

Generalized Polyneuropathies

Generalized polyneuropathies can be present due to:

- Diabetes mellitus
- Demyelinating conditions (Guillain-Barre Syndrome; chronic inflammatory demyelinating polyneuropathy;
- Charcot Marie Tooth Disease (Type I or II)
- Alcoholism
- Autoimmune disease (rheumatoid arthritis, lupus)
- HIV (caused by the virus itself, by certain drugs used in the treatment of HIV/AIDS or its complications, or as a result of opportunistic infections) (16)
- Vitamin B deficiency
- Toxin exposure (which may include some chemotherapy drugs or anti-retroviral agents; illicit drug use, such as glue-sniffing; or exposure to heavy metals found in industrial settings such as arsenic, lead, mercury, and thallium) (17)

Symptoms of Painful Peripheral Neuropathy

Symptoms and prognosis vary. In painful peripheral neuropathy, the pain is generally constant or recurring. The painful sensations may feel like a stabbing sensation, pins and needles, electric shocks, numbness, or burning or tingling. Symptoms in diabetic polyneuropathy and other generalized neuropathies typically start in the hands or feet and climb towards the trunk. Often the pain is most troublesome at night and can disturb sleep.

The sensations may be more severe or prolonged than would be expected from a particular stimulus. For example, someone who has facial pain from trigeminal neuralgia (tic doloureux) may find it excruciating to have something brush across a cheek. Even a light breeze or wind may trigger the pain.

The nature of the pain may feel different than pain caused by a normal injury. Neuropathy may affect not only nerves that transmit pain messages, but also non-pain sensory nerves that transmit other tactile sensations, such as vibration or temperature.

Painful peripheral neuropathy may also occur along with damage to motor nerves, or to autonomic nerves that govern basic physiological states, such as blood pressure – both of which cause non-sensory symptoms, such as muscle weakness or lightheadedness.

Diagnosis of Painful Peripheral Neuropathy

Diagnosis of painful peripheral neuropathy may require several steps. A clinical examination will involve taking a complete patient history and checking tendon reflexes, muscle strength, motor function and the sense of touch. Additionally, urine and blood specimens may be requested to check for metabolic or autoimmune disorders. Other tests might be needed.

Follow-up tests in the diagnosis of painful peripheral neuropathy may include:

- Nerve conduction velocity testing to see how fast electrical signals move; and
- Electromyography, which measures the electrical impulses of muscles at rest and during contraction
- For facial pain syndromes, brain scans using computed tomography (CT) and/or magnetic resonance imaging (MRI)
- A spinal tap (lumbar puncture) to test for breakdown of myelin
- A biopsy of the nerves may even be ordered to inspect the extent of nerve damage

Treatments for Peripheral Neuropathy

Once neuropathy has developed, few types can be fully cured, but early treatment can improve outcomes. Some nerve fibers can slowly regenerate if the nerve cell itself is still alive. Eliminating the underlying cause can prevent future nerve damage. Good nutrition and reasonable exercise can speed healing. Quitting smoking will halt constriction of blood vessels, so that they can deliver more nutrients to help repair injured peripheral nerves.

Mild pain may be relieved by over-the-counter analgesic (pain relief) medication. For patients who have more severe neuropathic pain, anticonvulsants or antidepressants are commonly prescribed; their action on the central nervous system can calm overactive nerves. Topical patches that act through the skin – for instance, delivering the anesthetic lidocaine or chili-pepper extract capsaicin – may also provide some relief. Another option is administration of a local anesthetic and steroid (cortisone) blocks.

When pain does not respond to those methods, alternatives can include cannabinoids or opiate analgesics. If these measures are ineffective, in a small, select group of patients, opioids may be gradually introduced after carefully considering concerns and side effects. (18) Meanwhile, to relieve the most severe cases of neuropathic pain, nerves may be surgically destroyed, although the results might be only temporary and the procedure can lead to complications.

For some patients, a treatment regimen will also include physical or occupational therapy to rebuild strength and coordination.

Neuromodulation May Be an Option to Manage Painful Peripheral Neuropathy

In cases in which drugs are ineffective or side effects intolerable, an option for some patients may be spinal cord stimulation or peripheral nerve stimulation.

By 2017, about 34,000 patients a year were receiving spinal cord stimulation (SCS) implants. The therapy was first FDA-approved to manage chronic pain in 1989. Spinal cord stimulation starts with a trial phase. In a sterile setting, a slim electrical lead with a series of electrical contacts is guided beneath the skin into the epidural space above the spinal cord. The patient goes home with an external battery pack that provides neurostimulation for several days. If this trial treatment reduces pain from 50-70%, the patient may choose to receive a permanent system. To power a permanent SCS system, in a follow-up procedure, a pacemaker-like pulse generator is implanted beneath the skin. (19-20)

Patients must carefully follow instructions to prepare for the procedure and abide by a few restrictions once the implant is in place, such as avoiding bending or twisting motions. Like all surgical treatments, receiving an implant carries risks of infection or bleeding. Hardware-related complications may also arise. Most complications are easily reversed, but SCS implants do pose a small risk of more serious problems, such as neurologic injury.

Sometimes spinal cord stimulation effectiveness may lessen over time. In patients who eventually develop a tolerance to neurostimulation, a potential future option is delivery of a pain-relief agent to targeted sites in the body, using an intrathecal drug delivery system. For instance, ziconotide, a non-opiate drug now often employed to treat complex regional pain syndrome (CRPS), has been suggested by specialists as a possibly viable alternative pain-relief agent. (21)

For appropriately screened patients, meanwhile, peripheral nerve stimulators can have an 80% to 90% near-term success rate. (22)

Conclusion

Irrespective of the type of peripheral neuropathy they have, many patients can find some relief if the underlying cause is addressed and a holistic treatment approach is maintained, but they will require careful interdisciplinary monitoring and follow-up.

For further information see: WIKISTIM at <http://www.wikistim.org> – This free-to-use collaborative, searchable wiki of published primary neuromodulation therapy research was created in 2013 as a resource for the global neuromodulation community to extend the utility of published clinical research. The goals of WIKISTIM are to improve patient care and the quality of research reports, foster education and communication, reveal research needs, and support the practice of evidence-based medicine.

Please note: *This information should not be used as a substitute for medical treatment and advice. Always consult a medical professional about any health-related questions or concerns.*

References

1. Merck Manual. (2014) Complex Regional Pain Syndrome (CRPS). Available at: <http://www.merckmanuals.com/professional/neurologic-disorders/pain/complex-regional-pain-syndrome-crps> (accessed July 19, 2016).
2. North RB et al. Spinal cord stimulation versus reoperation in patients with failed back surgery syndrome: an international multicenter randomized controlled trial (EVIDENCE Study). *Neuromodulation* 2011;14:330–6.
3. Breivik H, Collett B, Ventafridda V, Cohen R, Gallacher D. Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. *Eur J Pain*. 2006 May;10(4):287-333. Epub 2005 Aug 10. PubMed PMID: 16095934.
4. Zhuo M, Wu G, Wu LJ. Neuronal and microglial mechanisms of neuropathic pain. *Mol Brain*. 2011 Jul 30;4:31. Review. <http://www.molecularbrain.com/content/4/1/31> (accessed July 17, 2016).
5. Zorowitz RD, Smout RJ, Gassaway JA, Horn SD. Usage of pain medications during stroke rehabilitation: the Post-Stroke Rehabilitation Outcomes Project (PSROP). *Top Stroke Rehabil*. 2005 Fall;12(4):37-49.
6. NICE. (2008) Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin. Available at: www.nice.org.uk/TA159 (accessed July 17, 2016).
7. Krames E et al. Using the SAFE principles when evaluating electrical stimulation therapies for the pain of failed back surgery syndrome. *Neuromodulation* 2011;14:299–311.
8. Ekre O et al. Long-term effects of spinal cord stimulation and coronary artery bypass grafting on quality of life and survival in the ESBY study. *Eur Heart J* 2002;23:1938–1945.
9. Deer TR, Mekhail N, Provenzano D, Pope J,

Krames E, Leong M, Levy RM, Abejon D, Buchser E, Burton A, Buvanendran A, Candido K, Caraway D, Cousins M, DeJongste M, Diwan S, Eldabe S, Gatzinsky K, Foreman RD, Hayek S, Kim P, Kinfe T, Kloth D, Kumar K, Rizvi S, Lad SP, Liem L, Linderth B, Mackey S, McDowell G, McRoberts P, Poree L, Prager J, Raso L, Rauck R, Russo M, Simpson B, Slavin K, Staats P, Stanton-Hicks M, Verrills P, Wellington J, Williams K, North R; Neuromodulation Appropriateness Consensus Committee.

The appropriate use of neurostimulation of the spinal cord and peripheral nervous system for the treatment of chronic pain and ischemic diseases: the Neuromodulation Appropriateness Consensus Committee. *Neuromodulation*. 2014 Aug;17(6):515-50; discussion 550. doi: 10.1111/ner.12208. PubMed PMID: 25112889.

10. Medscape. (Jan. 7, 2015) Spinal Cord Stimulation. Available at: <http://emedicine.medscape.com/article/1980819-overview> (accessed July 18, 2016).

11. Liem L, Russo M, Huygen FJ, Van Buyten JP, Smet I, Verrills P, Cousins M, Brooker C, Levy R, Deer T, Kramer J. One-year outcomes of spinal cord stimulation of the dorsal root ganglion in the treatment of chronic neuropathic pain. *Neuromodulation*. 2015 Jan;18(1):41-8; discussion 48-9. doi: 10.1111/ner.12228.

Epub 2014 Aug 21. PubMed PMID: 25145467.

12. Nguyen, JP, Nizard, J, Keravel, Y, Lefaucheur, JP. Invasive brain stimulation for the treatment of neuropathic pain. *Nat Rev Neurol*. 7, 699–709 (2011); published online 20 September 2011.

13. Jin DM, Xu Y, Geng DF, Yan TB (July 2010). Effect of transcutaneous electrical nerve stimulation on symptomatic diabetic peripheral neuropathy: a meta-analysis of randomized controlled trials. *Diabetes Res. Clin. Pract.* 89 (1): 10–5.

14. Azhary H, Farooq MU, Bhanushali M, Majid A, Kassab MY. Peripheral neuropathy: differential diagnosis and management. *Am Fam Physician* (2010) Apr 1;81(7):887-92

15. The Foundation for Peripheral Neuropathy.

<https://www.foundationforpn.org/what-is-peripheral-neuropathy/facts-risk-factors/>. (accessed July 17, 2016)

16. Baron, R. Mechanisms of Disease: neuropathic pain—a clinical perspective. *Nature Clinical Practice Neurology* (2006) 2, 95-106

17. University of Chicago, Center for Peripheral Neuropathy.

http://peripheralneuropathycenter.uchicago.edu/learnaboutpn/typesofpn/inflammatory/hiv_aids.shtml (accessed July 17, 2016).

18. Rutchik, JS. (2011, Sept 26). Toxic Neuropathy. Medscape Reference. Retrieved 10/1/12 from <http://emedicine.medscape.com/article/1175276-overview>.

19. Kumar A, Felderhof C, Eljamel MS. Spinal cord stimulation for the treatment of refractory unilateral limb pain syndromes. *Stereotact Funct Neurosurg* 81(1-4):70-74, 2003.

20. Vallejo R, Kramer J, Benyamin R. Neuromodulation of the cervical spinal cord in the treatment of chronic intractable neck and upper extremity pain: A case series and review of the literature. *Pain Physician* 10(2):305-311, 2007.

21. Reverberi C, Dario A, Barolat G. Spinal cord stimulation (SCS) in conjunction with peripheral nerve field stimulation (PNFS) for the treatment of complex pain in failed back surgery syndrome (FBSS). *Neuromodulation*. 2013 Jan-Feb;16(1):78-82; discussion 83. doi: 10.1111/j.1525-1403.2012.00497.x. Epub 2012 Sep 17. PubMed PMID: 22985076.

22. Novak CB, Mackinnon SE. Outcome following implantation of a peripheral nerve stimulator in patients with chronic nerve pain. *Plast Reconstr Surg*. 2000 May;105(6):1967-72.