Peripheral Nerve Disorders

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■ PERSPECTIVE

Background

The nervous system is traditionally divided into central nervous system (CNS) and peripheral nervous system (PNS) components. The PNS can be further subdivided into 12 cranial and 31 spinal nerves. Disorders of the cranial nerves are discussed in Chapter 103. Because diseases of the neuromuscular junction and the myopathies are located distal to the neuron itself, they are also considered separately in Chapter 104. Radiculopathies, which are disorders of the roots of the PNS, are so commonly associated with musculoskeletal neck and back pain that they are mentioned only briefly here and are discussed in detail in Chapter 51.

The simplest approach to diseases of the PNS parallels the CNS model of separating focal from nonfocal disease. In the PNS, the first broad category is the focal group, which can be divided into those with evidence of single versus multiple lesions of peripheral nerves, known respectively as *simple mononeuropathies* and *multiple mononeuropathies* (or *mononeuropathy multiplex*). The second broad category, which constitutes the nonfocal group of peripheral neuropathies, contains the polyneuropathies. These tend to produce bilaterally symmetrical symptoms and signs, reflecting the widespread nature of the underlying pathologic process.

The evaluation of PNS disease involves a goal-directed history and physical examination targeted at answering the following three questions, each of which corresponds to a stratum of the algorithm presented in Fig. 105-1:

1. Are the sensorimotor signs and symptoms symmetrical or asymmetrical?
2. Are the sensorimotor signs and symptoms distal or both proximal and distal?
3. Is the modality involved exclusively motor, sensory, or mixed sensorimotor?

By systematically combining responses to these questions, one can identify seven discrete categories of peripheral neuropathy, each of which contains a finite set of possible diagnoses. Because pure motor or sensory findings tend to occur mainly in an asymmetrical, distal distribution, this is the only category in Figure 105-1 subdivided into pure motor and pure sensory abnormalities.

Epidemiology

Although Guillain-Barré syndrome (GBS) is the most commonly encountered emergent peripheral neuropathy in developed countries, its annual incidence is just over 1 to 2 cases per 100,000 population.[1] In contrast to the low incidence of acute peripheral neuropathies, several of which are associated with short-term mortality, the vast majority of peripheral neuropathies seen in the emergency department (ED) are subacute or chronic and are associated not with mortality but with long-term morbidity.

Current estimates suggest that about 1.5% of the U.S. population suffers from peripheral neuropathy.[2] Over 7% of the population has diabetes mellitus, with a prevalence rate of 20% in individuals older than 60 years. Roughly 50% of these individuals have peripheral neuropathy.[3]

■ PRINCIPLES OF DISEASE

Anatomy

The spinal component of the PNS is shown schematically in Figure 105-2. The anterior and posterior nerve roots exit the spinal cord at each segmental level. Just distal to the dorsal root ganglion they converge to form a mixed (motor and sensory) spinal nerve, of which there are 31 pairs: 8 cervical, 12 thoracic, 5 lumbar, 5 sacral, and 1 coccygeal. The spinal nerves immediately bifurcate into anterior (ventral) and posterior (dorsal) rami. The posterior ramus travels to the back. The anterior ramus innervates the anterolateral portion of the body and supplies all peripheral nerves for the upper and lower extremities through the brachial and lumbosacral plexus, respectively. Interweaving of fibers occurs within a plexus, producing a mixed sensorimotor innervation of peripheral nerves exiting the plexus.

In addition to the motor and sensory modalities of the PNS, the autonomic nervous system has a peripheral component. Anatomically and functionally, the autonomic nervous system is divided into two parts: a sympathetic (thoracolumbar) component and a parasympathetic (craniosacral) component. Autonomic dysfunction may cause systemic abnormalities, such as orthostasis, or local problems, such as atrophic, dry skin.

Pathophysiology

The PNS has only three basic responses to a wide array of pathologic stimuli. As shown in Figure 105-2, these are (1) the myelinopathies, where the primary site of involvement is limited to the myelin sheath surrounding the axon; (2) the axonopathies, where the primary site of involvement is the axon, with or without secondary demyelination; and (3)

Figure 105-1. An approach to peripheral neuropathy in the emergency department. AIDP, acute inflammatory demyelinating polyneuropathy (Guillain-Barré); CIDP, chronic inflammatory demyelinating polyneuropathy; DSPN, distal symmetrical polyneuropathy. *A proximal distribution of sensorimotor findings may dominate the clinical picture in patterns 3, 4, and 5, depending on the location of the lesion(s).
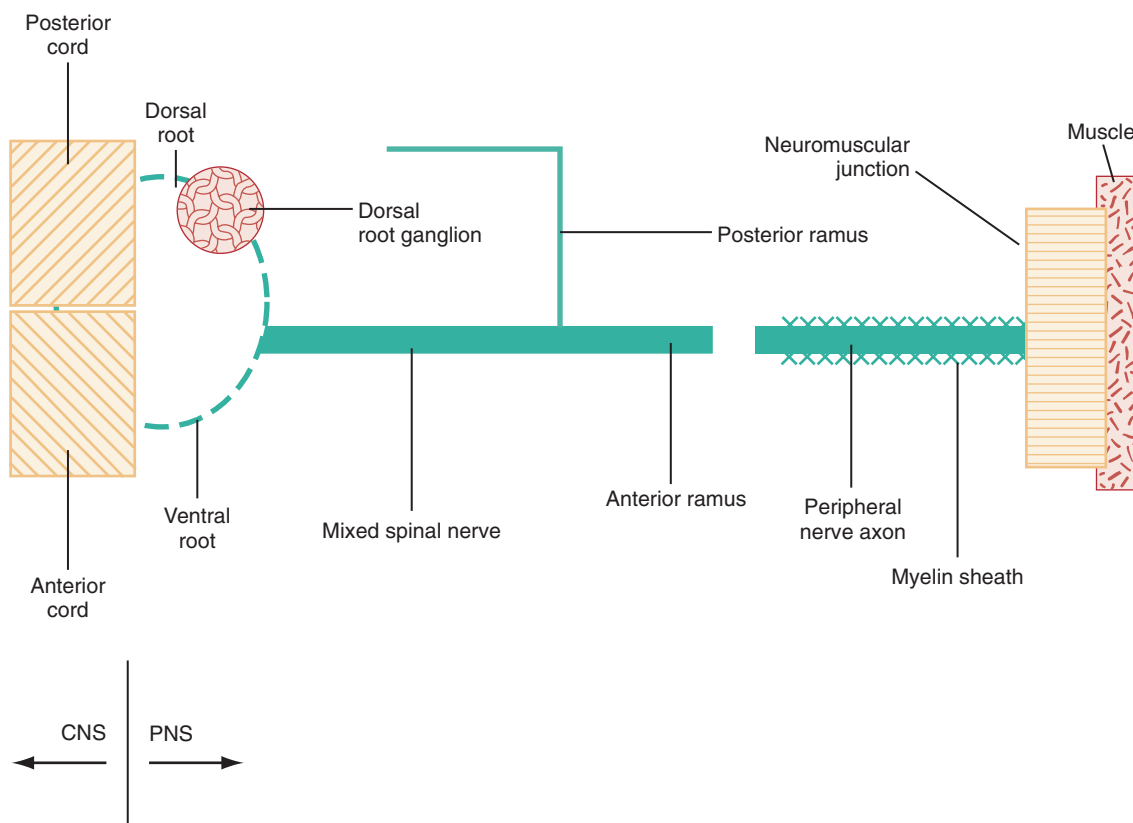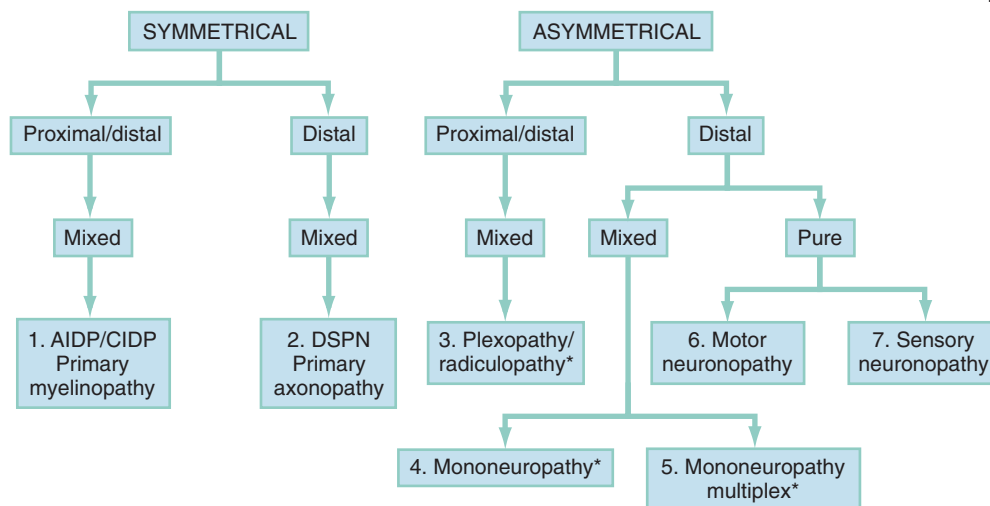

Figure 105-2. Schematic representation of macroscopic and microscopic anatomy of the peripheral nervous system and its interface with the central nervous system. See text for explanation.

the neuronopathies, where the cell body of the neuron itself is the primary site of involvement, ultimately affecting the entire peripheral nerve. Although overlap occurs, each of these prototypes has a distinctive clinical presentation, electrophysiologic profile, and microscopic appearance.

Electrophysiologic testing, that is, nerve conduction studies (NCSs) and needle electromyography (EMG), detects underlying pathologic abnormalities. Because neither test is readily available in the acute care setting, they are discussed only briefly here. Information gathered from NCSs and EMG can be used to obtain objective information on the anatomic distribution of involvement (symmetrical vs. asymmetrical and distal vs. proximal and distal) and the modalities involved (sensory, motor, or mixed). NCSs and EMG can also identify the level of the neuraxis affected by the disease process (i.e., root, plexus, or nerve); if the nerve is affected, electrophysiologic testing can help determine whether the lesion is mononeuropathic (either caused by an isolated mononeuropathy or mononeuropathy multiplex) or polyneuropathic. Finally, EMG and NCSs can distinguish axonal from myelinopathic disease, further narrowing the differential diagnosis. Prognosis is determined by the nature of pathologic involvement of the PNS. Primary demyelination spares the axon and thus carries the best prognosis. The prognosis is worse in axonopathies because reestablishing nerve function is dependent on the much slower process of axonal regeneration. Neuronopathies, which begin

BOX 105-1 CAUSES OF ACUTE, EMERGENT WEAKNESS AND POSSIBLE RESPIRATORY COMPROMISE

Autoimmune
  Demyelinating
    Guillain-Barré syndrome
    Chronic inflammatory demyelinating polyneuropathy (CIDP)
  Myasthenia gravis
Toxic
  Botulism
  Buckthorn
  Seafood
    Paralytic shellfish toxin
    Tetrodotoxin (puffer fish, newts)
  Tick paralysis
  Metals
    Arsenic
    Thallium
Metabolic
  Dyskalemic syndromes
    Acquired (especially with thyrotoxicosis)
    Familial
  Hypophosphatemia
  Hypermagnesemia
  Porphyria
Infectious
  Poliomyelitis
  Diphtheria

Table 105-1 Patterns and Prototypes of Peripheral Neuropathies

TYPE	PATTERN DISTRIBUTION	PROTOTYPICAL DISEASE MODALITIES
1	Proximal and distal, symmetrical, sensorimotor polyneuropathy	GBS
	Proximal and distal	Symmetrical
	Motor > sensory	
2	Distal, symmetrical, sensorimotor polyneuropathy	Diabetic DSPN
	Distal	Symmetrical
	Sensory > motor	
3	Proximal and distal, asymmetrical, sensorimotor neuropathy	Brachialplexopathy
	Proximal and distal	Asymmetrical
	Sensory and motor	
4	Distal, asymmetrical, sensorimotor mononeuropathy	CTS (median mononeuropathy)
	Distal	Asymmetrical
	Sensory and motor	
5	Distal, asymmetrical, sensorimotor mononeuropathy multiplex	Vasculitic mononeuropathy multiplex
	Distal	Asymmetrical
	Sensory and motor	
6	Distal, asymmetrical, pure motor neuronopathy	ALS
	Distal	Asymmetrical
	Motor	
7	Distal, asymmetrical, pure sensory neuronopathy	Pyridoxine toxicity
	Distal	Asymmetrical
	Sensory	

ALS, amyotrophic lateral sclerosis; CTS, carpal tunnel syndrome; DSPN, distal symmetrical polyneuropathy; GBS, Guillain-Barré syndrome.

with primary destruction of the nerve cell body, produce pure motor or pure sensory syndromes. Eventually the entire nerve is affected, resulting in the worst prognosis of the three.

■ CLINICAL FEATURES

The differential diagnosis for any patient presenting with sensory, motor, or sensorimotor complaints, particularly if localized to the extremities, should include a peripheral neuropathy. Within this group, patients with focal weakness are most concerning because they are at greatest risk for respiratory compromise. Box 105-1 lists the causes of acute, emergent weakness that may affect respiration. Although several of the disorders listed are myopathies (see Chapter 106) rather than peripheral neuropathies, they are lumped together because it is important to identify patients at risk for respiratory failure early in the course of evaluation.

As soon as the emergent causes of weakness have been excluded—which is possible in the majority of patients—the individuals with focal weakness should be assessed next to exclude CNS disease (e.g., stroke) (see Chapter 99). One can then proceed through the systematic approach to peripheral neuropathy outlined in Figure 105-1. Another way to look at the algorithm displayed in Figure 105-1 is shown in Table 105-1, with the distinguishing features of each of the seven peripheral neuropathic patterns described by distribution and modality and represented by a disease prototype.

Type 1: Demyelinating Polyneuropathies

The pattern of symmetrical weakness, usually worse distally, accompanied by variable sensory findings is characteristic of acute GBS. This pattern is discussed first because it is the most common cause of weakness associated with acute respiratory failure seen in emergency practice.

Guillain-Barré Syndrome

GBS is a heterogeneous and unpredictable disorder, with marked variation in latency between antecedent infection and symptom onset. The clinical signs, cadence of disease progression, degree of respiratory compromise, laboratory findings, and time required for convalescence are also highly variable. The most common form of GBS is an acute inflammatory demyelinating polyneuropathy (AIDP), comprising 90% of the cases seen in the United States.[1] Less common variants include acute motor axonal neuropathy (AMAN), acute motor and sensory axonal neuropathy (AMSAN), and the Miller Fisher syndrome. AMAN accounts for most of the remaining cases seen in the United States afflicting those of Asian decent. Miller Fisher syndrome is a rare form of GBS characterized by the triad of ophthalmoplegia, ataxia, and areflexia (Box 105-2).[1,4]

The majority of patients seek treatment days to weeks after resolution of an upper respiratory or gastrointestinal illness, presenting with progressive, symmetrical distal (and usually to a lesser extent proximal) weakness. Signs and symptoms are usually worse in the lower extremities and are associated with diminution or loss of deep tendon reflexes (DTRs), variable sensory findings, and sparing of the anal sphincter. Up to 32% will have all four extremities affected at the time of presentation and 10% will have weakness that begins in the upper

BOX 105-2 DEMYELINATING POLYNEUROPATHIES

Guillain-Barré syndrome
  Acute inflammatory demyelinating
    polyradiculoneuropathy (AIDP)
  Acute motor axonal neuropathy (AMAN)
  Acute motor and sensory axonal neuropathy (AMSAN)
  Miller Fisher syndrome
Chronic inflammatory demyelinating
  polyradiculoplexo-neuropathy
Malignancy
HIV
Hepatitis B
Buckthorn
Diphtheria

extremities.[1] However, the ocular muscles are usually spared. Urinary retention secondary to autonomic dysfunction may occur, contributing to a clinical picture easily mistaken for a spinal cord lesion or conus medullaris syndrome.

The most commonly infectious organisms associated with GBS are *Campylobacter jejuni* (in patients with a history of diarrhea), cytomegalovirus, Epstein-Barr virus, and *Mycoplasma pneumoniae*. AIDP is caused in part by macrophage invasion of the myelin sheath. The macrophage is believed to detect antigens in the myelin that are nearly identical to the antigens present on certain infectious organisms.[1,5,6]

In practice, patients with symmetrical weakness of relatively acute onset, decreased or absent DTRs, and variable degrees of sensory loss should be managed as if they have GBS or one of its variants, which places them at risk for respiratory compromise. Conversely, patients with predominantly sensory signs and symptoms are less likely to develop acute respiratory distress and have a more favorable prognosis.[7]

About half of patients with GBS have autonomic dysfunction, experience a peak of disease severity within a week of onset, have some form of cranial nerve involvement (usually VII), and suffer long-term sequelae of their illness. Nearly one third require ventilatory support. Both the mortality and the recurrence rate are about 3%.[8]

In addition to electrophysiologic testing, there are three ancillary tests that may be helpful in the diagnosis of GBS. Cerebrospinal fluid (CSF) analysis is useful when it demonstrates the characteristic picture of markedly elevated protein with only a mild pleocytosis. In the clinical setting of suspected GBS, this finding is highly specific. Early in the disease, however, patients may have normal CSF values. Consequently, a normal CSF cannot be used to exclude GBS because of the limited sensitivity of this test. Selective enhancement of the anterior spinal nerve roots on magnetic resonance imaging (MRI) is suggestive, but not diagnostic, of GBS.[9] The GBS disability score, which combines age, presence or absence of diarrhea, and a score of the patient's ability to ambulate independently at 2 weeks, has been shown to be predictive of prognosis at 6 months, particularly related to independent activity.[10]

Management. Individuals with suspected GBS must have their respiratory function tested. A decrease in forced vital capacity (FVC) has been shown to correlate with the need for intubation in patients with GBS. An FVC of less than 20 mL/kg was associated with pending respiratory failure and the need for intubation, whereas patients with an FVC of greater than 40 mL/kg did not require intubation.[11,12] Likewise, patients with a negative inspiratory force (NIF) of less than 30 cm water are more likely to require mechanical ventilation.[12] Other tests, such as the forced expiratory volume in 1 second

(FEV_1) or peak flow rate (PFR) can also be used to assess respiratory function. Patients unable to perform these tests and those with less than 100% of predicted values should have an arterial blood gas obtained. Evidence of alveolar hypoventilation (elevated carbon dioxide [P_{CO_2}]) in a patient with an unsecured airway requires a level of intensive monitoring that is impractical in many emergency departments. Therefore, patients with weakness, CO_2 retention, or other evidence of early ventilatory failure should be considered for early, prophylactic intubation.[13]

Among patients with possible GBS who have normal pulmonary function, extensor neck strength can be monitored to predict impending ventilatory failure. Patients with probable GBS should receive neurologic consultation and be admitted to the hospital. Either plasma exchange or intravenous immunoglobulin (IVIG) should be administered. There is sound evidence that both are superior to placebo and that combination or sequential therapy confers no therapeutic advantage over either intervention alone. Plasma exchange is cumbersome and not available at many hospitals. IVIG is more readily available and is usually administered in a dose of 400 mg/kg/day for 5 days. However, IVIG is quite expensive, costing roughly $50 to $80 per gram.[14] Although not approved by the Food and Drug Administration, IVIG is supported in certain national guidelines.[15] Corticosteroids are no longer recommended for treatment of GBS.[16] Oral steroids have been shown to delay recovery. Intravenous steroids alone have been shown to impart no benefit, and though the combination of intravenous steroids and IVIG has hastened recovery, there was no affect on long-term outcome.[17–19] The marked elevation in blood pressure seen in some patients with GBS should not be treated because it is typically transient and may be followed by precipitous and unpredictable hypotension.

Type 2: Distal Symmetrical Polyneuropathies

Most polyneuropathies are characterized by a pattern of distal, symmetrical sensorimotor findings, worse in the lower than upper extremities, with a stocking-glove distribution of sensory abnormalities that gradually diminishes as one moves proximally. The motor findings and loss of DTRs, which lag behind the sensory features, follow a similar pattern of progression from distal to proximal. The diffuse, distal, symmetrical nature of this pattern is most consistent with a toxic-metabolic disease process, as yet unidentified, that causes a length-dependent axonopathy. Distal symmetrical polyneuropathy (DSPN) is the most common type of peripheral neuropathy seen in emergency practice. Only the most common causes of DSPN are discussed, with a more complete listing of causes shown in Box 105-3.

Diabetic Distal Symmetrical Polyneuropathy

The preponderance of cases of DSPN occur in diabetics, also termed diabetic polyneuropathy. Initial symptoms usually consist of "positive" sensory complaints (e.g., dysesthesias such as tingling or burning) beginning on the plantar surfaces of both feet. At the early stages of a typical DSPN, there may be some asymmetry.[20] At this juncture, it may be impossible to distinguish a focal neuropathic process such as a mononeuropathy from a polyneuropathy, although in this location, prior probability strongly favors a polyneuropathy. As the process advances, the plantar surfaces of both feet become dysesthetic before the dorsum of either foot is involved. Weakness of dorsiflexion of the big toe is usually the first motor sign, followed by weakness of foot dorsiflexion, footdrop, loss of Achilles' reflex, and later a "steppage gait."

BOX 105-3   **DISTAL SENSORIMOTOR POLYNEUROPATHIES**

Diabetes mellitus
Alcoholism
Neoplastic or paraneoplastic
Hereditary motor and sensory neuropathies
    (Charcot-Marie-Tooth)
Cryptogenic sensorimotor polyneuropathies (CSPN)
HIV
Toxins
    Organic or industrial agents
        Acrylamide
        Allyl chloride
        Carbon disulfide
        Ethylene oxide
        Hexacarbons
        Methyl bromide
        Organophosphate-induced delayed polyneuropathy
            (OPIDP)
        Polychlorinated biphenyls (PCBs)
        Trichloroethylene
        Vacor
    Metals
        Arsenic
        Gold
        Mercury (inorganic)
        Thallium
    Therapeutic agents
        Amiodarone
        Antiretrovirals

        Dapsone
        Disulfiram
        Isoniazid
        Metronidazole
        Nitrofurantoin
        Paclitaxel (Taxol)
        Phenytoin
        Statins (HMG-CoA reductase inhibitors)
        Thalidomide
        Vinca alkaloids (vincristine, vinblastin)
Nutritional
    Beriberi (thiamine or vitamin B_1)
    Pellagra (niacin, B vitamins)
    Pernicious anemia (vitamin B_{12})
    Pyridoxine deficiency (vitamin B_6)
End-organ dysfunction
    Acromegaly
    Chronic pulmonary disease
    Hypothyroidism
    Renal failure (uremic neuropathy)
Paraproteinemias
    Amyloidosis
    Monoclonal gammopathy of unknown significance
        (MGUS)
    Multiple myeloma
    Waldenström's macroglobulinemia
Porphyria

HMG-CoA, hydroxymethylglutaryl coenzyme A.

Sensory loss continues to move proximally, and before it reaches the knees, the fingertips are usually involved. DTRs are progressively lost, as is proprioception. If the latter becomes severe, patients may develop sensory ataxia. As the neuropathy continues to progress, sensory abnormalities ultimately involve all modalities and extend to a diamond-shaped periumbilical area. Far advanced disease may affect sensation over the skull vertex and facial midline structures. Atrophy and areflexia occur as weakness worsens. Severely impaired patients may be unable to ambulate or grasp objects. These symptoms have a significant impact on the patient's quality of life, affecting not only physical functioning but emotional, sleep, and social functioning. Many of these patients display signs of depression or anxiety.[21] Polyneuropathies can be difficult to diagnose and are best approached by performing electrodiagnostic studies on patients with a constellation of symptoms and signs suggesting a particular neuropathy.[22]

Management. As with virtually all peripheral neuropathies, referral is indicated for management of diabetic DSPNs. If discomfort is severe, the etiology of the neuropathy seems likely to be diabetic, and if referral is delayed, it may be necessary to provide the patient with some symptomatic relief. Because treatment of neuropathic pain has traditionally been linked to etiology rather than an underlying mechanism, the choice of pharmacologic agents is empirical, with substantial practice variation in the United States and worldwide.[23] In the United States the first choice is often a nonsteroidal anti-inflammatory drug, which has little proven efficacy and a high potential for renal impairment.[3] Based on placebo-controlled randomized clinical trials, tricyclic antidepressants and anticonvulsants appear to have the best NNTs (number of patients needed to treat in order to provide at least 50% relief of symptoms in one patient). These are generally in the range 3 to 5,

with confidence intervals whose upper limits reach 10 in some instances.[24] Imipramine or amitriptyline may be started at a dose of 25 mg at bedtime (10 mg in elderly patients) and titrated slowly up to a dose of 300 mg. Carbamazepine at a dose of 200 to 400 mg every 8 hours or gabapentin at a dose of 900 to 3600 mg/day are also effective treatments.[25,26] Tramadol in two studies has shown an NNT below 5.[24] Although tramadol is a mixed opioid, development of dependence in long-term use appears to be uncommon. In a recently published guideline, the following medications were recommended for the treatment of neuropathic pain: gabapentin, opioids, tramadol, and tricyclic antidepressants.[3] Also being used is pregabalin at 150 to 600 mg/day, with a mechanism similar to that of gabapentin, and dulexetine at 60 mg/day, which is a selective serotonin and norepinephrine reuptake inhibitor.[3] Among the selective serotonin reuptake inhibitors (SSRIs), paroxetine and bupropion appear to be effective, but fluoxetine is not.[27] The summary NNT for the SSRIs has a confidence interval that reaches 50, suggesting that, pending further data, these agents should be considered second-line drugs.[24] Topical capsaicin provides relief in some patients, but the burning associated with its application has limited its usage. Improving glycemic control can prevent, diminish, or reverse early diabetic DSPNs. Patients will typically spend over $1,000 per year for pain relief from diabetic DSPN.[3]

Alcoholic Distal Symmetrical Polyneuropathy

Although the association between alcoholism and peripheral neuropathy has been well established for centuries, demonstration of a direct neurotoxic effect of alcohol remains elusive. The preponderance of evidence, from both observational studies in humans and experimental data from animal models,

suggests that the association between alcohol and peripheral neuropathy may be confounded by nutritional status (i.e., deficiency states might be the true underlying cause of alcoholic peripheral neuropathy).

The clinical and pathologic picture of alcoholic neuropathy is similar to that of the DSPN of diabetes. However, in alcoholism severe myopathy and cerebellar degeneration often complicate the clinical picture.[28] Autonomic skin changes with atrophy and hair loss accompany the sensorimotor abnormalities. Often other systemic effects of alcoholism are so severe that the patient may not notice the neuropathic symptoms. All patients with suspected alcoholic DSPN should receive dietary supplements and referral for outpatient management.

Human Immunodeficiency Virus Neuropathies

With the widespread use of highly active and effective antiretroviral treatment, peripheral neuropathies have become the most common neurologic complication of HIV infection. The typical HIV neuropathy is a DSPN, which appears to be triggered by a combination of dideoxynucleoside therapy and poorly characterized immune-mediated mechanisms associated with HIV.[29,30] These patients require referral for specialized care. In addition to standard therapies for DSPN, lamotrigine has been shown to be moderately effective in the treatment of HIV-associated painful neuropathies.[31]

Toxic and Metabolic Neuropathies

Many toxic agents and metabolic derangements produce a typical DSPN. Box 105-3 lists some of the most common toxic and metabolic causes of peripheral neuropathy. On the basis of preliminary results from a case-control study, the statins have been added to this list.[32]

Type 3: Asymmetrical Proximal and Distal Peripheral Neuropathies (Radiculopathies and Plexopathies)

Radiculopathies are discussed in detail in Chapter 103. Plexopathies, which are discussed briefly in this chapter, are uncommon and often the result of trauma (Box 105-4). Generally, a plexopathy, whether brachial or lumbosacral, is identified by a process of elimination (i.e., a pattern of sensorimotor and reflex abnormalities that fit neither a radicular nor individual peripheral nerve distribution). Although this approach does not exclude a mononeuropathy multiplex on physical examination alone, a careful history should determine whether the patient is at risk for developing a mononeuropathy or plexopathy on the basis of underlying disease.

Most plexopathies are often the result of blunt trauma and are usually seen in young men following motor vehicle accidents. Most present for evaluation several months after injury because of the need to recover from concurrent injuries. Therapeutic intervention is often delayed in order to maximize the potential for spontaneous recovery. Several surgical repairs exist, including neurotization or nerve transfer.[33]

Radiation (actinic) plexopathy occurs after a variable period of latency following treatment, which may extend to 20 years or more. Almost all series include women who received radiation treatment for breast cancer. Among neoplastic causes, most originate from the lung or breast. Patients with probable neoplastic brachial plexopathy need imaging studies and may require immediate radiation therapy. Pain control is the focus of management.

Thoracic outlet syndrome remains a controversial disorder.[34] Although the pendulum has swung over the past 50 years from

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BOX 105-4 **ASYMMETRICAL PROXIMAL/DISTAL PERIPHERAL NEUROPATHIES**

Brachial plexopathy
    Open
        Direct plexus injury (knife or gunshot wound)
        Neurovascular (plexus ischemia)
        Iatrogenic (central line insertion)
    Closed
        Traction injuries
            "Stingers"
            Traction neurapraxia
            Partial or complete nerve root avulsion
        Radiation
        Neoplastic
        Idiopathic brachial plexitis
        Thoracic outlet
Lumbosacral plexopathies
    Open
    Closed
        Traction injuries
            Pelvic double vertical shearing fracture
            Posterior hip dislocation
            Retroperitoneal hemorrhage
        Vasospastic (deep buttock injection)
        Neoplastic
        Radiation
        Idiopathic lumbosacral plexitis
        Infectious
            Herpesvirus (sacrococcygeal)
            Herpes simplex II
            Herpes zoster
        Cytomegalovirus (CMV) polyradiculopathy (HIV)

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a postulated vascular cause to a neurogenic etiology, current evidence supporting the high prevalence of compression of the brachial plexus as a cause of thoracic outlet syndrome is in fact only slightly better[35] than earlier evidence favoring a vascular etiology.[36] Nevertheless, the disorder is currently felt to be most commonly due to compression of the medial or lower portion of the brachial plexus by a cervical rib or fibrous band.[37] The syndrome is characterized by gradually progressive weakness and wasting of median and ulnar hand muscles with ulnar forearm and hand sensory signs and symptoms. Patients with this clinical picture should be referred for NCSs and EMG, which are said to be diagnostic.[37] The treatment of true neurogenic thoracic outlet syndrome requires surgical removal of the rib or aberrant fibrous band to decompress the brachial plexus.[38] An excellent discussion of this entity from a different perspective can be found in Chapter 85.

Because of the complexity of plexopathies, there is no reason to expect that one can or should do more in the ED than localize the probable pathologic process to the brachial or lumbosacral plexus. Depending on severity and suspected etiology, one should either admit or refer the patient to a neurologist with experience in PNS disease.

Type 4: Isolated Mononeuropathies

The pattern of asymmetrical, sensorimotor, usually distal, peripheral neuropathy is characteristic of a mononeuropathy. Mononeuropathies are of two main types: isolated and multiple. The isolated mononeuropathies are discussed in this section, while the multiple mononeuropathies, also termed

BOX 105-5 **ISOLATED MONONEUROPATHIES**

Upper extremity
   Radial nerve
      Axilla
      Humerus
      Elbow (posterior interosseous neuropathy)
      Wrist (superficial cutaneous radial neuropathy)
   Ulnar nerve
      Axilla
      Humerus
      Elbow
      Condylar groove
      Cubital tunnel
   Wrist (Guyon's canal)
   Hand
      Superficial terminal ulnar neuropathy
      Deep terminal ulnar neuropathy
         Proximal hypothenar
         Distal hypothenar
   Median nerve
   Axilla
   Humerus (musculocutaneous mononeuropathy)
   Forearm
      Anterior interosseus
      Pronator syndrome (?)
   Wrist (carpal tunnel)
   Hand (recurrent motor branch)
   Suprascapular mononeuropathy
      Axillary mononeuropathy
Lower extremity
   Sciatic nerve
   Femoral nerve
      Iliacus compartment (proximal)
      Saphenous mononeuropathy (distal)
   Lateral femoral cutaneous (meralgia paresthetica)
   Peroneal nerve
      Common peroneal mononeuropathy (fibular head,
         popliteal fossa)
      Deep peroneal mononeuropathy (anterior
         compartment)
   Tibial nerve
      Popliteal fossa (proximal)
      Tarsal tunnel (distal)
   Sural nerve
      Popliteal fossa, calf (proximal)
      Fifth metatarsal base (distal)
   Plantar nerve
      Distal to tarsal tunnel
      Interdigital neuropathies (Morton's neuroma)
   Obturator mononeuropathy

Figure 105-3. Radial nerve, major branches, right arm, lateral view. (From Stewart JD: Focal Peripheral Neuropathies, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, 2000.)

Radial Mononeuropathy

The radial nerve arises from C5-T1 roots. After exiting the brachial plexus, it passes behind the proximal humerus in the spiral groove and takes a lateral (radial) course down the upper arm (Fig. 105-3). At about the level of the antecubital fossa, it bifurcates into the posterior interosseous (pure motor) and superficial radial (pure sensory) nerves.

The radial nerve controls extension of the fingers, thumb, wrist, and elbow (triceps). In contrast to the median and ulnar nerves, the radial nerve provides only *extrinsic* motor innervation to the hand (i.e., it does not supply motor fibers to any muscles that both originate and insert within the hand). In further contrast to the median and ulnar nerves, which supply most of the sensation to the hand, the radial nerve makes a contribution only to a cutaneous dorsal area overlying the first dorsal interosseus muscle, sometimes extending part of the way up the dorsa of the thumb, index, and long fingers.

Radial mononeuropathy caused by involvement at the level of the axilla is uncommon. When it occurs, it is usually associated with other upper extremity mononeuropathies or a brachial plexopathy. Although improper use of crutches may cause this syndrome, it usually occurs after an extended period of unconsciousness during which the arm is positioned in such a way that prolonged, deep compression is applied to the axilla. Axillary radial mononeuropathy is distinguished from the more common humeral form by the finding of triceps involvement in addition to typical wrist and finger drop. Triceps involvement occurs because the innervation to the triceps is proximal to the point where the nerve is most vulnerable as it winds around the humeral shaft (see Fig. 105-3).

Most radial mononeuropathies are due to so-called Saturday night palsies. The euphemism is derived from the association of radial mononeuropathy with improper positioning of the arm during deep, commonly inebriated sleep. Consequently, the radial nerve is trapped for a prolonged period between the humeral shaft and some firm surface, causing an external compression mononeuropathy. "Bridegroom's palsy" is another eponym for radial mononeuropathy, so named because the radial nerve may be compressed by the bride's head resting on the bridegroom's arm during sleep.

Because innervation of the wrist and finger extensors occurs distal to this area of the humeral shaft, findings are characterized by wrist and finger drop and mild numbness over the skin of the first dorsal interosseus muscle. Depending on the level,

mononeuropathy multiplex, are discussed in the next section, as a type 5 peripheral neuropathy.

Isolated mononeuropathies are usually caused by trauma, either blunt or penetrating (Box 105-5). If the trauma is blunt, the injury may be secondary to compression from an internal or external source. Entrapment neuropathies are a subset of compression neuropathies occurring at anatomic locations where nerves traverse potentially constricting compartments or tunnels.[39] Isolated mononeuropathies may be acute, intermittent, or chronic and continuous. Antecedent peripheral neuropathy may be a risk factor for development of compression neuropathy (so-called double-crush syndrome), particularly in diabetics.[40]
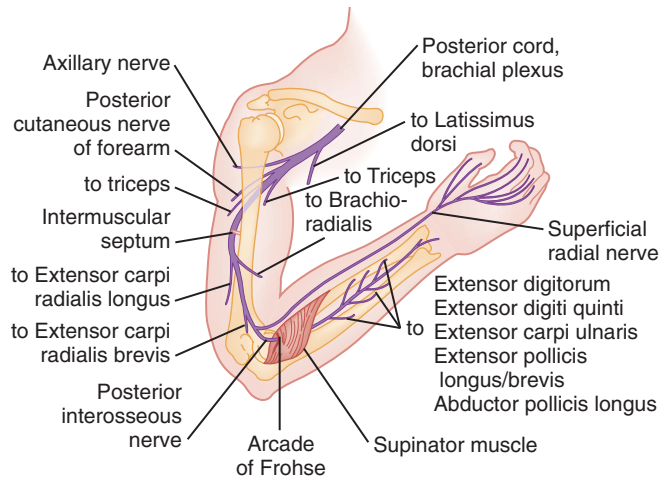
degree, and duration of compression, some fascicles of the nerve may remain functional, resulting in a partial radial mononeuropathy. Thus, the superficial radial nerve may remain intact, resulting in no loss of sensation, or loss of wrist and finger extension may be incomplete.

Because the finger drop of radial mononeuropathy places the hand at a mechanical disadvantage, examination of ulnar function by testing interossei may produce false-positive findings of weakness. To adjust for this, the examiner should ask the patient to place the palm on a horizontal supporting surface such as a stretcher. With the fingers extended and no longer "dropped" at the metacarpophalangeal joints, interosseous strength can now be fairly tested. Failure to perform this maneuver may cause misdiagnosis of a simple radial mononeuropathy as a brachial plexopathy in an effort to explain what appears to be radial and partial ulnar nerve involvement.

About 90% of radial nerve palsies occurring during sleep, coma, or anesthesia recover fully, usually within 6 to 8 weeks. Evidence of denervation on EMG studies predicts a slower rate of recovery. Tourniquet injuries to the radial nerve usually recover spontaneously within 2 to 4 months. If axonal degeneration is seen on electrophysiologic testing, recovery may take longer, although virtually all radial mononeuropathies caused by tourniquets eventually resolve. About 75% of radial nerve injuries associated with a closed humeral shaft fracture recover spontaneously. In contrast, surgical intervention is needed to free the nerve from entrapment associated with complex fractures.

While patients are waiting for spontaneous recovery to occur, the hand should be maintained in about 60 degrees of dorsiflexion. Although a simple dorsal plaster or fiberglass splint treats the wristdrop, atrophy and contractures can be minimized, and function of the hand can be improved if wide rubber bands anchored to the splint at a point proximal to the wrist are attached to individual fingers to provide passive dorsiflexion.

Ulnar Mononeuropathy

The ulnar nerve includes C7-T1 roots and passes through the brachial plexus to descend medially, without branching, to the ulnar (medial) condylar groove at the elbow. It then enters the cubital canal, where it gives off branches to the ulnar wrist flexor and the deep flexors of the fourth and fifth digits.

Just proximal to the wrist, two important sensory branches leave the main trunk to supply cutaneous sensation to part of the hand (Fig. 105-4). These are the palmar and dorsal cutaneous branches, which do *not* pass through Guyon's canal. The palmar branch supplies sensation to the hypothenar eminence and the dorsal branch innervates the ulnar side of the dorsum of the hand, extending out nearly to the tip of the fifth and ulnar half of the fourth digit.

At the wrist, the nerve enters Guyon's canal (Fig. 105-5) between the pisiform and hook of the hamate, then bifurcates into the superficial terminal sensory branch and the deep motor branch.

The superficial sensory nerve supplies ulnar sensation to the palmar side of the fifth and half of the fourth digit (see Fig. 105-5). The deep motor nerve supplies the hypothenar muscles, then crosses to the radial side of the palm to innervate
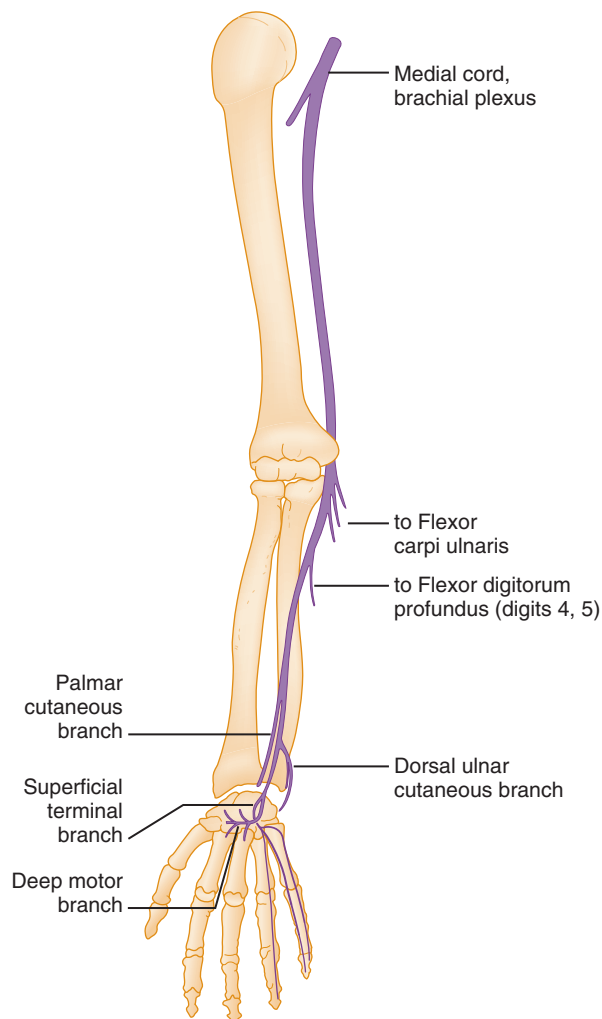

Figure 105-4. Ulnar nerve, major branches, right arm, anterior view. (From Stewart JD: Focal Peripheral Neuropathies, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, 2000.)
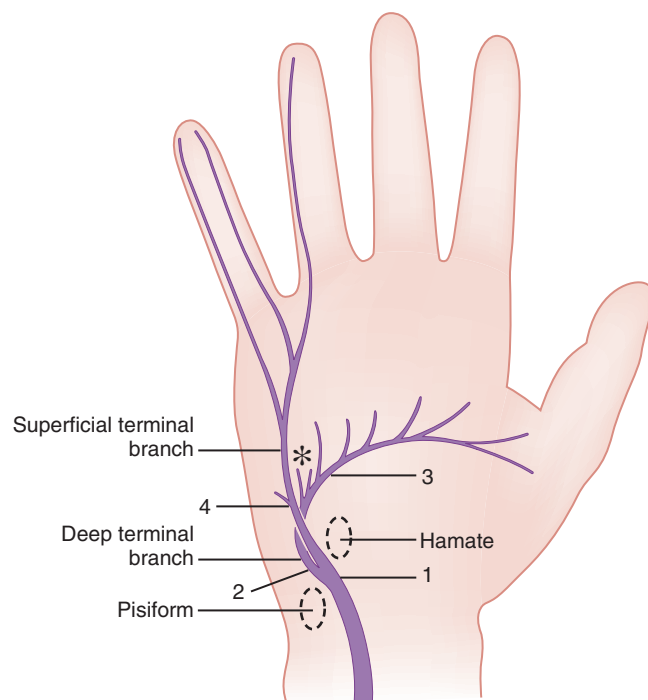
Labels: Medial cord, brachial plexus; to Flexor carpi ulnaris; to Flexor digitorum profundus (digits 4, 5); Palmar cutaneous branch; Superficial terminal branch; Deep motor branch; Dorsal ulnar cutaneous branch

Figure 105-5. Distal ulnar nerve and branches, right hand, palmar view. Numbers indicate four main sites of distal ulnar mononeuropathy in the wrist and hand. *Denotes hypothenar branches. (From Stewart JD: Focal Peripheral Neuropathies, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, 2000.)

Labels: Superficial terminal branch; Deep terminal branch; Pisiform; Hamate; 1; 2; 3; 4

the ulnar intrinsics (all interossei and the ulnar lumbricals of the fourth and fifth digits), terminating in the first dorsal interosseus. The interossei abduct and adduct the fingers and are all innervated by the ulnar nerve. The lumbrical muscles flex the metacarpal phalangeal joints and are evenly divided between the ulnar (fourth and fifth) and median (second and third) digits. The ulnar nerve can be thought of as the complement to the median nerve in the hand because it supplies all of the muscles and all palmar sensation not innervated by the median nerve.

The ulnar nerve may be injured at two locations near the elbow: in the ulnar condylar groove and distally in the cubital canal. Because the condylar groove is shallow, the ulnar nerve runs superficially in this location and is vulnerable to injury, usually from external pressure or from a fracture or dislocation. The ulnar nerve has a propensity to develop a "tardy ulnar palsy," occurring years after a traumatic event. Many of these delayed ulnar mononeuropathies can be localized to the elbow on electrophysiologic testing.

Some ulnar mononeuropathies occur secondary to compression just proximal to entry into the cubital canal or are entrapped within the canal itself. Transient symptoms may occur during prolonged flexion or with repeated flexion and extension at the elbow.

Although distinguishing a condylar from a cubital ulnar mononeuropathy is difficult, it is usually possible to localize the problem to the region of the elbow or the wrist. In addition to prior probability heavily favoring the elbow, the presence of sensory abnormalities in an ulnar distribution in the hand and fingers (i.e., usually including the fifth digit and "splitting" the fourth digit) strongly suggests that the lesion is at the level of the elbow rather than the wrist. The ulnar cutaneous innervation to the hand branches off from the main trunk proximal to the nerve entering Guyon's canal (see Figs. 105-4 and 105-5). Thus, a lesion at the wrist should not produce sensory abnormalities, whereas one at the elbow would be expected to do so.

Compression of the ulnar nerve within Guyon's canal is rare. When it does occur, it affects all of the ulnar intrinsics (i.e., the two ulnar [fourth and fifth] lumbricals) and all the interossei. However, the ulnar extrinsics (i.e., the deep flexors of the fourth and fifth digits) are not affected, nor is the ulnar flexor of the wrist. The only sensory abnormalities are those in the distribution of the superficial terminal sensory branch, sparing other areas of ulnar innervation (see Fig. 105-5).

There are three ulnar mononeuropathies that occur distal to Guyon's canal in the hand. The two most common ones involve the deep terminal branch, either proximal or distal to the separation of the hypothenar branches (see Fig. 105-5). If the lesion is proximal, it produces weakness of all the ulnar innervated muscles of the hand without sensory loss. If it is distal, the hypothenar ulnar intrinsics are spared but the picture is otherwise similar. Usually, this occurs secondary to a laceration or repeated compression in the hand from use of certain tools, a cane, or the handle of a crutch.

Involvement of the superficial terminal branch (see Fig. 105-5) arises as pure sensory loss of the palmar surface of the fifth digit and ulnar half of the fourth digit caused by direct compression of this branch just distal to Guyon's canal. The dorsal surface of these two digits should have normal sensation except for the distal tips. This configuration of findings is due to the intact innervation provided by the dorsal and palmar cutaneous branches that enter the hand without passing through Guyon's canal (see Fig. 105-4).

Most ulnar mononeuropathies will spontaneously resolve. However, if muscle atrophy, particularly in the hypothenar area, is detected, then surgery may be considered.[41,42]
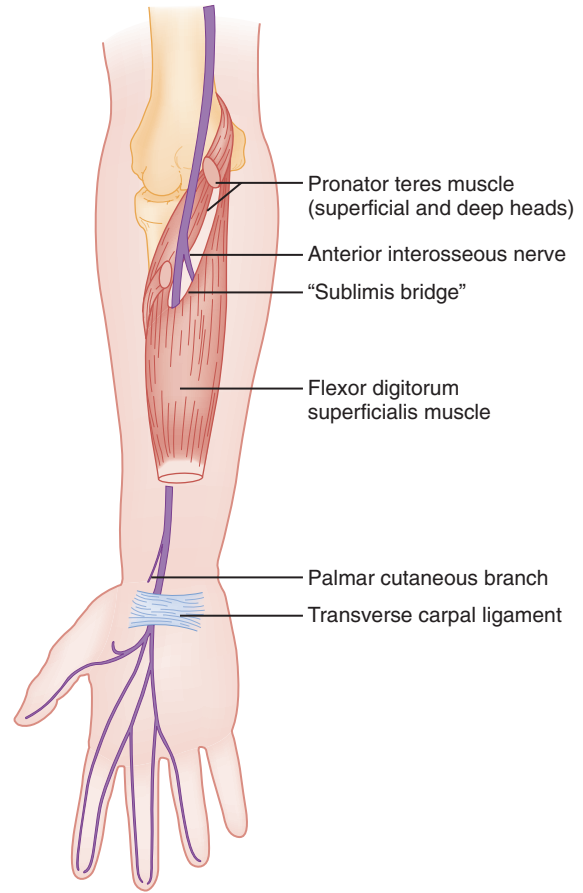

Figure 105-6. Median nerve, major branches, right arm, anterior view. (From Stewart JD: Focal Peripheral Neuropathies, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, 2000.)

Median Mononeuropathy

The median nerve arises from C5-T1 spinal nerve roots and exits the brachial plexus through the lower trunk (Fig. 105-6). Median mononeuropathy is usually diagnosed as carpal tunnel syndrome (CTS), which is the most common of all entrapment neuropathies. CTS has a prevalence of 3 to 6% in the U.S. population.[43] Although the patient may complain of bilateral symptoms, a careful history usually reveals that symptoms in one hand preceded those in the other. Awakening at night and shaking the hand is a common symptom of CTS. Symptoms are often worsened by activity. For unclear reasons, the pain may spread as high as the arm or shoulder, although the paresthesias are generally confined to the fingers. Many patients on initial questioning state that their entire hand is involved, although this is not supported by careful sensory examination. Complaints that the hands are clumsy or weak, especially when holding a glass or opening a screw-top container, are frequent. The skin of the fingers innervated by the median nerve may be drier and rougher to the touch than the corresponding ulnar skin, depending on the duration of entrapment.[44]

When there is motor involvement in CTS it is confined to the median intrinsics, which innervate the *l*umbricals (flexion of the metacarpal phalangeal joints), and subserve thumb *o*pposition, *a*bduction, and *f*lexion, known as the LOAF muscles. However, the hallmark of CTS is sensory involvement, with motor abnormalities occurring later. The typical pattern of sensory innervation of the hand by the median, ulnar, and radial nerves shows marked individual variation.

BOX 105-6 | **CONDITIONS ASSOCIATED WITH CARPAL TUNNEL SYNDROME**

Acromegaly
Amyloid
Diabetes mellitus
Hypothyroidism
Obesity
Pregnancy
Renal failure
Rheumatoid arthritis

Figure 105-7. Sciatic nerve, major branches, right leg, posterior view. (From Stewart JD: Focal Peripheral Neuropathies, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, 2000.)

The most specific finding for CTS is splitting of the fourth digit (i.e., normal sensation of the ring finger on the ulnar palmar side with abnormal sensation on the median [radial] palmar side of the same finger). The most sensitive finding is abnormal sensation of the distal palmar tip of the index finger. If sensory findings are absent in the presence of motor findings consistent with median nerve involvement, it is highly unlikely that the patient has CTS, and an alternative diagnosis should be sought. If neither sensory nor motor symptoms are evident, none of the provocative tests originally reported to reproduce the sensory symptoms of CTS—of which the most common are Tinel's sign (percussion of the median nerve at the wrist) and Phalen's sign (maximal palmar flexion at the wrist)—has shown adequate sensitivity or specificity to determine which patients should be referred for electrodiagnostic studies.[45–47] As suggested earlier, the best way to examine patients for sensory findings is to touch the distal palmar tips very lightly, asking the patient whether the sensation feels "abnormal."

CTS appears to be associated with the conditions listed in Box 105-6. Of these, the two most common are diabetes mellitus and pregnancy. CTS associated with systemic illness is commonly bilateral. Although CTS in pregnancy may be self-limiting, about half the women in one series were still symptomatic at 1-year follow-up.[48] All patients with suspected CTS should be referred for NCSs. However, because of the dissociation between clinical and electrodiagnostic indicators of CTS early in the disease, patients with normal electrodiagnostic findings in the presence of symptoms suggestive of CTS (with or without signs) should have an MRI[49] or sonogram.[50] At present, the sensitivity of MRI is good but its specificity is poor.[51] Ultrasound has been shown to be useful particularly in patients with symptoms and a negative NCS. This is done by measuring the cross-sectional area of the median nerve at the end of the pisiform.[52] Thus, if all diagnostic studies in a symptomatic patient are negative, or if only the MRI result is positive, they should be repeated within a few months if symptoms do not resolve.[44] This recommendation is based on the theory that the CTS will progress over time to the point that an objective indicator such as the NCS will become positive.

Because of the possibility of development of a disabling "median hand" after inadvertent direct injection of the median nerve, one should not inject the carpal tunnel with steroids in the ED. The physician to whom the patient is referred can decide after NCS whether to recommend splinting, injection, or surgical division of the transverse carpal ligament. Endoscopic repair appears to provide excellent results.[53]

Sciatic Mononeuropathy

The sciatic nerve includes L4-S3 spinal nerve roots that pass through the lumbosacral plexus and divide into two terminal branches: the common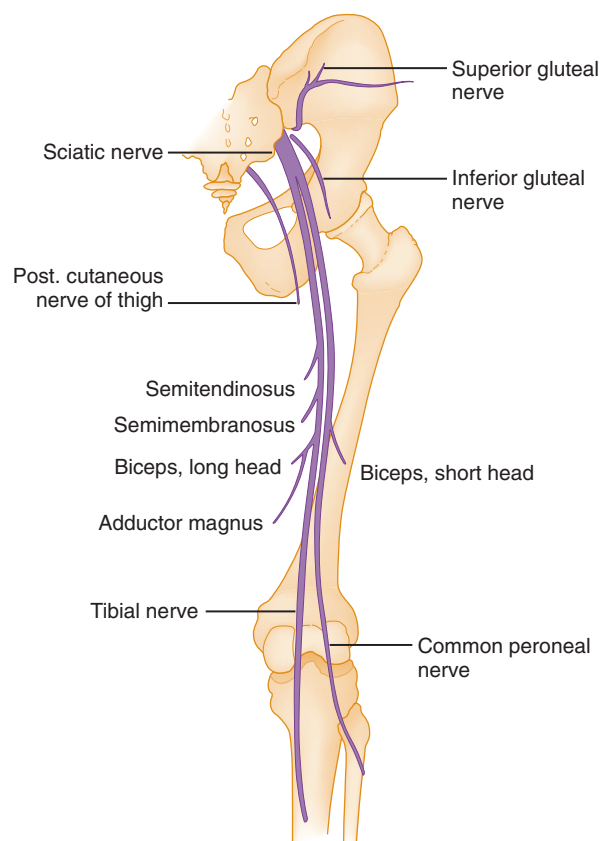 peroneal and tibial nerves. The nerve exits the pelvis through the sciatic notch, passes behind the hip, and remains deep in the thigh until its terminal bifurcation in the proximal popliteal fossa (Fig. 105-7).

Lesions of the sciatic nerve occur with posterior hip dislocation or with virtually any form of penetrating or blunt trauma that causes formation of a buttock hematoma. Other causes include deep gluteal injection and prolonged supine immobilization on a firm surface. Because the sciatic nerve innervates the hamstrings and provides all sensorimotor function distal to the knee, a complete sciatic mononeuropathy is a devastating injury. Ambulation is extremely difficult because of inability to flex the knee and a flail foot (i.e., neither flexion nor extension is possible at the ankle). Fortunately, many sciatic mononeuropathies are incomplete. For unknown reasons, a partial lesion typically involves only the trunk of the sciatic nerve, which subsequently becomes the common peroneal nerve, sometimes making the two difficult to distinguish from one another clinically. On electrophysiologic studies, evidence of involvement of gluteal muscles or of any muscles innervated by the tibial nerve readily distinguishes a partial sciatic mononeuropathy from a lesion of the common peroneal nerve. Treatment of footdrop requires a posterior splint to maintain the ankle at 90 degrees until a brace can be obtained (see later section on "Common Peroneal Mononeuropathy").

Lateral Femoral Cutaneous Mononeuropathy

Lateral femoral cutaneous mononeuropathy (meralgia paresthetica) is a common syndrome believed to be caused by injury to this pure sensory nerve as it passes through or over the inguinal ligament, where it may become entrapped or kinked. Along with facial nerve neuropathy, meralgia paresthetica is

one of the most commonly reported mononeuropathies associated with HIV. External pressure and obesity may also contribute to nerve injury, causing numbness and dysesthesia over the skin of the upper lateral thigh. Regression usually occurs spontaneously, but recurrence is common and may require a release procedure for the inguinal ligament.

Common Peroneal Mononeuropathy

The common peroneal nerve is a continuation of one trunk of the sciatic nerve. It is most vulnerable to injury where it winds around the fibular neck (Fig. 105-8). It then passes through the fibular canal and bifurcates into its terminal branches, the superficial and deep peroneal nerves. The superficial peroneal nerve innervates the peroneal muscles (foot everters) and supplies sensation to the lateral, distal lower leg and dorsum of the foot. The deep peroneal nerve traverses the anterior compartment and supplies innervation to the dorsiflexors of the foot and toes, plus cutaneous sensation between the first and second toes.

Most common peroneal mononeuropathies are idiopathic and thought to be related to compression where the nerve is superficially located lateral to the fibular neck. Because this common neuropathy is often noted on awakening, it may be secondary to position during sleep. Leg crossing may also be a risk factor for development of this mononeuropathy. The most striking feature of a complete common peroneal mononeuropathy is footdrop caused by weakness of foot dorsiflexion. At testing, the everters of the foot are also weak, but the inverters, which are innervated by the tibial nerve, remain strong. This is the single most reliable clinical feature distinguishing sciatic from common peroneal mononeuropathy. Analogous to radial mononeuropathy in the upper extremity, sensory abnormalities in the leg and foot are inconstant and easily overlooked in peroneal mononeuropathy. Most patients with peroneal palsy recover. Those who do not should be studied electrophysiologically to ensure that the point of compression is not proximal to the fibular neck (i.e., in the popliteal fossa). If the point of peroneal injury appears to be in the region of, or distal to, the fibular neck on EMG, patients whose footdrop does not resolve should be considered candidates for exploration to determine whether the nerve is compressed within the fibular canal.

Treatment of common peroneal palsy may require a posterior splint to maintain the ankle at 90 degrees until the nerve regenerates. This splinting prevents the foot from falling into sustained equinus (plantar flexion), which in turn allows the intermalleolar distance to narrow, effectively locking the talus out of the ankle mortice.

The treatment of isolated mononeuropathies depends on their etiology, location, and natural history of spontaneous recovery. All penetrating neuropathies should have surgical exploration and repair performed. Blunt trauma may cause a mononeuropathy indirectly by entrapment of a nerve within a fracture, hematoma, or compartment, requiring surgical intervention. Alternatively, nerves may be injured at a point where they are superficial, either by a single direct blow or by sustained pressure caused by immobility (pressure palsies). Most of these resolve spontaneously over time, depending on the severity of injury and length of the nerve. If entrapment can be confirmed by imaging or electrophysiologic studies, a release procedure is indicated. In many instances, when there is disagreement between clinical and EMG findings, MRI may be helpful in selecting patients for exploration by visualizing entrapment or traction.[54] Characteristic sonographic findings have also been reported in several mononeuropathies.[55]

The mononeuropathies that do not require timely surgical exploration should be referred for further workup to confirm the location of the neuropathic lesion.

Type 5: Mononeuropathy Multiplex

Mononeuropathy multiplex is characterized by an asymmetrical, sensorimotor, usually distal pattern of peripheral neuropathy (Box 105-7). As with isolated mononeuropathies, sensory abnormalities tend to be located in the same general anatomic region as the accompanying motor findings. Whether DTRs are affected depends on which nerves are involved. For example, if the process includes the femoral nerve, the patellar reflex is likely to be diminished or absent.

Figure 105-8. Common peroneal nerve, major branches, right leg, anterolateral view. (From Stewart JD: Focal Peripheral Neuropathies, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, 2000.)

Labels: Sciatic nerve; Common peroneal nerve; Fibular tunnel; Peroneus longus muscle; Superficial peroneal nerve; to Peroneus brevis; to Extensor digitorum brevis; Tibial nerve; Deep peroneal nerve; to Tibialis anterior; to Extensor digitorum longus; to Extensor hallucis longus

BOX 105-7	MONONEUROPATHY MULTIPLEX

Vasculitis
  Systemic vasculitis
    Polyarteritis nodosa
    Rheumatoid arthritis
    Systemic lupus erythematosus
    Sjögren's syndrome (keratoconjunctivitis sicca)
  Nonsystemic vasculitis
Diabetes mellitus
Neoplastic
  Paraneoplastic
  Direct infiltration
Infectious
  Lyme disease
  HIV
Sarcoid
Toxic (lead)
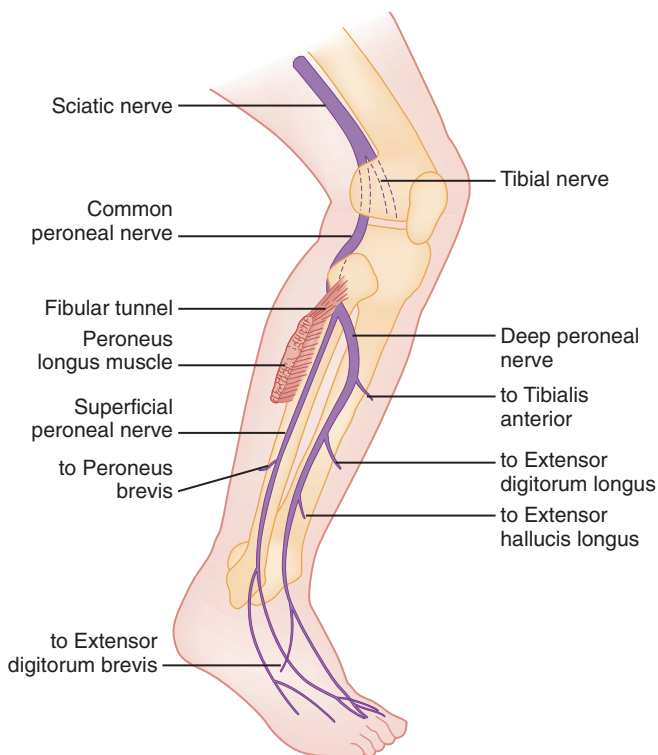Transient (polycythemia vera)
Cryoglobulinemia (hepatitis C)

Vasculitis

Mononeuropathy multiplex is strongly associated with vasculitis, which is the most common indication for sural nerve biopsy in most series. However, because diabetes mellitus is far more prevalent than vasculitis, the most common cause of mononeuropathy multiplex among ED patients is diabetes.

Diabetes Mellitus

Although the role of ischemia in diabetic neuropathies is controversial, evidence for a vascular cause is stronger in the asymmetrical diabetic multiple mononeuropathies than in the more common DSPNs seen in diabetes.

Lyme Disease

The PNS manifestations of Lyme disease can be divided into early and late. The early PNS syndromes commonly include facial nerve involvement (rarely other cranial nerve palsies) and radiculoneuritis. Late PNS involvement occurs as a DSPN, mononeuropathy multiplex, or radiculoneuropathy. The most common neurologic abnormality in Lyme disease is unilateral or bilateral facial nerve palsy, usually occurring within a month of exposure. Patients may also complain of headache and constitutional symptoms. Early in the course of Lyme disease, severe neuritic pain may develop in a radicular distribution, often in or near the dermatome where the tick bite occurred. There may also be associated sensory changes, motor weakness, and decreased reflexes consistent with nerve root involvement. Patients with chronic Lyme disease present with sensory symptoms, particularly distal paresthesias in the lower extremities. Less commonly, they develop a picture consistent with mononeuropathy multiplex or a radiculopathy. The latter is much less severe than the early radiculoneuritis of Lyme disease.

The most useful diagnostic tests for patients with suspected Lyme disease are a serum enzyme-linked immunosorbent assay, Western blot, and CSF examination. CSF abnormalities suggestive of Lyme disease are a lymphocytic pleocytosis, elevated protein, and normal glucose. The CSF is almost always abnormal in early radiculitis, sometimes abnormal with isolated facial palsy, and typically normal in chronic Lyme disease. Facial nerve palsy without CSF abnormalities may be treated with oral doxycycline 100 mg twice a day for 2 weeks. Intravenous ceftriaxone is the drug of choice for all other neurologic syndromes associated with Lyme disease. The adult dosage is 2 g/day, and the pediatric dosage is 75 to 100 mg/kg/day. Treatment with ceftriaxone should be continued for at least 2 weeks.

Type 6: Amyotrophic Lateral Sclerosis

Although *amyotrophic lateral sclerosis* (ALS) and *motor neuron disease* (MND) are often used synonymously, the latter represents a spectrum of diseases ranging from primary lateral sclerosis, in which degeneration is confined to upper motor neurons, to progressive muscle atrophy, in which only lower motor neurons are involved. ALS, which requires the presence of both upper and lower motor neuron findings, resides in the middle of this spectrum, representing the most common form of MND. The incidence of ALS is 1.5 to 2.5 per 100,000.[56]

In ALS, the primary pathologic process in the PNS component of the disease is a neuronopathy of the anterior horn cell. Because this structure is located proximal to the point where

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BOX 105-8	**OBJECTIVE CLINICAL FINDINGS CONSISTENT WITH AMYOTROPHIC LATERAL SCLEROSIS**

Upper motor neuron signs
   Hyperreflexia
      Sustained clonus, especially at ankle
      Finger flexors and jaw jerk
   Spasticity, especially of gait
   Positive Babinski sign
Lower motor neuron signs
   Positive motor phenomena
      Fasciculations
      Cramps
   Negative motor phenomena
      Asymmetrical distal weakness
      Atrophy
Combined upper and lower motor neuron signs
   Dysarthria
   Dysphagia
   Respiratory compromise

---

motor and sensory fibers merge to form mixed spinal nerve roots, the signs and symptoms of MND are purely motor (see Fig. 105-2). In the CNS, there is a loss of Betz cells from the motor cortex with secondary degeneration of the corticospinal tracts. Box 105-8 lists some representative upper, lower, and mixed motor signs. Patients typically demonstrate asymmetrical distal weakness without sensory findings. Positive motor phenomena in the form of fasciculations are found in almost all patients at diagnosis but are rarely an initial complaint. Although there is electrophysiologic evidence of autonomic involvement in ALS, this is generally subclinical.

Most patients with an asymmetrical, distal, pure motor neuropathy have ALS, for which only supportive treatment is currently available. However, there are some preliminary studies of recombinant human insulin–like growth factor 1 that have shown marginal improvement in this otherwise fatal disease.[57] All patients in whom this diagnosis is suspected should be referred for electrophysiologic confirmation against standardized criteria. Confirmation is particularly important because multifocal motor neuropathy, a rare disease that masquerades as ALS, responds dramatically to cyclophosphamide and immunoglobulin administration.[58]

Type 7: Sensory Neuronopathy (Ganglionopathy)

This category of peripheral neuropathy is characterized by a selective or predominant involvement of the dorsal root ganglion, producing a relatively pure sensory syndrome analogous to the pure motor syndrome of ALS. Although all sensory modalities are affected, proprioception is profoundly altered, leading to sensory ataxia and loss of DTRs without weakness. The distribution is typically asymmetrical and distal at the outset, but depending on severity and extent of progression, it may become functionally symmetrical. Sensory ganglionopathies can now be confirmed by MRI of the spinal cord and surrounding areas, showing degeneration of central sensory projections that localize the disease process to the dorsal root ganglion.[59] Some of the more common causes of this type of peripheral neuropathy are listed in Box 105-9.

BOX 105-9 SENSORY NEURONOPATHIES (GANGLIONOPATHIES)

Herpes
    Herpes simplex I and II
    Varicella zoster (shingles)
Inflammatory sensory polyganglionopathy (ISP)
Paraneoplastic
Primary biliary cirrhosis
Sjögren's syndrome (keratoconjunctivitis sicca)
Toxin induced
    Pyridoxine (vitamin B_6) overdose
    Metals
        Platinum (cisplatin)
        Methyl mercury
Vitamin E deficiency

BOX 105-10 ANCILLARY DIAGNOSTIC TESTING IN SUSPECTED PERIPHERAL NEUROPATHY

Obtained in most patients
    Complete blood count (CBC)
    Erythrocyte sedimentation rate (ESR)
    Glucose
    Creatine kinase (CK)
    Creatinine
Obtained only if indicated
    Human chorionic gonadotropin (HCG)
    Magnesium
    Phosphate
    Vitamin B_{12}
    Hemoglobin A_{1c}
    Serum protein electrophoresis (SPEP) with immune
        fixation electrophoresis (IFE)
    Venereal Disease Research Laboratory (VDRL) or rapid
        plasma reagin (RPR) screen with fluorescent
        treponemal antibody-absorption (FTA-ABS) test, as
        appropriate
    Thyroid function
    HIV
    Lyme enzyme-linked immunosorbent assay (ELISA) and
        Western blot
    Rheumatoid factor and antinuclear antibody
    Blood, urine, hair, or nails for metal, depending on
        suspected chronicity of exposure
    Specific serum antibodies to components of peripheral
        nervous system
    Cerebrospinal fluid for cells, protein, Lyme titer
    Electrodiagnostic testing
        Nerve conduction studies
        Electromyography
    Neurodiagnostic imaging
        Magnetic resonance imaging
        Computed tomography
        Sonography
    Quantitative sensory testing
    Nerve biopsy
        Sural
        Intraepidermal nerve fiber density

■ ANCILLARY DIAGNOSTIC TESTING

Relatively few blood tests contribute to the diagnosis of peripheral neuropathy, and only a small number of these are available in the ED. CSF analysis may be helpful in GBS and Lyme disease. Additional tests that may be indicated in patients referred for evaluation are listed in Box 105-10, along with others that may be ordered selectively, depending on the clinical picture. Expensive batteries of tests purporting to measure a wide variety of antibodies to components of peripheral neuropathies are commercially available but have not been shown to be useful as screening tests.

KEY CONCEPTS

■ In the emergency department, it is not usually possible to arrive at the diagnosis of a specific peripheral neuropathy because of the need for confirmatory ancillary testing that is beyond the scope of emergency practice. Rather, the focus should be on identifying one of seven categorical patterns of peripheral neuropathy, shown in Figure 105-1 and listed in Table 105-1, after other non-PNS causes have been eliminated.

■ One of these seven patterns can usually be identified by combining three clinical features that are readily obtainable from a goal-directed history and physical: (1) right-left symmetry or asymmetry, (2) proximal-distal location, and (3) sensorimotor modalities affected. This approach is summarized as an algorithm in Figure 105-1.

■ Identification of one of the seven types of peripheral neuropathy determines the need for ancillary diagnostic testing, therapeutic intervention, disposition, and the timing of neurologic referral.

■ Respiratory compromise is the primary life-threatening event seen in some peripheral neuropathies; GBS is by far the most common peripheral neuropathic cause of respiratory arrest.

■ Any patient with symmetrical weakness, distributed both proximally and distally, with loss or diminution of DTRs and variable sensory abnormalities should be treated as having GBS.

The references for this chapter can be found online by accessing the accompanying Expert Consult website.