderly, people who have, you know, advanced diabetes, hypertension, et cetera. But generally, for an average, you know, sort of young, healthy person who has transverse myelitis, these treatments are pretty safe.

**Krissy Dilger:** [00:37:22] Great. Thank you so much. Moving on to the topic of rehabilitation, Dr. Narayan, when should someone begin rehabilitation? And do you recommend rehabilitation for all people diagnosed with TM or just those with paralysis?

**Dr. Ram Narayan:** [00:37:41] The first question is very easy. Yeah, the answer is very simple: as soon as possible. So, I would say if somebody gets diagnosed with transverse myelitis, the very next day, when the physical therapist is available, you should get the physical therapist to see you for transverse myelitis. So, this typically should happen when the patient is admitted in the hospital itself. If the patient did get admitted, it should happen in the hospital itself.

[00:38:07] You don't want to wait for the patient to be discharged and then later establish care with physical therapy. Physical therapy starts at the earliest possible time, number one. And, and there are studies to support that the earlier therapies begin and the more aggressive the therapy regimen is, and the more appropriate it is, and, when it is offered by the, you know, the most appropriate kind of physical therapist, meaning a physical therapist that is particularly trained in this area or that is, that understands this condition much better, the outcomes are much better.

[00:38:42] Okay. So, that's number one. Number two, do you recommend physical therapy for all patients? First thing is, I would say by and large, yes. And the reason is, you do not need to have paralysis for you to get into a physical therapy regimen. Even if this was just a sensory impairment where you do not, where, where the patient may not have any weakness per se, of the muscles in the legs, they just may have sensory symptoms like numbness or tingling, et cetera, I would still recommend a physical therapist to evaluate this patient. Because lack of sensation in the legs might mean lack of balance and a fall risk because of that, number one. Number two, there are, weakness is not the only symptom of transverse myelitis as Dr. G clearly pointed out. There are so many other symptoms.

[00:39:33] For example, spasticity is another very important symptom in transverse myelitis where the legs can be stiff and that can sometimes affect the, the mechanics of walking. So, that is also another reason to see the physical therapist. So, the answer is you do not need complete paralysis. And I would say every transverse myelitis patient should get evaluated by a physical therapist at least once. And then depending on what the physical therapist thinks and, and based on the assessment of the physical therapist, we could, you know, we could make a plan for, for, you know, for the future.

**Krissy Dilger:** [00:40:14] Great. Thank you so much. We got a question from the community. Dr. G, can you shed some light on decompensation and how a patient might guide their provider in helping them to recover and/or adjust to the worsened or new symptoms?

**Dr. Elena Grebenciucova:** [00:40:32] Yeah, no, absolutely. So, decompensation, meaning that somebody had transverse myelitis, and maybe somewhat improved and has reached a plateau in symptoms. But then over time, maybe over a course of a few weeks or over a course of few months, there has been worsening. And you know, here we have to ask a question, what's underlying this decompensation or this worsening.

[00:40:59] So turns out there's quite a few causes, quite a few reasons. One of the most common scenarios is an undiagnosed infection happening in the body. So, when a patient with transverse myelitis has something as simple as a urinary tract infection, or maybe they have a tooth abscess, or maybe they have some sort of a viral infection brewing and they don't even have a cough yet or a sore throat, or maybe they're thinking it's allergies, but in reality, it's a viral illness.

[00:41:30] During those periods of time, the scar tissue, the sort of the damaged areas of the spinal cord, they tend to have a harder time, you know, maintaining function, and people often feel decompensation. So, all of their old symptoms come back and even feel significantly worse. So, when we encounter a patient with transverse myelitis for whom everything suddenly became worse, right?

[00:41:57] Or over the past few days or a week, first and foremost, we screen for infections. We talk to them, we examine them, we check their temperature, we check the labs. It's very important to know that people with transverse myelitis may experience urinary tract infections without having the typical symptoms of UTI.

[00:42:19] So, you know, an average person with a UTI may have burning with urination or increased frequency of urination and kind of knows that's what's going on, but the sensation in the bladder, and the bladder-brain communication in patients with spinal cord damage for transverse myelitis is impaired. So, that person may not always know that they have a UTI, and that comes as a surprise when we find that during urinalysis, treat the patient, and upon the treatment and resolution of the infection, the symptoms of transverse myelitis improve.

[00:42:51] Now, okay. So, that's a common scenario. Sometimes shortly after any viral illness, or sometimes even after vaccination, because either a vaccination or an infection, ultimately, they stimulate your immune system. Right? So sometimes we see patients get a vaccine or maybe they had a recent infection and suddenly, for a few days, while they're having a little fever and feeling a little weak. They have a little worsening of their old symptoms. That's also a transient recrudescence of symptoms. It's typically benign. And when we see this post vaccination, it is benign. It is not something to worry about, but obviously to let your doctor know, just to make sure that it's benign and it typically resolves within a few days post vaccination, as you start feeling better.

[00:43:40] It's just the fact that when the body's immune system is activated, that those damaged areas, the scar tissue is under a little bit more stress. And that is benign. That is okay. It typically resolves. Other scenarios is when a patient with transverse myelitis, particularly in the setting of COVID pandemic, you know, has been sort of not as active as usual, right?

[00:44:04] So maybe they have been staying at home way more, right, because of the pandemic and restrictions. They haven't been exercising as much, the, you know, to the extent of their ability. They, maybe they haven't been taking those walks. Or maybe because they've been, you know, isolated and very sad, staying at home and not feeling that great.

[00:44:25] They haven't been really, you know, going places, haven't been ambulating very much. And so, that can contribute to deconditioning. And with deconditioning comes worsening in weakness. And so, what we do in this instance is, of course, we examine the patient to make sure that that's all, the deconditioning is all that we are seeing. And sometimes we take an MRI to confirm that, right?

[00:44:51] And ultimately that patient needs, you know, intensive physical therapy regimen and, you know, trying to either ambulatory, trying to increase their exercise routine but not stress themselves too much, but to the extent that it's safe for them and to the extent that they're able to kind of increase the activity, recondition those muscles and muscle memory.

[00:45:16] So, that's very important. Another thing that we see when we say decompensation is somebody who has nerve-related, the neuropathic pain or tingling as a result of their transverse myelitis. And a lot of times, if the patient has been having poor diet and becomes vitamin deficient, like vitamin B6 and B12, we can see worsening. In people with diabetes who, you know, likewise, you know, haven't been to their doctor, you know, haven't been eating well.

[00:45:47] You know, when their blood glucose is not well controlled, we see worsening of sensory symptoms, burning symptoms, you know, that can mimic worsening or decompensation of transverse myelitis in people who suffer from depression. And remember that everybody's affected by depression differently. We think

about depression as somebody who's very sad and crying and doesn't have interest in things. But in some people, depression also can be more silent. And maybe they're just more irritable, and maybe they just want to sleep all the time, or maybe they're in, they have insomnia. They're not getting enough sleep.

[00:46:23] They're not getting enough rest. So, in cases of depression that affects, you know, their livelihood, their sleep, very often we see decompensation and symptoms, particularly reemerge and so worsening of perception of pain. And in those instances, we really strongly suggest to, you know, for, for these patients to reach out for, you know, therapy, talk therapy or establish care with psychiatry to guide them, to reach out to family members, even if it's just simply via Skype, you know, to try and sort of increase their social interactions to help with those symptoms.

[00:47:01] And of course, when there is a pain decompensation, talking to your neurologist about pain management is very important. But also making sure that the pain decompensation is truly from transverse myelitis and not from something else like low back pain because of a slipped disc or maybe some, you know, muscle strain, a muscle spasm, which is very common in people with transverse myelitis. Another part of decompensation comes from spasticity.

[00:47:27] And, you know, people with transverse myelitis often experience muscle spasms, right? And some patients with transverse myelitis, you know, develop stiffness in their muscles and very painful spasticity. And these patients are at very high risk of worsening spasticity when their activity level decreases, when their sleep is poor, when their diet is poor, when they, particularly if they haven't been able to stretch their legs or their arms, that they were previously doing that. Or, say they haven't been doing that and they have been less active.

[00:48:05] So, managing spasticity is very important. And so, you know, stretching, you know, when it's safe for people who do not have major impairment in balance. You know, stretching, passive or active stretching, is very important. Eating a healthy diet with plenty of electrolytes, with potassium and magnesium is very important. You know, hydrating plenty is very important because dehydration can lead to worsening of spasticity. Avoiding the extremes of temperatures, very important. For people with transverse myelitis, we know that the hot weather, just like the cold weather, can make symptoms appear so much worse, and that's both pain and weakness and spasticity.

[00:48:51] So, avoiding the extremes of temperature or limiting the time in extremes of temperature is very important. Management of spasticity, of course, has to go through your treating neurologist. And of course, as many of you know, involves muscle relaxants, combination of muscle relaxants, physical therapy, and you know, dietary changes, hydration changes, you know, stretching regimen.

[00:49:17] So, these many, many causes of decompensation, and it's just so important to talk to your physician, to be examined and, you know, to discuss with them, what is it that could be causing this decompensation? Do you need an MRI? What else needs to be done to help you?

**Krissy Dilger:** [00:49:36] Okay, thank you so much. And, Dr. Narayan, how long after onset should someone continue to do rehabilitation? Is there a cutoff for when progress will stop?

**Dr. Ram Narayan:** [00:49:48] I have a strong feeling about this. The answer is, there is no answer to this question. So, it is, so, as I said, so there are a few things. One is when I put a timeline and say, well, what you get at six months is what you get in terms of your recovery, then majority of patients quit trying at that point of time. Not just patients, interestingly enough, even doctors and physical therapists would start, quit trying.

[00:50:17] So, we do not want to say that, number one. Number two, but even in actual clinical practice, we see that a majority of the patients, particularly the young patients, and I see also children with transverse myelitis, they tend to do much better than a predicted timeline.

[00:50:37] So, if you had in your mind that, you know, this is going to be the maximum improvement at this point of time, you know, X number of months, they almost always outbeat that and continue to improve beyond that. So, time and again, we get humbled about this. And so, we say you will improve as long as you keep trying.

[00:50:54] Now, the improvement may not be as much as you had as in a particular point of time in the disease course, but it would still be there. Now, the other thing, no worsening or remaining stable is in itself an improvement. So, that's also something to remember. So, long story short, we don't want to put a timeline and say, this is going to be the time of maximum recovery, beyond which there is not going to be a recovery. We don't want to say that, number one. And number two, as I mentioned earlier, transverse myelitis encompasses a broader category of conditions. And, for example, spinal artery stroke may respond differently to therapy. Acute flaccid myelitis, which is a, you know, disease caused by a virus, that tends to behave differently to therapy. And then the garden variety transverse myelitis, immune mediated transverse myelitis, or transverse myelitis that happens because of another inflammatory condition like MS or NMO, they tend to behave differently with therapy. So, because of all these different factors, both biological and patient related factors, we don't want to say when the improvement is going to be at its maximum. I think what is important for patients is to keep trying persistently and consistently with physical therapy until they get to their maximum level of recovery.

**Krissy Dilger:** [00:52:17] I think that's a really important point you just made. And I really appreciate you expanding upon that because it's really important for our community to know that recovery can take longer than, you know, two years or whatever their doctor might have originally told them. We're almost at the end of our time. So, I guess I would just ask if either of you have anything you'd like to add that we didn't get to today? Dr. G?

**Dr. Elena Grebenciucova:** [00:52:43] Yes, absolutely. I think in advocating for yourself, if you've been diagnosed with transverse myelitis, it's really important that your MRIs are done on a high-quality MRI machine. And MRI machines come in two different strengths, 1.5 Tesla and 3 Tesla. 3 Tesla is currently the standard of care that gives you better resolution and so we can see the lesions a little bit better. So, I always caution the patients to make sure that, when they schedule MRIs outside, that they specifically ask when scheduling if it's a 3 Tesla MRI because that MRI can show things much better. And, as Dr. Narayan mentioned, you know, spinal cord is a difficult area to image.

[00:53:26] So, you want to get a high quality, the best type of imaging that you can. And the second thing that I would like to, you know, mention is that it's so important for people who had transverse myelitis to,

you know, continue, you know, following up with a neurologist to make sure that they are not having new concerning symptoms, that their exam is unchanged, and definitely for periodic imaging to make sure that this was just a one-time event and this is not evolving into multiple sclerosis or something else.

**Krissy Dilger:** [00:54:01] Okay, great. Thank you. And, Dr. Narayan, is there anything you'd like to add?

**Dr. Ram Narayan:** [00:54:05] Yeah. So, as Dr. G mentioned earlier, transverse myelitis is a rare condition and research in this area is vital to understanding the disease better, both in terms of disease markers, what we call biomarkers, and predictors of how, you know, things are going to be in the future.

[00:54:27] So, we really appreciate your participation in research studies that have conducted throughout the country. Because this is a rare disease, there are quite a handful of us that have a special interest in transverse myelitis throughout the country. And so, we would strongly encourage you guys to reach out to the SRNA and find out about what research studies are going on in this area to get enrolled.

**Krissy Dilger:** [00:54:53] Great. Thank you both so much for joining us. We really appreciate it. And I'm excited to offer this resource to our community. Also, we received a lot of questions today and I just wanted to ensure everyone we've written them all down and we are going to plan on having another podcast to hopefully address some of these questions because they're really great questions and we would love to offer another session like this to get to them. So, look out for that in the future. As a reminder, this podcast was recorded and will be made available on our website and our resource library. You can also find other podcasts and videos from past symposia, research summaries, and other resources in that resource library.

[00:55:35] So, in the meantime, if your question wasn't answered, you may be able to find some resources on that on our website. If you have any questions, please feel free to email us at [info@wearesrna.org](mailto:info@wearesrna.org). Alright, great. Thanks so much everyone and have a great rest of your day.

**Dr. Elena Grebenciucova:** [00:55:51] Thank you so much for having us, bye.

**Dr. Ram Narayan:** [00:55:54] Thanks.