

# Peripheral Neuropathies

Dr. Rafa G. Carretero  
Internal Medicine Department  
Hospital Universitario de Móstoles

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## 1 Introduction

Peripheral neuropathies encompass disorders of peripheral nerve cells and fibers, which manifest secondary to a wide range of pathologies. These nerves include cranial nerves, spinal nerve roots, nerve trunks, along with nerves of the autonomic nervous system. There are several methods used to classify peripheral neuropathies, including categorizing them as mono-neuropathies, multifocal neuropathies, and polyneuropathies. Further subclassifications can be made by separating peripheral neuropathies as axonal, demyelinating, or mixed, which is essential for treatment and management purposes. The most frequently encountered symptoms of peripheral neuropathy include numbness, paresthesias, burning in the limbs, pain, weakness, and loss of deep tendon reflexes.

Peripheral neuropathies usually develop over months to years, while some may develop more rapidly and be progressive in nature. Peripheral neuropathies have a broad range of severity and clinical manifestations, as they can affect motor, sensory, and autonomic fibers. Neuropathies can be both painful and debilitating for patients.

## 2 Etiology

Peripheral neuropathies stem from a variety of origins, including metabolic, systemic, and toxic causes. Several causes of peripheral neuropathies exist, but diabetes mellitus (DM) is the most common etiology. Other underlying etiologies worth considering include:

- Diabetes mellitus
- Chronic alcoholism
- Nutritional deficiencies (Vitamins B1, B6, B12)
- Inflammatory conditions (vasculitis)
- Hypothyroidism
- Autoimmune disease (Sjogren syndrome, lupus, rheumatoid arthritis)
- Infections
- Guillain-Barre syndrome
- Toxins (heavy metals, chemicals)
- Chemotherapy agents
- Medications (antibiotics, cardiovascular medications)
- Tumors (secondary to compression or associated paraneoplastic syndromes)
- Inherited conditions (e.g., Charcot-Marie-Tooth disease, familial amyloidosis)
- Trauma/injury

### 3 Epidemiology

The most prevalent subtype is diabetic peripheral neuropathy, which can lead to significant complications: foot ulcers, poor wound healing potential, limb compromise, local to systemic infection, septicemia, and even death. The most common mononeuropathy is carpal tunnel syndrome.

### 4 Pathophysiology

The exact pathophysiology of peripheral neuropathy is contingent on the underlying disease. Although a wide assortment of distinct diseases can ultimately lead to peripheral neuropathies, the mechanisms in which peripheral nerves suffer injury exhibit similar patterns. These reactions include segmental demyelination, along with Wallerian and axonal degeneration.

**Segmental Demyelination:** This process refers to the process of degeneration of the myelin sheath, with sparing of the nerve axon. This type of reaction can present in mononeuropathies, sensorimotor, or, principally, motor neuropathies. These are often inflammatory and sometimes immune-mediated.

**Wallerian Degeneration:** This occurs after a nerve axon degenerates due to a lesion or physical compression; the portion distal to the axon passively wastes away, likely due to a lack of nutrients from the cell body. This reaction results in focal mononeuropathy that is secondary to trauma or infarction of the nerve.

**Axonal Degeneration:** This type of degeneration usually manifests as symmetrical polyneuropathy (around 80%) and tends to cause weakness, most notably weakness in dorsiflexion of the ankles and foot, with accompanied trophic changes to muscle. The axon degenerates in a pattern that starts distal and progresses proximally; this is thought to be because the most distal portion of the axon is particularly vulnerable due to its distance from the cell body, which provides metabolic support. Examples of diseases causing axonal degeneration include diabetes, HIV, and Guillain-Barre syndrome.

## 5 History and Physical

The clinical presentation of peripheral neuropathy widely varies depending on the underlying disease process. Patients may complain of symptoms initially starting in their digits and progressing to their proximal limbs. Symptoms range and include changes in sensation, weakness, atrophy, pain, numbness, and even autonomic disturbances. Clinically, these symptoms may resemble that of myelopathies, radiculopathies, autoimmune diseases, and diseases of muscles. Advanced disease may progress to reduced or absent deep tendon reflexes, stocking-glove pattern sensory loss, muscle wasting, and weakness. Aside from a meticulous review of past medical history, providers should inquire about toxic exposures, present and past medications, trauma, dietary and nutritional deficiencies, and alcohol use.

Complications of peripheral neuropathies include pain, altered sensation, muscle atrophy, and weakness. Diabetic peripheral neuropathy is infamous for complications, including foot ulcers which can lead to gangrenous digits and limbs, sometimes progressing to amputation.

Advanced (more specific) symptoms:

- Loss of sensation
  - Hypoesthesia
  - Difficulty discriminating textures
  - Cottony feeling in hands
  - Unsteady gait because of sensory ataxia
  - Painless burns and traumas
- Positive symptoms:
  - Painful symptoms
  - Burning sensation
  - Hyperalgesia
- Motor symptoms:
  - Flaccid distal weakness
  - Hyporreflexia
  - Muscle atrophy if axonal injury

## 6 Evaluation

Evaluating patients with neuropathy involves a detailed history and physical, including a review of current and past medications. Although there are no standard laboratory or imaging studies to test for peripheral neuropathies, the following studies may aid in the

diagnosis and help narrow down the underlying cause of the neuropathy, such as inflammatory, infectious, metabolic, and so on:

- Determination of vitamin B12 or folate deficiency
- Electrolyte imbalances
- Testing for diabetes
- Testing for vitamin and mineral deficiencies such as copper, B1, B6, folate, B12
- Heavy metal toxicities such as mercury, lead, and arsenic
- Infectious workup HIV, syphilis, and so on
- Thyroid function testing.[13]
- Testing for specific autoimmune diseases
- Nerve conduction study and electromyography (EMG)
- MRI or CT scans in cases where compression of the nerve is of concern
- Nerve biopsy
- Genetic testing (if suspicion of inherited neuropathies)

## 7 Treatment and Management

Treatment of peripheral neuropathies should focus on the treatment of the underlying disease process. For example, glucose control in diabetic neuropathy and alcohol cessation in alcoholic neuropathy. Nutritional deficiencies can have therapy with supplementation of the depleted vitamins or minerals. Unfortunately, not all peripheral neuropathies are reversible. Physical therapy and occupational therapy can be initiated to aid in the improvement of a patient's overall strength and function. Chronic inflammatory demyelinating neuropathy is treated using corticosteroids initially but can also be treated using intravenous immunoglobulin, plasma exchange, and some immunosuppressant drugs.

Neuropathic pain, particularly in those suffering from small-fiber neuropathies, does not typically respond to simple analgesics. Instead, effective treatment for pain associated with peripheral neuropathies can be with membrane stabilizers, certain anti-epileptics, and tricyclic antidepressants.

In those diseases where peripheral nerves suffer damage through Wallerian or axonal degeneration, the prognosis is poorer, as the recovery of the nerve is more challenging. For clinical improvement to take place, the axon must regenerate itself and reinnervate the affected muscle or organ. The prognosis of diseases which occur secondary to segmental demyelination is more favorable because remyelination is achieved more quickly, allowing the return of function of the axon.

Patients require education on the signs and symptoms of peripheral neuropathy. Patients should be made aware that they have an increased risk of injury due to loss of sensation; they should be conscious of any new cuts or damage to their skin as wound healing can be delayed, and the risk for infection increases. Recommend always wearing socks with closed-toed shoes to decrease the risk of infection. Patients should take caution when exposing themselves to hot or cold environments to avoid burns and frostbite. Patients with alcohol-induced neuropathy should get information on cessation.

## 8 Special types of neuropathies

**Compression neuropathies** The typical example is the carpal tunnel syndrome, affecting the median nerve. It is a mono-neuropathy.

**Hereditary motor and sensory neuropathy (HMSN)** The typical example is the Charcot-Marie-Tooth disease. Usually they are polyneuropathy.

**Metabolic neuropathies** The typical example is diabetes neuropathy. They can present with sensory, motor, and autonomic neuropathy. In the case of diabetes, implicated causes of peripheral nerve damage include oxidative stress damage, accumulation of sorbitol, and advanced glycosylation end products. The characteristic polyneuropathy and distal sensory peripheral neuropathy are present in about 80% of diabetic neuropathy patients. This is often described as a “stocking-glove distribution”, which can take several years to develop. However, any kind of neuropathy can appear during the development of diabetes: mononeuropathy, multiplex mononeuropathy (multiple mononeuritis), polyneuropathy, radiculopathy, and even cranial nerves.

**Toxic and nutritional deficit-related neuropathies** They are polyneuropathies presenting with distal sensory deficits, paraesthesia, burning pain, distal muscle weakness, and impaired motion.