

## **Episode 3 - Prof. Bart Morlion - Understanding the Pain Puzzle**

### **Neuropathic Pain Fundamentals**

Speaker 1

Welcome back to Inside the Silent Storm. I'm Dr. Lim, and today we're tackling one of the most challenging aspects of diabetic peripheral neuropathy. The pain itself. If you have ever wondered why neuropathic pain feels so different from other types of pain, why it is described as burning, shooting, or electric-like, or why it often doesn't respond to traditional pain medication.

Speaker 1

Today's episode will provide those answers by exploring the fundamental signs of neuropathic pain, and how understanding these mechanisms can lead to better treatments. I'm joined today by Professor Bart Morlion, an expert in pain medicine. Together, we will unravel why neuropathic pain is such a unique and challenging puzzle for both patients and clinicians. Professor Morlion is the Director of the Leuven Center for Algology and Pain Management at the University Hospitals of Leuven, and clinical professor at the University of Leuven, Belgium.

Speaker 1

He teaches pain management, pharmacology and evidence-based medicine at the medical school. Professor Morlion, thank you for helping us understand this complex and often misunderstood aspect of diabetic peripheral neuropathy. Hello, Professor Morlion, it's really nice to have your insights. Really trying to explain to us the puzzle of pain. So how many types of pain that we're looking at right now?

Speaker 2

Yes, indeed. If we look at the types of pain, there is, what we call the mechanistic descriptors of pain proposed by, IASP, the International Association of Pain. And they distinguish three types. So first of all, nociceptive pain, which actually is a type of pain with just a normal activation of nociceptors and nociceptors, which, are critical in the pain system.

Speaker 2

And this is actually the, the physiological form of pain, like, you know, when you cut your finger or you had an operation. So this is the very physiological way of our alarming system. On contrast, then we have neuropathic pain. And neuropathic pain is not normal because there is some disease or a lesion in the somatosensory nervous system.

Speaker 2

And this can be in the periphery. It can be a peripheral, neuropathic pain, like for instance, shingles or a radiculopathy, but also diabetic neuropathy, for instance. Or it can be centrally located in the spinal cord, like we see with, spinal cord injury or like we see post-stroke pain. And it's, and then thirdly, this is has been decided quite recently.

Speaker 2

We as especially clinicians knew that some of their patients didn't fit in these two categories. And in the past it had many names. It started with functional pain, dysfunctional pain. But now we have an official definition. It's called nociplastic pain. And nociplastic pain actually is, pain based on an altered nociceptive process, not fitting in the definition of nociceptive pain and not fitting into the definition of neuropathic pain.

Speaker 2

But these patients are definitely in pain.

Speaker 1

Then they should be grateful that diabetic peripheral neuropathy has been classified as the one type, one type of the neuropathic pain.

Speaker 2

Indeed. So this is a typical example and a very prevalent example, of peripheral neuropathy, peripheral neuropathic pain because of the polyneuropathy. And it's so prevalent because worldwide we see such an explosion of diabetes, especially type II patients. And knowing that, almost half of them will develop a polyneuropathy and half of them a painful polyneuropathy, that means this is about millions of patients in the world.

Speaker 1

And I understand that there's been confusion about how to screen and how to diagnose diabetic peripheral neuropathy. Could you give us a simplified workflow, especially for primary care practitioners?

Speaker 2

I think the first important step is to take a history and first listen to the story of the patient, because many patients will actually give the clues to neuropathic pain, because it's had been shown several times that patients with proven neuropathic lesions and pain always explained and reported the same type of complaints. And it's about burning pain.

Speaker 2

It's about painful cold. It's about the feeling of arms, pins and needles, electric shocks. And now I named five typical descriptors of neuropathic pain. And based on these observations, many colleagues have been starting work. And can we make pain questionnaires with a high specificity and sensitivity to as a screening instrument, to make the diagnosis of neuropathic pain easier.

Speaker 2

And this works. This works also in the primary care setting and for GP's. To give you one example, my nurses in the pain central, they know it by heart these pain questionnaires, they even don't even need paper or the questionnaires themselves because they're so simple. For clinical practice, I would recommend to you have the painDETECT also very specifically focused on neuropathic pain also very useful for diabetes specific patients.

Speaker 2

Little problem is it's not, free usable. So, and the other one is an even very much shorter for pain questionnaire. It's the DN4, it stands for Douleur Neuropathique 4 Questions. It's French. Now you know that it was developed first in France but it has spread to world. And it's available in almost every single language which is validated very high sensitivity and specificity.

Speaker 2

So I, I would recommend especially for primary care physicians, health care providers, which are not dealing with neuropathic pain on a daily basis. Have a look at this DN4. And for you find it very easily in the internet. And it's it's very useful.

Speaker 1

Thanks for the pointers. Professor Morlion. So after we have to use either painDETECT or DN4, DN4 is freely available, has been validated. Either has high sensitivity and specificity for screening of diabetic peripheral neuropathy. And after that, remember we still need to examine our patients, right?

Speaker 2

Of course. You, as especially as a doctor, you should not only treat patients based on screening instruments and maybe even apps. Looking for, neuropathic pain. No, it's important, to examine the patients. And you. It starts with a neurological examination. But you shouldn't be a neurologist to be able to diagnose this. So I always tell, my students and fellows that even, with very simple means, like a cotton swab, like a toothpick.

Speaker 2

It's already a good start to diagnose neuropathic pain, because then you will be able to look for sensory, sensory changes in a certain anatomic area. If this if you see that these, these changes, are also in the area where the patient reports pain and it's linked to a dermatome, or the nerve distribution of a peripheral nerve, for instance, then you, have much more, confirmation that this type of pain is, is neuropathic.

Speaker 2

And with the cotton swab, you can look for allodynia and light touch, which, elicits pain. We call this, allodynia. And so, I know there are very fancy devices to do a QST, Quantitative sensory testing. And for studies, it's very useful. But I must admit, even in the pain center, we do not use these, expensive devices.

Speaker 2

We go for the bedside testing and also testing for cold and warmth can be done with very simple means.

Speaker 1

So meaning questionnaires plus clinical bedside examination would suffice. From at the routine clinical practice. So diagnosed.

Speaker 2

I would say that's good for over 80% of getting a very firm diagnosis. Nevertheless, some of, additional, technical investigations like, clinical neurophysiology, nerve conduction study, or EMG can be helpful even to further make a confirmation of your diagnosis. For instance, in some patients with radiculopathy, Yes. If at a certain stage maybe you would do an MRI to look, is there a spinal problem?

Speaker 2

Yes or no?

Speaker 1

Okay. And since we are talking about, how we screen, how we diagnose, etc.. So sometimes our GP's will actually ask when we actually started diagnosing and we start to manage people with diabetic peripheral neuropathy. Some of them, they may not respond to the conventional treatment. Is it related to some peripheral nerve pain pathophysiology. Or is this central brain system processing sensitization?

Speaker 2

Both both. It's it's a combination of both. Of course in diabetic polyneuropathy you have these peripheral changes in the small especially the small nerves. But as you know it's not only the sensory system also motor and autonomic system, will will change. And it has to do with the hyperglycemia and mitochondrial changes. So that's looking and deep diving into the cellular mechanisms.

Speaker 2

But ongoing pain if this barrage keeps on going you will find also in these patients the manifestations of central sensitization. And where when you are able to control the peripheral action, maybe still some central nerve activity keeps on going and that's, that can be challenging. And you talked about doctors who prescribe medication. I noticed that still nowadays doctors prescribe the classical painkillers for this type of pain.

Speaker 2

And we know that this doesn't work, paracetamol, NSAIDs, do not work in these type of patients. So you should go for we do not have an official term. I like to use the term anti neuropathic medication, but it's about certain group of certain groups of antidepressants like tricyclic like SNRIs, like duloxetine as an example.

Speaker 2

But especially also the gabapentinoids, because, like pregabalin gabapentin, because we know that there are some in these patients problems also with their, electrolytes channels like calcium channels, like sodium channels.

Speaker 1

And can I can I just because I, I have a simple mind. I mean, I'm just thinking if for a person with diabetic peripheral neuropathy, the pain stimulus actually comes from both central and peripheral. And hence do you, do you use like combinations certain like medication A, they target on the central region more and medication B, they target the peripheral region more?

Speaker 2

With this this medication I named gave the examples of antidepressants and gabapentinoids, they're actually working on both systems. So already and for instance, if you look at gabapentinoids, they will interact with hyperactive calcium channels and they will modulate and becoming less active. But these channels are, are, very generally spread.

Speaker 2

So you will have, effects not only in the peripheral system but also in the central nervous system. And on the other hand, if you look at the very old, tricyclics, we know that on one hand, they, have, serotonin and noradrenaline or no epinephrine, depending which part of the world we were living in.

Speaker 2

Re uptake inhibiting actions. But this, this specific, pharmacodynamic action will enhance your, descending inhibition. It will empower the, body's own analgesic system. That's the way I tried to explain it to my patients. If we look then at, the, tricyclics again, they have also sodium, stabilizing properties. So, they have many, different actions.

Speaker 2

But exactly this, this multitude and actions is a problem with this tricyclics, especially also in diabetic patients. Because to give you one example, if you encounter a patient with painful



diabetic neuropathy, for instance, in the feet and it's, climbing up, then actually even without a diagnosis or clinical manifestations, you can be sure that also the autonomous neuropathy is going on already.

Speaker 2

And if you would start then with these old medications, then you could get into trouble with cardiac arrhythmias, with, cardiac interference. So that's the reason I especially in diabetic patients, I will not take although it's in the guidelines, I will not choose these tricyclics as a first choice. I will I think it's safer to use than in this case, drugs like pregabalin or like an SNRI, like duloxetine and in some patients.

Speaker 2

Yes. We it doesn't do the job enough. And then we head for combinations.

Speaker 1

Thanks for explaining the contraindications of the TCAs because always been written that cardiac arrhythmia tend to avoid. So that's that's a reason why. Thank you very much for some early on for that. Yeah. I mean I just I have lots of follow up questions related to the pain processing and the sensitization. Just, just something that came out from, out of my mind.

Speaker 1

We do you see tachyphylaxis when with a long term use of, of anti neuropathic medication.

Speaker 2

Tachyphylaxis in the classical sense, like we witnessed, for instance, with local anesthetics. And so I trained as an anesthetist. We know this phenomenon of tachyphylaxis very well if you keep on going with sodium channel blockers for instance, in this, spinal, area, like with epidural. So we notice this effect will wear off after, a few even days, and shortly after some weeks.

Speaker 2

But this is not observed, with this anti neuropathic, medication. But to be fair, it doesn't work in every single patient. So often you need to start, this medication, you need to be sure that the patient is compliant. So the patient needs some information that this medication will not work immediately. Not after the first pill.

Speaker 2

Do not forget to explain this to your patients, because otherwise they will call you at night and say, this is, humbug, this, pill, because it doesn't work. It's a you need to build up all these anti neuropathic medications slowly. You need to look for what's tolerated and only after. So, certain course of weeks you can say is my patient now responding well or less well to this, medication.

Speaker 1

Thank you very much, Professor Morlion. So mainly the tips would be to diagnose ,questionnaires plus clinical examination when necessary, refer for, QST or even NCS., etc., treat early. But for diabetic peripheral neuropathy, they involve both central and peripheral pain pathways.

Speaker 2

And of course do not forget to control, the glycemia. And you shouldn't forget to treat also.

Speaker 1

The underlying condition.

Speaker 2

Underlying condition.

Speaker 1

Definitely. Thanks very much, Professor Morlion.

Speaker 2

Thank you, Professor Morlion.

Speaker 1

This deep dive into the mechanism of neuropathic pain has been truly eye opening. What strikes me most is how the pain experienced by our patients living with diabetic peripheral neuropathy is not just all in their head, is the results of very real, measurable changes in how the nervous system processes information. Understanding these mechanisms helps explain why traditional approaches to pain management often fall short for neuropathic pain, and why we need specialized strategies.

Speaker 1

The concept of central sensitization particularly helps us understand why treating neuropathic pain requires a comprehensive approach that goes beyond just targeting the peripheral nerves. For our listeners experiencing neuropathic pain, I hope today's discussion validates your experience and helps you understand that this unique type of pain requires specialized care and understanding from your health care team. In our next episode, we will shift from the science to the human experience as we explore living with fire patients tell their stories of diabetic peripheral neuropathy.

Speaker 1

We will hear directly from individuals living with diabetic peripheral neuropathy about how this condition affects their daily lives, their relationships, and their mental health. These personal stories remind us that behind every scientific mechanism we've discussed today is a real person seeking relief and hoping for a better quality of life. Thank you for joining us as we continue our journey inside the Silent Storm.

Speaker 1

Thank you for joining us on this journey. And remember in the fight against diabetic peripheral neuropathy. Knowledge truly is power. Until next time, take care of yourself and each other.