

## Symptom Management: Spasticity

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**Intro:** [00:00:00] ABCs of NMOSD is a 10-part education podcast series to share knowledge about neuromyelitis optica spectrum disorder, or NMOSD, a rare relapsing autoimmune disorder that preferentially causes inflammation in the optic nerves and spinal cord. ABCs of NMOSD Podcast Series is hosted by SRNA, the Siegel Rare Neuroimmune Association, and in collaboration with the Sumaira Foundation for NMO, the Connor B. Judge Foundation and Guthy Jackson Charitable Foundation. This education series is made possible through a patient education grant from Viela Bio.

**GG deFiebre:** [00:00:59] Hello and welcome to the ABCs of NMOSD Podcast Series. This podcast is about Managing Spasticity in NMOSD. My name is GG deFiebre, and I'm from the Siegel Rare Neuroimmune Association.

[00:01:13] ABCs of NMOSD is made possible through a patient education grant from Viela Bio. Viela Bio is dedicated to the development and commercialization of novel life-changing medicines for patients with a wide range of autoimmune and severe inflammatory diseases.

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[00:01:41] For this podcast we were joined by Dr. Jacqueline Nicholas. Dr. Nicholas is a board-certified neurologist specializing in neuroimmunology, multiple sclerosis, and spasticity.

[00:01:52] Dr. Nicholas received her undergraduate degree from Miami University in Oxford, Ohio, and her medical degree from the University of Toledo College of Medicine in Toledo, Ohio. She trained at the University of Pittsburgh Medical Center where she completed an internship in internal medicine and a neurology residency where she served as Chief Neurology Resident.

[00:02:11] Dr. Nicholas completed a fellowship in clinical neuroimmunology, multiple sclerosis, and spasticity at The Ohio State University Medical Center in Columbus, Ohio, while also completing her Master of Public Health degree at The Ohio State University College of Public Health. She received a prestigious three-year Sylvia Lawry Physician Fellowship Award to fund her fellowship training.

[00:02:34] To start, can you just tell us a little bit about what spasticity is and what tone is in NMOSD?

**Dr. Jacqueline Nicholas:** [00:02:41] Sure. Spasticity is defined as a increase in muscle tone with some type of movement. Clinicians will describe it as a velocity-dependent increase in muscle tone. That means if we just very slowly move someone's limb, around a joint, for instance, flex the arm slowly, we may not pick up any increase in that muscle tone, where we feel some degree of stiffness or a catch. But if we move it really quickly, then we may actually pick up that there's some tightness or a catch there. And that's what we define as true spasticity - when there's some type of movement that

leads to an increase in muscle tone. But there are many different symptoms that people experience with spasticity, where it can be described as being: my muscles just feel very stiff, or people will describe having cramping or spasms, or they may describe that when they're trying to move their body or their legs, they can have what's called like an extensor spasm where the legs will stick straight out and remain stiff and it's very hard to bend them back into a seated position. People experience the clinical symptoms of spasticity quite differently.

**GG deFiebre:** [00:04:03] And then what causes spasticity in NMOSD? What is the reason that it happens?

**Dr. Jacqueline Nicholas:** [00:04:09] Typically in NMOSD, a common reason for spasticity would be if somebody has had a transverse myelitis and certainly in NMO, the myelitis can be quite severe and obviously many times, longitudinally extensive. When individuals have a transverse myelitis, they would be at an increased risk of developing spasticity. Certainly in NMO, although less common, we can see brain lesions, particularly in the brainstem, and this would be another area, could lead to spasticity. One of the common manifestations that many of my patients have had with that condition is something called dystonic spasms, where they may feel like one side of their body just gets very tight, and the arm may flex and the leg may flex at the hip and the knee, and the individual just can't relax it. And it's truly just caused by the damage within the spinal cord and sometimes the brain. And so anybody that experiences spasticity has to have some type of damage within the central nervous system, which includes the brain or spinal cord.

**GG deFiebre:** [00:05:19] And by transverse myelitis you mean someone that has had inflammation or damage to the spinal cord within NMOSD?

**Dr. Jacqueline Nicholas:** [00:05:27] Absolutely.

**GG deFiebre:** [00:05:28] Okay. And then why is it that some people have spasticity and others don't? Is there a reason within NMOSD that that might be the case?

**Dr. Jacqueline Nicholas:** [00:05:38] It can be very challenging, and to be frank, there's not a simple answer. So two people who have a lesion in the same level of the spinal cord or had inflammation at someplace in the spinal cord could be entirely different in how their symptoms occur.

So one person may have some weakness but not develop spasticity, whereas another individual could develop quite severe spasticity. But we think it has to do more with the degree of damage within the nervous system that prevents that normal signaling -there's an inhibit inhibitory signal that can occur. When you go to think "I want to catch a baseball" and you lift up your arm to catch that ball coming at you, the muscles that would prevent you from doing that, the antagonist muscles, those should not be contracting. Only the muscle to raise your arm and sort of flex the elbow and open your fingers to catch that baseball. But the problem with spasticity is that agonist and antagonist muscles, the muscles that do the opposite actions, can be contracting at the same time, and so that can prevent movement and be quite problematic.

**GG deFiebre:** [00:06:51] And you talked a little bit about this, do we know why someone might have severe spasticity and why someone else might not? Two people might both have spasticity, but someone has very severe spasticity. Do we have any understanding of why that might be the case?

**Dr. Jacqueline Nicholas:** [00:07:06] We tend to see, based on the degree of damage that somebody has had in their brain or their spinal cord, that sometimes that can correlate. Again, it varies significantly from person to person. I can share that in my personal experience as a neuroimmunologist and spasticity doctor, I tend to see patients who have had weakness as one of the problems that they've developed as a result of the damage in their spinal cord or their brainstem in the setting of NMOSD.

[00:07:39] I tend to see that it's more likely to occur in those individuals who've had weakness because it's sort of the body's natural way of helping, where those muscles can stiffen up and sometimes that spasticity can be favorable to some degree. Where if you had a complete weakness in one leg or both legs, it could be very hard to walk on legs that are kind of like jello.

[00:08:03] Whereas that stiffness, if the limbs and the muscles that are very loose, stiffen up, even if somebody's weak, that can help to support them better and allow them to be more effective at moving. But the problem really arises when the stiffness becomes so severe that the individual has trouble moving the limb or bending at the knees or other joints, depending on what the individual is trying to do. So there are some benefits of it and also some, some significant disadvantages as well.

**GG deFiebre:** [00:08:33] I know you talked a little bit about the benefits, so are there any other benefits to spasticity besides maybe providing some strength to a muscle that would otherwise be weak?

**Dr. Jacqueline Nicholas:** [00:08:45] I would say that that overall is the true benefit of spasticity because, that, for some individuals, when we manage spasticity, we want to be careful to loosen the muscles significantly enough to provide them with comfort and potentially better function.

[00:09:01] But at the same time we need to sometimes maintain some of that spasticity because that may allow for better function. So for instance, after a relapse of NMOSD where somebody has had a long spinal cord lesion, initially, they could be very weak in their limbs. And if the limbs remained very, very weak and very loose, it'd be very hard for that individual to accomplish certain motor tasks that they may want to carry out. And so that stiffness does help to some degree to be able to do some of the things that someone needs to do. But again, the problem really lies in when that stiffness is so severe that it's causing problems with pain, or it's inhibiting that individual's ability to work with neurophysical therapy or neuro-occupational therapy to really get that good rehab and try to strengthen and improve mobility.

**GG deFiebre:** [00:09:59] Got it. And then just going back a bit, I know you mentioned that someone can have damage to the spinal cord or the brainstem. Do you see any differences in how spasticity presents, depending on where in the central nervous system the damage is?

**Dr. Jacqueline Nicholas:** [00:10:14] Interestingly, I don't. As neurologists, we sometimes encounter people who have spasticity for a number of different reasons and can see it quite severe when they

have damage within the brain versus the spinal cord and various areas. So I wouldn't say that there's particular areas where we're more likely to see more severe spasticity.

**GG deFiebre:** [00:10:36] Got it. And then, what is clonus?

**Dr. Jacqueline Nicholas:** [00:10:40] Clonus is a word that means continuous muscle contraction. So one of the common things that someone's doctor might do while evaluating them would be to put a hand on the bottom of the foot and then to quickly bend that foot up. And sometimes somebody can feel their foot repeatedly just pressing down and it's an involuntary movement where it can just repeatedly jerk.

[00:11:03] Some people that have clonus, again, that's a common sign of damage within the brain or the spinal cord. And we can certainly see that in people that have spasticity. I'd say also that, many people with spasticity will describe that they might be laying down at night to go to bed and they feel that their legs just jerk or repeatedly kind of kick, and it's outside of their control. That's something called myoclonus or a muscle jerk. And again, that's a loss of neuronal control, or those normal signals that normally would inhibit your body from making movements that you don't want to make. But the problem is when that damage occurs, the signaling is confused, and then you can have these motor signals sent to the limbs to just randomly move.

[00:11:53] A lot of times people will notice that if the weather's really cold outside - cold can be a common stimulus for this - or if somebody touches their body, or if they try to move, that can be another trigger. So there are many reasons why that can happen.

**GG deFiebre:** [00:12:10] Okay, thank you. And then how long does it take spasticity to develop if it is going to happen? Is this something that happens immediately when someone is first having symptoms of NMOSD? What is the course of how spasticity might present?

**Dr. Jacqueline Nicholas:** [00:12:26] When somebody initially has a neurologic injury, it typically doesn't occur immediately. So, oftentimes when the initial damage occurs, let's say it's occurring in the spinal cord, somebody can have almost what's called spinal shock or such significant weakness and loss of muscle tone, where the limbs can almost feel incredibly floppy and loose. And then over time, over days to weeks to months, people will start to notice that they feel some tightness or some stiffening in those areas. And again, that can be mild to severe in range of how it occurs, but usually it does take some time for that spasticity to develop.

[00:13:12] And, one of the things that's very important for anybody who's experiencing spasticity is to know that it's important to get ahead of it early. Because spasticity can worsen over time and if it's not adequately treated with either stretching, therapy, and/or medications that we'll talk about tonight, sometimes those muscles can become so stiff that they get contracted permanently, where the tendons and ligaments can be fused to the bone. And then that can be very painful and limit mobility significantly, because then somebody can no longer straighten a limb or open their hand. And that can lead to a number of other complications, including trouble with maintaining good hygiene, and leading to things like ulcers of the skin. So it is something that's really important to get on top of when you notice these symptoms.

**GG deFiebre:** [00:14:08] All right. And that's a great transition to how spasticity is treated. If you don't mind, if you could just go over line treatments for what physicians generally do to treat spasticity in patients with NMOSD.

**Dr. Jacqueline Nicholas:** [00:14:22] When we evaluate somebody with spasticity, we really want to determine, is this something that is affecting multiple muscles or is it really just a few select muscles? And that sometimes can help to guide our treatment. I would say that most commonly, most individuals are started on a regimen of good stretching exercises. And, making sure that they're well hydrated and that they're minimizing those triggers that we talked about, like getting cold or infection, things that can really increase spasticity.

## First-Line Treatments

[00:14:56] And then, very commonly, first-line treatments would include oral antispasmodics. So Baclofen is an oral medication that's often dosed anywhere from once a day to sometimes up to three to four times a day. And that's something that's taken by mouth and usually has to be slowly titrated up because it can make people feel tired. But over time, many people can tolerate that well if it's increased very slowly, although some people still can't tolerate it because it can make them feel too sleepy or have difficulty with her thinking more clearly. So, sometimes other options would have to be used. That medication really activates a receptor called Gabba, which is involved in the overexcitability of the nervous system when there's been some type of damage so that's a very common one. And I would say that one that we see used quite commonly in spasticity associated with NMOSD.

[00:15:54] There are other agents. Tizanidine is another type of muscle relaxer that is commonly used, and that's another one that has pretty similar side effects to Baclofen in terms of sleepiness, but does require some blood work monitoring because it's broken down by the liver.

[00:16:10] And then there are other medicines that I would say are less commonly used, and those would be medications like benzodiazepines. Those would be things like, valium or diazepam, and those medicines we tend to not use as commonly because they can make people very sleepy, and oftentimes they need to be continually increased over time due to tolerance.

[00:16:34] Those oral medications would probably be our most common first line treatments.

## Second-Line Treatments

[00:16:39] Second-line treatments would be when the oral medications are not effective enough. Then we would look at if somebody has some severe stiffness. So let's say that somebody feels that their leg is very stiff in terms of noticing that they have trouble bending their knee because maybe their quadriceps muscle feels so tight that it's overpowering the other muscles that would help to bend the knee, like the hamstring muscles. So if that was the major problem, then their doctor could use something called botulinum toxin, which is a neurotoxin that can actually be injected into the muscles with a tiny needle into different areas within the muscle to spread it out. And then, to decrease the communication between the nerve and the muscle junction so that it's not overactive

and tight, but to decrease it to where it's a bit looser. And so Botox would be something that's more reserved when there's focal spasticity. So again, certain muscles that are stiff. Sometimes, people who have had lesions from NMOSD can have trouble with a foot turning down and in when they try to walk, and it just is sort of stuck in that position and have trouble getting their heel to the ground, or the toes could curl and be very painful because they're curling under. Those are muscles that are very easily targeted with botulinum toxin injections.

[00:18:03] Now, one of the challenges with Botox is, again, the only way it can be administered is via a needle and so it has to be injected specifically into the different muscles that are affected. Whereas the pills that we talked about taking by mouth, you can take that and then that's spreading out to affect all your muscles.

[00:18:23] Sometimes these options are even used in combination. And then, if somebody has pretty severe spasticity that hasn't responded to those options and is more diffused, Then there's this device called an intrathecal Baclofen pump and intrathecal means that it's giving the medication directly into the spinal fluid.

[00:18:44] That can be really beneficial, because when somebody takes something like Baclofen by mouth, only about 2 to 3% of it is actually getting to where you need it, which is in the spinal fluid to bathe those receptors within the brain and the spinal cord to reduce that spasticity. And then the rest of it is really circulating in your body and leading to the side effects of the sleepiness and those other side effects. So, if somebody is not benefiting enough or having significant side effects and they have severe spasticity, an intrathecal Baclofen pump would be an option. And typically, doctors will do an assessment where they do an injection of liquid Baclofen into the spinal fluid, pretty similar to how we might take spinal fluid if we were to do a lumbar puncture or a spinal tap.

[00:19:33] They would inject in some of the liquid Baclofen into the spinal fluid and then do some assessments over the course of many hours to see if the muscles got looser or not. And if they got looser to any degree, then people would know that that Baclofen pump would actually be an option to treat their spasticity. But there's a lot of ins and outs of that pump, and somebody has to be really committed and know about the potential risks of Baclofen withdrawal and overdose. But it has been a lifesaver for some of my patients with severe spasticity.

[00:20:05] And then I would say that if somebody is having spasticities to the point that we talked about, where they can develop contractures and limbs can be stuck in certain positions, then sometimes that would require a surgical tendon release or something of that sort by an orthopedic doctor to help with that, sometimes podiatrists as well.

[00:20:30] There's a less common treatment that I would say I typically don't see this used in adults, but sometimes it was discussed more in the past for things like cerebral palsy, but something called a dorsal rhizotomy where a surgeon would actually cut some of the neurons within the spinal cord to alleviate some of that spasticity, but also trying to maintain some of the motor function.

[00:20:56] That, again, would be in a more severe case. But I can't stress enough how important those lifestyle factors are. They may not do the whole job of controlling the spasticity, but the regular stretching exercises, making sure you're well-hydrated, and certainly making sure that any

active infections are being treated, because any kind of noxious stimuli to the body can actually increase spasticity. And that's why people many times see fluctuations in their spasticity throughout the day or from week to week.

**GG deFiebre:** [00:21:30] Great. Thank you so much for that overview. That's a really good transition to our next question, which is about how exercise can potentially reduce spasticity. Is there any kind of evidence that this is the case?

**Dr. Jacqueline Nicholas:** [00:21:43] There is pretty good evidence for this. If somebody is not stretching those muscles, again, as those spastic muscles are tight, it's because the muscles are contracting. If those muscles are allowed to continue to contract and we're not trying to stretch them back out, those muscle tendons can get shorter and tighter and again, eventually could result in a fusion of those muscles and ligaments to the bone to where it couldn't be effectively treated with some of the treatments that we discussed outside of surgery.

[00:22:16] There is quite a bit of evidence about that. And I'll also say that in my experience, any of the medication options that we discussed, it's imperative that somebody do those stretching exercises along with them. I find that when people get botulinum toxin injections, for instance, people who do a really great job with stretching those muscles throughout the day or if they're not sure how to stretch them, working with a physical or occupational therapist, we really see improved benefits in that setting compared to just doing the injections and not stretching over time. And so this has been shown in numerous studies to be beneficial.

**GG deFiebre:** [00:22:54] Great. Thank you. We did get one question: this person over time, their spasticity has continued to worsen, and they're not necessarily seeing that the spasticity is associated with changes in their MRIs. What are the potential reasons behind, an increase in spasticity like this?

**Dr. Jacqueline Nicholas:** [00:23:12] That's a really great question, and I think that that's always something that can be perplexing for our patients who are dealing with NMOSD, because they may not have had a new relapse in quite some time. They're doing well on the current medicine they're on to prevent new damage. But, sometimes they can feel that those muscles are getting tighter and tighter over time. Common reasons for that are that after damage has occurred in the spinal cord or the brain or brainstem, we can see, because of the damage has occurred over time, that there can be some accelerated shrinkage of the brain or even the spinal cord. As that is shrinking and muscles are not used as much or not stretched as much, we can certainly see that those muscles become tighter or stiffer. The other thing that we always want to assess for, if we find certainly that there's nothing new happening on the MRI, would be: is there any kind of noxious stimuli to the body that could be increasing this spasticity?

[00:24:16] So again, sometimes people can have infections that they're not aware of, like urinary tract infections, where maybe because of the damage done from the NMOSD, they don't feel it the same way as they may have before when they had a UTI. Just checking some of those basic screening tests for infection can be really important, because sometimes when you then treat that infection, the spasticity returns to the level it was before, significantly reduced.

[00:24:43] Sometimes spasticity could actually be a sign that there's an infection going on. The other thing is also to make sure that there's not any sores or wounds on the body. Certainly with NMOSD, people can have loss of sensation or change in sensation and maybe may not be aware of a change in their skin integrity.

[00:25:05] Another thing that I look for in that case, is I make sure that there's not any ulcers or sores on the buttocks or in between the legs or anywhere where somebody may not be able to see as commonly. Because sometimes that can be a sign that there's some type of wound on the body that needs to be addressed. And again, addressing that then in turn reduces that noxious sensory stimuli to the body and that reduces the spasticity. But it can also be a normal progression over time, that the spasticity just gradually worsens. And so again, another very important reason to get in front of it and treat it and monitor it over time.

**GG deFiebre:** [00:25:46] Great. Thank you. We got a question from someone who has pain and spasticity all the time, and when it's bad, it can be an 8 to 10 out of 10. And their doctor won't prescribe narcotics for the nerve pain. But this person has tried all the routine meds, and while tizanidine and Baclofen help, they don't decrease their symptoms enough to handle really bad days. And so they're really worn out from the pain and spasticity, and they asked to be referred to another pain doctor, but were sent to someone who handles migraines and headache pain rather than NMO. And so, the spasticity doctor was the one who increased their tizanidine and an added Baclofen. They also use lidocaine, cool showers, CBD cream, cooling mats, and nothing really seems to be working for them. Do you have any additional things that you might suggest that they try to do to help the pain and spasticity in this case?

**Dr. Jacqueline Nicholas:** [00:26:41] Sure. That sounds pretty unbearable, and I'm sorry to hear about that. I think that, in this individual, it sounds like they're saying that their bad days are quite severe. And that even tizanidine and Baclofen, although it helps a little bit, aren't really targeting or giving them the full benefit. So, it can be a challenge to know exactly what to say to this person without being able to examine them. But I would say I would first check and see, are the tizanidine and the Baclofen at adequate doses. Sometimes, elevating those over time can be helpful. The other thing that I would say is it sounds like there's a pretty significant pain component here.

[00:27:19] Certainly spasticity can cause pain, from the spasms or the tightness, but also with NMOSD, we know that this can be a very painful condition for a number of reasons. And oftentimes, the painful skin sensations or dysesthesias from the neurologic damage can be quite severe. And so sometimes focusing on treating the pain, separate from just loosening the muscles, can help in turn reduce spasticity.

[00:27:46] So there are a number of neuropathic pain medications that we use and even other medicines that are off label for that use. That would be one area that I might explore. There are certain medications that are called serotonin and norepinephrine reuptake inhibitors [SNRIs], and that class of medication sometimes can also really help, from that different pathway of targeting the pain, to reduce that neuropathic pain.



[00:28:14] In addition, I would want to make sure that that individual is plugged in with neuro-physical therapy and occupational therapy to make sure that they're getting an adequate stretching program. And then if this individual, the neurologic exam would be incredibly helpful to know further what's going on, because if there were muscles that were focal muscles that were really tight, for instance, sometimes people tell me their calves are the worst place or their thighs. Sometimes even using small amounts of botulinum toxin injection in those areas where they're having this significant spasm or discomfort can be helpful. Also if this is somebody who, on exam, was noted to have severe spasticity, another consideration would be that intrathecal Baclofen pump.

[00:29:00] But again, it would be hard for me to know without seeing the patient. And then, I would say that there are also a number of other alternative options that are available. Sometimes pain cannot be treated simply with one mechanism. And that's why we mentioned talking about taking the Baclofen or the tizanidine like they're doing, but also in combination with a neuropathic pain medication. I know I mentioned the SNRIs, but there are also medications like Gabapentin and pregabalin or Lyrica that can be helpful as well. And then sometimes we use tri-cyclic antidepressants, which in my opinion, aren't really great to treat depression, but we use them specifically for pain. Medications like amitriptyline or nortriptyline can be very helpful.

[00:29:43] Some of the alternative treatments can be helpful too, like acupuncture or relaxation therapy, like mindfulness training can be incredibly helpful. Those are really the things that I would start with first in the scope of neurology. And then, there is a significant bit of research that is being done as well to better understand the effect of cannabinoids on pain. I know that that can be a taboo issue and that's something that has been looked at in the setting of diseases like multiple sclerosis, where people can have inflammation in their spinal cord in shorter areas, whereas in NMOSD we certainly see longer areas of inflammation. There are some reports that it's beneficial for spasticity there. Although there's a lot of ongoing studies that I think need to be sorted out so that doctors can better understand long-term and short-term risks and benefits of that.

[00:30:40] But, depending on the state somebody lives in, that would be another option that they could potentially explore. And then if all of those options were not significantly helpful, then seeing a pain specialist who sounds like maybe specializes more in what this person is suffering from. It sounds like this person is more seeing somebody who specializes in pain associated with headaches. Seeing somebody who could really address the whole picture. I think that in certain instances, pain may require a narcotic medication if the neuropathic pain medications aren't helpful.

[00:31:13] So I think it's really a comprehensive approach and look at what could be done, but it sounds like there are a lot of opportunities for improvement for this individual.

**GG deFiebre:** [00:31:23] Great. Thank you so much. And so we did talk a little bit about Botox, but are there any long-term effects that need to be considered when using Botox long-term?

**Dr. Jacqueline Nicholas:** [00:31:34] Botulinum toxin, there are a couple of different forms of the toxin. The most common form that's used for spasticity is called onabotulinum toxin A. Really with repeated use, most individuals will continue to respond. It's given every three months, the benefit

should last close to three months for that type of toxin. But, some people may develop, after an initial benefit to the toxin, may begin to notice that it's not helping as much over time with subsequent injections. One of the reasons for that could be that somebody has developed an immune response against the toxin.

[00:32:12] If that occurs, typically, I switch the botulinum toxin to a different form. So another common form that's used is called abobotulinum toxin A. Sometimes just switching to a different type of botulinum toxin can result in improved benefits. The other thing that I would say is, one risk of Botox, we kind of start at a low dose, so we think may help and then assess for benefit and then slowly increase over time. Because Botox, again, is blocking that communication between the nerve and the muscle junction.

[00:32:44] We don't want to give so much that we cause somebody to be incredibly weak to where they can't work with therapy, but we also want to give enough to where we've provided comfort and potentially allowed for improved mobility if they do have motor function there. So again, just making sure that the dose isn't being overdone.

[00:33:03] And then the other thing is that sometimes when people get repeated injections, because it's really decreasing that communication there at the nerve muscle junction, if somebody is getting those repeatedly, we can see atrophy of that particular muscle where the muscle is shrinking. Again, that's something that the specialist who's administering that needs to be mindful of and monitoring over time. But there are many people who get this over years and years and years and find significant benefit and don't have any of these issues.

**GG deFiebre:** [00:33:34] Got it. Thank you. And then is Botox to treat spasticity any good without subsequent rehab?

**Dr. Jacqueline Nicholas:** [00:33:42] I would say that it is helpful, but it is significantly more beneficial when people receive the Botox to then go for some therapy or rehab to work to stretch those muscles. And once those muscles are a little bit looser, again, sometimes people are then better able to work with a therapist to try to strengthen them. Again, that's not the case for everybody, depending on the degree of injury. But, we definitely see an improvement in the muscle tone and the looseness over time in individuals who do that as opposed to just getting the injections and then not working with therapy to do the stretches.

**GG deFiebre:** [00:34:22] Okay, thank you. And then, in rehab someone might be using electrical stimulation. Can this be used to treat spasticity as well?

**Dr. Jacqueline Nicholas:** [00:34:31] I would say that this is a less commonly used treatment. Usually it's done with something like a TENS unit, which can basically be applied over the muscle and provide some electrical stimulation to the muscle. There have been some small studies, particularly in stroke, I would say not as many in NMOSD specifically, that have suggested that it can be beneficial for spasticity in the legs or the lower limbs. Whereas, there hasn't been as much benefit reported in the upper limbs. Sometimes people will do this in the physical therapy setting, or there are portable devices that can be purchased for home use. But I would say that most people that utilize this would do it in combination with other treatment options.

**GG deFiebre:** [00:35:18] Okay, thank you. Does spasticity change the muscle or bone ligament or other structures over time? And if so, how does it do this?

**Dr. Jacqueline Nicholas:** [00:35:27] It definitely can, and probably the most concerning part and what we see happen, especially if it's not addressed, is that as those muscles get tighter and tighter, they can shorten. And again, those ligaments and tendons can fuse and fuse to the bone so that there's no longer the ability to move the limb at a joint. So for instance, if somebody has stiffness it's in their arm and the arm is stuck flexed at the elbow - I've seen a number of people where they didn't think it was an issue because they didn't have pain, they noticed that it was tight but just didn't really do the stretches, and then those muscles and tendons and the joint became fused and then they couldn't move it. And then that leads to atrophy of the muscle and certainly a lot of pain when somebody can't move a limb around a joint. And so really it can often be a progressive tightness and stiffening. Now that's not the case for everybody. Sometimes people have more mild spasticity where it manifests more as, just feeling tight or some spasms, but not where it's so tight that it would cause a limb to become stuck. But that would really be the main change that we can see over time.

**GG deFiebre:** [00:36:39] Got it. And then is there anything else that you want to mention about spasticity?

**Dr. Jacqueline Nicholas:** [00:36:45] I want to share that neurologists in general, I don't think that we get excellent training in our residency programs and our training programs to become neurologists, to really understand that spasticity is very treatable and that there are a lot of options out there aside from oral medications to treat spasticity. I became very passionate about treating spasticity when I was in my fellowship training and started taking care of people who had NMOSD and other causes of transverse myelitis or brain inflammation, where it was really a symptom that was pretty common.

[00:37:21] For many, they reported the problem but had only been treated with oral muscle relaxers that sometimes they couldn't tolerate. And, as I went on in my training and did a spasticity fellowship, I realized that there are many, many options out there to help somebody with spasticity.

[00:37:37] If you're experiencing it and you feel like nothing you've done has helped, I encourage you to talk with your doctor about it because there are a lot of options, and sometimes a combination of options can help to better improve that. It's one of those symptoms that I think that people just need to know if you think you have it, please bring it up, tell your doctor, and ask them what can be done to help because having that can definitely affect quality of life, and we want to give you the best quality of life possible.

**GG deFiebre:** [00:38:06] All right. Great. Well, thank you so much for taking the time today. We really appreciate it.

**Dr. Jacqueline Nicholas:** [00:38:10] Thanks so much.