

# What is Neuropathic Pain, Numbness, and Tingling?

You can view this presentation at: [youtu.be/kFmH5tYiXL0](https://youtu.be/kFmH5tYiXL0)

[00:00:00] **Roberta Pesce:** Hi, everyone. Welcome to our first talk of the day focused on symptom management, specifically neuropathic pain, numbness, and tingling, which can all be devastating symptoms following a rare neuroimmune diagnosis. I'm joined today by Dr. Ram Narayan, neurologist, and Assistant Professor of Neurology in the Department of Neurology at Barrow Neurological Institute. We'll address these symptoms and the current therapies for treating them. Good morning, and over to you.

[00:00:35] **Dr. Ram Narayan:** All right. Good morning, one and all. My name is Ram Narayan. I am Assistant Professor of Neurology in the MS and Neuroimmunology Division at the Barrow Neurological Institute. And I will make an attempt to talk about, what is neuropathic pain, numbness and tingling relevant to the patient population that's dealing with rare neuroimmunological diseases. I thank the SRNA and my mentors, Dr. Greenberg and Dr. Levy, for this wonderful opportunity. All right. So, I do not have any disclosures relevant to the talk. So, this is the synopsis of what we're going to discuss today. What is neuropathic pain and how common is it? What are some causes and mechanisms of neuropathic pain? How is the diagnosis of neuropathic pain made? And the crux of the talk is going to be on management. And I've tried to cover topics that patients frequently ask me in the clinic, so I find, so I hope you would find this more relevant to you in the management of these conditions.

[00:01:50] So first of all, what is neuropathic pain? So, pain that's caused by disease of these somatosensory pathways, and somatosensory means it is the pathway that carries sensory signals from the skin out from any end organ, it could be the liver, the spleen, any internal organ or any external, the muscle or the bone, or the skin, to the higher, the highest center in the brain. So that is the somatosensory system. And it's a three-wire system. If you look at this picture here, so you would see here, here you can see that there are some wires that, the nerve fibers that come from the skin and that go to the spinal cord, that's your first wire. The second wire is the nerve fiber that comes from the spinal cord and goes all the way to a relay center in the brain called the thalamus, that's the second wire. And then the third wire is the nerve fiber that starts from the thalamus all the way to the somatosensory cortex, otherwise called the sensory cortex.

[00:02:58] Now, these pathways are directly involved in neurological conditions. And as an example, a very common condition is diabetic neuropathy, which tends to affect the peripheral pathways. When I say peripheral, anything outside the brain and the spinal cord, which is, you can think of that as the freeway, that

is the main, that is what we call the central pathway, and then the peripheral pathway is anything outside the brain and the spinal cord, so that would be all the nerves that come off the spinal cord and go all the way up to the skin. So diabetic neuropathy is a condition that affects the peripheral pathways, whereas in multiple sclerosis, neuromyelitis optica, in MOG antibody disease, in stroke, in transverse myelitis, you have the central pathways affected.

[00:03:53] And neuropathic pain is different from pain that comes from inflammation. So, if you have a cut on your skin, if there is peptic ulcer, or if you have any pain from your joint, or your muscles or your bones, those pain, those kinds of pain are different from neuropathic pain. And ten percent, sorry about that, ten percent of pain, of all patients with chronic pain have neuropathic pain characteristics. Now, this might look like a small number, but it's important to understand that 50 million adults in the United States have chronic pain. So, 10 percent of that is a good 5 million people that have neuropathic pain characteristics. So again, this is another picture of the complex pathways.

[00:04:47] And you can see, so this is for example, these are the peripheral nerve fibers that take the pain sensations to the spinal cord, and then they course all the way up through different centers in the brain stem, so this is what we call the medulla oblongata, and this is the midbrain, and then this is the highest center of the brain called the cerebral cortex. Now, if you look at each of these areas, they have distinct function. Now, one very important point for us to remember is it's really the spinal cord that plays a major mechanism, a major role, in the integration of pain signals that come from the brain to the skin and from the skin to the brain, so both the ascending and the descending pathways are controlled in the, at the level of the spinal cord and of course at other levels as well.

[00:05:39] So now, what causes neuropathic pain? So why do patients with these conditions, disease conditions, get neuropathic pain? Well, there are some of these mechanisms implicated, brain signaling changes. So, what this means is, whenever a nerve fiber is affected by a disease process, let's say diabetic neuropathy, the impulses that go from the skin to the spinal cord are going to be affected because of that, and then the spinal cord is going to many times thinks that there is an excessive signal coming from that area in the skin. So particularly when the spinal cord is chronically deprived of impulses, of regular, normal impulses coming from the skin, it sort of presumes that even for a trivial stimulus, it would presume that that is excessive stimulus coming, and that's one such mechanism.

[00:06:38] And if you look at all of these nerve fibers, they're all started with sodium and potassium channels, and it's considered that, that sodium channel abnormalities in the nerve fibers that are affected by these disease processes, which is, again, which can result in neuropathic pain. Now, second-order nociceptive neuronal alterations, now again, these are all very loaded medical words, but essentially it means that there is a lot of short-circuiting that goes on in the spinal cord when there is a disease process like MS or NMO. And then you have inhibitory modulation changes. It's important to recognize that the higher centers of the brain, you can think of that as the big boss, and that constantly inhibits a lot of trivial stimuli that go through.

[00:07:29] So as part of our life, as part of just living, we get exposed to tons and tons of trivial environmental stimulus, and a lot of those are gated, are controlled, at the level of the spinal cord by the higher centers of the brain, such that not every impulse makes it through to the brain, and only certain very important impulses make it all the way to the brain. And then of course, central, reduced central pain modulation, this is also very similar in the sense that the higher centers of the brain, some of the centers of the brain, particularly in the midbrain, there is a lot of modulation of these impulses. It decides which impulses go and which impulses come off the brain, and those pathways can also be affected.

[00:08:18] So in a sense, they're in a patient who has a neurological condition, neuropathic pain can be caused by multiple mechanisms, most of which are poorly understood, starting all of the way from the end organ, which is the skin, up to the brain. And at different levels, at the level of the skin itself and those nerve fibers, and then at the level of the spinal cord and the level of the intermediary centers, meaning the midbrain and the brain stem, and then at the level of the cerebral cortex as well. So now, how do we start suspecting neuropathic pain in a patient that reports pain as a main symptom to us? So, if you look at this cartoon here, there are different patterns that we recognize in a patient with neuropathic pain. And for the purposes of the talk, for this talk today, I will try and focus on central neuropathic pain.

[00:09:18] So if you look at patients, particularly MS patients and patients that have NMO and TM, they would report this kind of banding pain in their chest. We've described this as the anaconda sign in an up-to-date article, and it used to be called the MS hug, but because it's not a warm symptom, it doesn't feel warm, it rather causes a lot of distress, we call it an anaconda sign, and that's how it feels like. And here you have a patient who has a complete lack of sensation below a particular level of the chest and also has pain in that area, so that sounds like a paradox where somebody might have a lack of sensation and yet have a lot of pain in that area.

[00:10:02] And shared here you'll see a gentleman with pain in one entire leg and in a part of the other leg as well. And see here in this picture down, you see that there are multiple other distributions where patients can have neuropathic pain in multiple sclerosis, for example, which also results in neuropathic pain. So, the distribution of pain is one important clue for us to distinguish neuropathic pain from other causes of pain. So, when a patient comes to us, to the clinic, and we suspect neuropathic pain, one thing, one of the main things we base our decision on is our clinical exam, so we test them with a little pin. We test them with a vibrating tuning fork. We test their joint position sense, and we test their sense of temperature.

[00:10:58] So based on that, we come to a conclusion if a patient has impairment in one or more of these modalities, we come to a conclusion that, yes, the patient has pain, and the patient has a neurological disease that can cause pain, and the patient also likely has a lesion in the pathways that conduct sensory impulses, and therefore the patient probably has neuropathic pain. Sometimes it's not very straightforward, and we may need other additional testing, like a quantitative sensory test, a sweat test, and sometimes a nerve conduction study, and sometimes something called the somatosensory evoked potential or a skin biopsy. So, these are ancillary tests which are less commonly used.

[00:11:42] The majority of the time the diagnosis of neuropathic pain is based on a history and a clinical exam. So, the management is essentially multimodality, it is multidisciplinary, and it is important for us to recognize that neuropathic pain is a very distressing symptom. It does cause significant change in the quality of life of a person that goes through this, but more importantly, it is also challenging to treat. And there is not one particular guideline or algorithm that we learn to take care of these patients, and so you're going to find that different physicians adopted very different approach to this. And the key of all of this is going to be that this is all multidisciplinary. Now, in my clinic I usually start with a multimodality approach directly, even at the first visit.

[00:12:54] So we already start talking about medications, but along with it we talk about alternative systems like acupuncture or nerve or cord stimulation using electronic devices, and also psychotherapy. So, we talk about all of the four of this at the first visit itself. So, these are some medications that many of you in the audience might be familiar with. We start with first-line therapies typically, which is, which are, which comprises of antidepressants and anti-epileptics, and then we use second-line therapies like topical lidocaine and

tramadol, and then third-line therapies as well. Now, it is important to understand that the first-line, second line and third line come based on the best clinical evidence based on the outcomes of various studies that have looked at the efficacy of these medications.

[00:13:55] Now, something common to all of these medications, first thing is more often than not we find patients on two or more of these medications. And sometimes that's when patients run into adverse effects. So, it's very important to recognize the possibility of polypharmacy in these patients, particularly in the elderly. And this is, a lot of these patients may also have coexisting migraines, or coexisting backaches, or arthritis, depression, and some of the medications used are common between all of these conditions and might interact with each other. It's also important to recognize that a lot of these medications, particularly the antidepressants and the antiepileptics, now, I've provided the full list here, they don't work immediately. They may require chemical changes to happen in the nervous system over a period of a few weeks for them to take full effect.

[00:15:02] And another important thing is, it sometimes is frustrating for patients when they're started on a low dose of these medications. At low doses, not surprisingly, you're not going to see any positive effects on the neuropathic pain, but the clinician would have decided to start you on a lower dose because slow titration is the key to prevent adverse effects. Now, because we do not have any clear set guidelines we're going to, we typically do most of this on a trial-and-error basis, and it's important to recognize that one size does not fit all. A lot of our patients end up using nonsteroidal anti-inflammatory drugs like ibuprofen or naproxen or indomethacin, and these and other over-the-counter medications, these have limited utility in the treatment of neuropathic pain and have a long-term adverse effect.

[00:16:00] So opioids, important to recognize with opioids, there have been studies with mixed conclusions, but clinicians and patients have recognized that there is always a challenge of narcotic overuse and dependence in some of our patients. And also, in this particular patient population that goes through transverse myelitis, or MS or NMO, cognitive and bladder symptoms are very common, and opioids certainly do not help those. In fact, opioids can significantly make these symptoms worse. The next important thing that I get asked about patients is, regarding from patients is the about the use of medical cannabis. Now, cannabis, when we talk about medical cannabis or cannabinoids, there are two components to recognize. One is called a THC, which is tetrahydrocannabinol, and the other one is the CBD, which is cannabidiol.

[00:17:00] Now THC is the psychoactive part of the drug which, the psychoactive compound that gives people the high from the cannabis, whereas cannabidiol is thought to be neuroprotective and anxiolytic and anti-inflammatory. Now, so the role of medical cannabinoids have been studied in a Cochrane analysis. Now when you hear this word Cochrane analysis or meta-analysis, we consider that to be one of the highest levels of evidence for practice, for the practice of medicine. And so, they looked at about 16 studies involving about 1,700 patients, and they found that the benefits of cannabis-based medicine can potentially be outweighed by their potential harm, that was the conclusion.

[00:17:53] And of course, when we are interpreting studies, you might find, you might come across different articles that have proven benefit of cannabis or opioids in neuropathic pain, but we always have a very particular way in critiquing and analyzing studies because of the different ways that these, and the different settings that these studies are performed in. In my own personal experience, I really think that cannabinoids or CBD oil may have a role for anxiety and depression and spasticity, along with coexisting neuropathic pain in a select population of patients. And of course, there are these numerous devices with which I have very limited experience, but an expert that's dealing with neuropathic pain in an outpatient clinic may be well, with pain management for example, may be well aware of some of these. So, from noninvasive methods, like a spinal cord stimulator, actually, wait.

[00:19:00] Okay, so starting from a transcranial magnetic stimulation, which is largely noninvasive, you have things like motor cortex stimulation, deep brain stimulation which involve invasive methods to reduce neuropathic pain. A vagal nerve stimulator, that is again a noninvasive, or rather a minimally invasive procedure for treating neuropathic pain. All of these devices have mixed results for the treatment of neuropathic pain. And one very important thing is, one really important modality of treatment is called scrambler therapy. I was fortunate to get exposed to scrambler therapy when I was working with Dr. Levy at Johns Hopkins.

[00:19:40] And Maureen Mealy, who is a very popular name at the SRNA, she came, she did this study for her PhD and found out that scrambler therapy has a significant role in the treatment of neuropathic pain and neuromyelitis optica. And finally, about CBT, or cognitive behavioral therapy, so it is important for us to not undermine the role of psychotherapy in the treatment of chronic pain, particularly neuropathic pain, because a lot of this has to do with thoughts and emotions and behaviors.

[00:20:24] So CBT does have a significant role in the management of pain. And many times, I ask my patients to do it along with medications to improve outcomes. Lastly, the current practice of medicine, we try and find one therapy that suits all. But I guess we are slowly moving away from that, and we're trying to find markers of response to treatment and try and individualize treatment protocols for each and every patient. And now I'll stop and take questions. Thank you so much.

[00:21:11] **Roberta Pesce:** Thank you, Ram, for this very interesting talk. I don't believe we received any questions, but please feel free to stay on in the event chat if any questions come along and thank you so much for your talk.