

# Neuropathy, Neuropathic Pain, and Painful Peripheral Neuropathy

— *Many kinds, causes, and treatments*

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## Introduction

This article is intended for patients, caregivers, and the general public, as well as doctors and medical specialists. It has three sections. The first defines neuropathy. The second gives a broad overview of neuropathic pain. The final section concerns painful peripheral neuropathy, a common neurological complaint, its causes, diagnosis and treatment.

## I. What Is Neuropathy?

Neuropathy is a condition that results from damage to, or dysfunction of, the nervous system. Most often, the damage exists in the peripheral nervous system, which lies beyond the spine and brain, although brain injury, such as stroke, can also result in neuropathic symptoms.

The symptoms of neuropathy depend on the underlying nerves whose function has been affected. Neuropathy that damages sensory nerves can cause numbness, weakness and stabbing or burning pain – symptoms that may worsen if not treated early. If there has also been damage to the type of nerves that convey the sense of touch, vibration, and temperature, patients may experience tingling, numbness, or the sense of wearing an invisible glove or sock over their hands or feet.

If there is damage to motor nerves that control stability and movement, patients may have a lack of coordination, weakness, or cramping.

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Neuropathy is a leading cause of chronic pain, including painful peripheral neuropathy

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Finally, if the autonomic nerves that regulate internal organ function have also been damaged, patients may experience a reduction in saliva, tears, perspiration, or other organ or gland dysfunction.

## The Impact of Neuropathy

Neuropathy is a leading cause of chronic pain, which persists for three months or more. About 8% of people who report chronic pain suffer from some form of neuropathy, which affects about 20,000 people in the U.S. and 15 million in the U.S. and Europe combined, according to the American Chronic Pain Association.

## II. Neuropathic Pain

An estimated 10% of the population has neuropathic pain. Although the condition may be lifelong, neuropathic pain can often be reduced and even controlled, when managed by specialists who combine treatments that might include medications, injections and even nerve stimulation (neuromodulation).

The nerve injury generating this disordered response may be from a specific incident (an accident, stroke, or amputation), or a disease such as diabetes, a viral infection, or neurodegenerative condition. The problem may occur in the central nervous system (spine and brain) or peripheral nervous system (smaller nerves outside the spinal column).

Typical cases of neuropathic pain include nerve pain from spinal disorders, including pain that persists after surgery thought likely to correct it (Persistent Spinal Pain Syndrome Type 2 [PSPS Type 2], formerly known as failed back surgery syndrome [FBSS]); post-amputation pain; chronic pain from other nerve trauma or injury; complex regional pain syndrome; and neuropathies that may occur after a viral infection or from metabolic disorders like diabetes.

Patients who have PSPS Type 2 may have buttock and leg pain as well as associated back pain that has a basis that may go beyond neuropathic pain, involving another pain system called nociceptive. In such cases, the pain is considered of mixed origin and treatment strategies will take this into account. Likewise, complex regional pain syndrome (CRPS) is – as its name suggests – complex, often with components of nociceptive as well as neuropathic pain. (1)

In many ways, the sensation of neuropathic pain is unique. The area of pain may be widespread (diffuse), or limited to a single nerve or several nerves. The pain may be described variously as feeling like a stabbing, burning, electric shock, or a freezing sensation. It may worsen at night. Some people may experience temporary numbness, tingling, and pricking sensations, sensitivity to touch, or muscle weakness. Others may experience more extreme symptoms, such as burning pain, muscle wasting or even paralysis.

As a chronic condition, neuropathic pain impacts function and quality of life. Neuropathic pain underlies an estimated 30-65% of the activity seen at hospital pain clinics. In severe cases of chronic pain, the health-related quality of life is ranked as worse than other pain conditions, heart failure, or even cancer. (2-3)

### Types of Pain with Neuropathic Origin

Pain that falls under the broad category of a pain of neuropathic origin includes neuralgia, such as the facial pain syndrome trigeminal neuralgia. Another pain of neuropathic origin is neuritis. Neuritis is caused by inflammation of a nerve or group of nerves and may be accompanied by fever and swelling.

Some of the processes active in neuropathic pain involve, to some degree, changes in parts of the nerve pathway that process pain sensations. Release of the body's own pain-reducing chemicals may be dampened, and some nerve cells along the pathway may become excitable and overly active in signaling pain messages. Therefore, regardless of where the original nerve injury occurred, in many instances, the central nervous system can play a role in the continued experience of chronic pain symptoms. (4)

Some of the specific types of disordered pain that may be experienced in neuropathy include:

- Allodynia – pain from what is normally a non-painful touch, such as being stroked by a feather
- Dysesthesia – an unpleasant feeling, which is not actually painful *per se*
- Hyperpathia or hyperalgesia – prolonged or severe pain from a lightly painful incident, such as a pinprick
- Paresthesia – unusual sensations, such as pins and needles or a burning sensation

### Central or Peripheral Pain

While some neuropathies occur because of damage to peripheral (small) nerves and nerve endings, other types of neuropathic pain happen after an injury in the central nervous system (brain and/or spine). These neuropathic pain conditions that arise in the brain or spine are called central pain syndromes. One example of a central pain syndrome is post-stroke shoulder pain, which is estimated to occur in up to one-third of stroke survivors. (5)

### Treatment of Neuropathic Pain

The underlying cause or medical problem should always be treated. This can reduce or stop damage to the nervous system. Once the underlying cause has been treated, subsequent treatments should focus on reducing the remaining symptoms that might be ongoing, which may include neuropathic pain.

To manage pain that cannot be relieved by over-the-counter medications, standard medical treatment includes anticonvulsant or antidepressant medications that help reduce nerve pain. Sometimes, pain creams, patches or even injections may relieve some types of nerve pain.

In cases where medications are ineffective or cause intolerable side effects,

neuromodulation therapy using spinal cord stimulation (SCS) or peripheral nerve stimulation may be considered as an option to reduce pain.

In 2008, the United Kingdom's Department of Health policymaking advisory group, the National Institute of Clinical Excellence (NICE), issued guidance that SCS should be used for medically resistant (refractory) neuropathic pain, finding it both clinically effective and cost-effective, with lower lifetime healthcare cost and better long-term outcomes. (6-7) Typical cases in which neurostimulation may be used include chronic pain from failed back surgery syndrome, post-amputation pain, other traumatic neuropathies, complex regional pain syndrome (CRPS) and metabolic and viral neuropathies. (8-10)

In 2015, a wider set of SCS options emerged. Newer stimulation patterns and frequencies are now available. Another newer method targets a structure alongside the spinal cord, thought to act as a relay station for sending sensory information to the brain, the dorsal root ganglion (DRG). The DRG is a bundle of nerve cell bodies located at the edge of each spine segment. A clinical investigation published in 2015 showed that stimulating the DRG helped provide relief for some painful areas, such as the extremities, that had been hard to reach with conventional SCS. (11)

For some patients with medication-resistant central pain, deafferentation syndromes, or trigeminal neuralgia, two types of implanted brain stimulation systems have been reported to provide some relief: motor cortex stimulation or deep brain stimulation. (Deep brain stimulation is commonly used in movement disorders such as Parkinson's disease.) (12)

A non-invasive type of peripheral nerve stimulation that is delivered through the skin, transcutaneous electrical nerve stimulation (TENS), has also been reported to improve symptoms of diabetic peripheral neuropathy. (13)

### III. Painful Peripheral Neuropathy

Painful peripheral neuropathy is a common neurological disorder characterized by numbness, weakness, tingling and pain, often starting in the hands or feet.

#### Prevalence and Incidence of Peripheral Neuropathy

Peripheral neuropathy is a common problem. More than two out of every 100 persons are estimated to have peripheral neuropathy; the incidence rises to eight in every 100 people for people aged 55 or older. (14)

#### Types and Causes of Peripheral Neuropathy

There are more than 100 different types of peripheral neuropathy, according to the U.S. National Institute of Neurological Disorders and Stroke (NINDS). As said earlier, the symptoms will depend on the function of the underlying nerve or nerves affected.

Peripheral neuropathy can either be inherited, or develop due to injury or illness. For instance, a disease may cause nerve endings to become

sensitized and signal pain without an obvious cause. Or the nerve cell outer sheath, the myelin coating, could degenerate and disrupt normal transmission of nerve signals.

Some 30% of peripheral neuropathies occur as a complication of diabetes, and an estimated 26% of patients with diabetes have some degree of diabetic neuropathy, due to prolonged effects of high blood sugar levels. In another 30% of cases, the precise cause of a painful peripheral neuropathy is unclear (or "idiopathic"). Other neuropathy causes include physical injury to a nerve, tumors, exposure to toxins, alcoholism, kidney failure, autoimmune responses, nutritional deficiencies, shingles, HIV infection, and vascular or metabolic disorders. (15)

#### Peripheral Neuropathy Terminology

If only one nerve is affected, the condition is called mononeuropathy. If several nerves are involved, the disorder is called mononeuritis multiplex, and if the condition affects both sides of the body, it is called polyneuropathy. The condition may be general, or located in a particular area, which is called focal peripheral neuropathy.

#### Focal or Multifocal Peripheral Neuropathies

Focal or multifocal peripheral neuropathies include:

- Carpal tunnel syndrome (caused by pressure on the nerve due to inflammation from repetitive stress), or other so-called "entrapment" syndromes
- Radiculopathies, including sciatica (a shooting pain in the arms or legs due to irritation or compression of the nerve root in the spine)
- Phantom limb pain and stump pain
- Post-traumatic neuralgia
- Postherpetic neuralgia (15)

### 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 doreaux) 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.

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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](http://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](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.