Peripheral nerve disorders can result in varied findings, including proximal or distal weakness, symmetric or asymmetric symptoms, and acute or chronic manifestations. Motor symptoms range from weakness to paralysis, whereas sensory symptoms range from numbness to pain.

Evaluation of peripheral nerve disorders requires an understanding of the anatomy of the spinal cord and the peripheral nervous system (Fig. 97.1). The peripheral nervous system is composed of 12 cranial nerves and 31 spinal nerves. Spinal nerves are formed from motor fibers whose cell bodies reside in the ventral horn of the spinal cord and from sensory fibers whose cell bodies are found in the dorsal root ganglion. The motor and sensory fibers join to form one nerve as it exits the spinal canal. Spinal nerves from several spinal levels merge at the cervical, brachial, lumbar, and sacral plexuses. Peripheral nerves originate either at these plexuses or, if they are formed from nerves of only one spinal level, as they exit the vertebral foramina.

Peripheral nerves consist of mixed fibers with variable amounts of motor, sensory, and autonomic fibers; small and large fibers; and myelinated and unmyelinated fibers. These fibers, which are surrounded by endoneurial fluid and covered in perineurium, form fascicles that are bundled together by the epineurial sheath. This sheath forms a protective barrier akin to the blood-brain barrier in the central nervous system.

In patients with symptoms concerning for a peripheral nerve disorder, the history and physical examination are important in localizing the lesion. Spinal nerve, or nerve root, lesions are called radiculopathies and result in myotomal weakness or dermatomal sensory loss. Plexus lesions can be variable, with symptoms that cross myotomes and dermatomes or involve multiple peripheral nerves. Symptoms depend on which trunk or cord is involved. Peripheral nerve lesions cause weakness and sensory loss that is limited to a specific peripheral nerve.

Systemic diseases affect the peripheral nervous system as well, and multiple peripheral nerves may be involved. Examples include disorders of the neuromuscular junction (NMJ), demyelinating disorders, diabetes, and toxic effects of drugs or chemicals (Box 97.1).

### PATHOPHYSIOLOGY

Spinal nerve compression results in radiculopathy, radicular pain, or both. Radiculopathy is due to blocked conduction along a spinal nerve and results in a neurologic deficit: dermatomal sensory loss or myotomal weakness. Radicular pain is due to irritation or inflammation of the spinal nerve, neurologic deficits are absent, and patients have purely painful symptoms that may not be isolated to a dermatome.
Causes of spinal nerve compression are varied; if a patient is younger than 50 years, the symptoms are more likely to be caused by disk herniation, and if older than 50 years, by degenerative changes.

**PRESENTING SIGNS AND SYMPTOMS**

As noted, sensory loss and weakness follow a dermatomal or myotomal distribution. Diminished reflexes may also assist in determining the nerve root that is involved (Table 97.1).

In the cervical region, C6 and C7 are the most commonly affected, with higher roots less frequently involved. This is true for the lumbosacral spinal nerves as well, with more patients having signs in the L5-S1 distribution. Sciatica is a particularly common syndrome of radicular pain and involves more than one of the L2-S1 spinal nerves.

**DIAGNOSTIC TESTING**

A careful history and physical examination will help localize the symptoms of a radiculopathy. The straight leg raise should be used to test for lumbosacral involvement. While the patient is lying supine, the leg is raised with the knee in extension. The test is considered positive for spinal nerve involvement when symptoms are reproduced within 60 degrees of elevation.

If a patient has solely radicular pain, imaging may not be necessary because the symptoms resolve in 60% to 80% of patients within 6 to 12 weeks with conservative treatment. In patients whose symptoms fail to resolve, progress, or involve sensory loss or weakness, either computed tomography or magnetic resonance imaging (MRI) is indicated. Patients should also undergo imaging if they have a history of malignancy, long-term steroid use, human immunodeficiency virus (HIV) infection, diabetes, acute loss of neurologic function, or known trauma. In general, MRI is preferred because it has higher soft tissue resolution. For disk disease, it is important to note that the size of a disk herniation does not always correlate with clinical symptoms: patients without evidence of herniation may have significant symptoms, whereas patients with an incidental finding of disk herniation may have no symptoms.

**TREATMENT**

In the acute phase of injury, painful symptoms are typically treated conservatively with nonsteroidal antiinflammatory
most frequent being median mononeuropathy (Fig. 97.2). Women older than 55 years are most commonly affected, with a 4.6% prevalence in women and 2.8% in men. The second most frequent cause is ulnar mononeuropathy; specifically, cubital tunnel syndrome. Other common peripheral mononeuropathies include involvement of the radial nerve in the upper extremity and the peroneal and lateral cutaneous femoral nerves in the lower extremity.

PATHOPHYSIOLOGY, PRESENTING SIGNS AND SYMPTOMS, AND DIAGNOSTIC TESTING

For mononeuropathies, the history and physical examination largely lead to the appropriate diagnosis. Findings in patients with common mononeuropathies and diagnostic maneuvers are presented in Table 97.2. In patients with a history of trauma or acute symptoms, plain films may be necessary to rule out fracture or dislocation. Patients with subacute or chronic symptoms should be asked about chronic conditions. Mononeuropathies can occur with several systemic diseases, including diabetes mellitus, amyloidosis, HIV, and states that cause edema, such as pregnancy. Outpatient testing may be more appropriate for individuals with chronic symptoms. MRI or electrodiagnostic testing such as electromyography or nerve conduction studies may be necessary, and the patient should be referred to a neurologist. MRI may demonstrate chronic nerve injury, whereas electrodiagnostic testing may show slowing of nerve conduction. These studies may aid in deciding whether surgical repair or decompression is necessary for certain syndromes.

Mononeuropathies

EPIDEMIOLOGY

As with radiculopathy, compression of peripheral nerves is the most common cause of peripheral mononeuropathy, the drugs (NSAIDs) and physical therapy. Low-quality evidence suggests that there is no difference between bed rest and activity for patients with sciatica. However, a randomized controlled trial showed that the addition of physical therapy is more effective than counseling and pain medications alone, although it may not be as cost-effective. Persistent or severe symptoms may require more invasive measures, from local corticosteroid injections to neurosurgical intervention. For the cervical spinal nerves, some evidence has shown that conservative therapy consisting of pain control has favorable short-term outcomes when compared with surgical intervention, although long-term outcomes appear to be similar. Surgical outcomes can be dependent on the mechanism of injury; for example, with spinal stenosis, 70% of patients will still have persistent loss of function. Chronic pain symptoms may be treated with medications used for neuropathic pain, such as antidepressants or anticonvulsants.

Fig. 97.2 Anatomy of the carpal tunnel.
### TREATMENT

Primary treatment should be aimed at the precipitating event for both acute and chronic mononeuropathy.

With acute mononeuropathy, the primary cause of injury is generally trauma. Fractures and dislocations should be reduced appropriately and immobilized with the guidance of surgical consultation.

Initial treatment of chronic mononeuropathy is typically conservative and supportive. Modification of behavior is a key component of treatment and prevention of further injury. For carpal tunnel syndrome, behavior modification includes weight loss and avoidance of caffeine, nicotine, and alcohol. Patients should be instructed to decrease any possible trauma related to repetitive use by making changes in workplace ergonomics, reducing repetitive use, and changing posture. Some neuropathies may require supportive devices; for example, the carpal tunnel may benefit from wearing a wrist splint, the ulnar nerve from wearing a sling or a long arm posterior splint, the radial nerve from wearing a volar splint, and the peroneal nerve from wearing a posterior splint. NSAIDs are typically prescribed for relief of symptoms, although they may be ineffective without appropriate

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### Table 97.2 Specific Peripheral Mononeuropathies

<table>
<thead>
<tr>
<th>PERIPHERAL NERVE</th>
<th>SYNDROME</th>
<th>COMPRESSION SITE</th>
<th>CAUSES</th>
<th>SIGNS AND SYMPTOMS</th>
<th>TESTING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median</td>
<td>Carpal tunnel</td>
<td>Carpal tunnel: by carpal bones and the flexor retinaculum (see Fig. 97.2)</td>
<td>Repetitive use, trauma</td>
<td>Burning, numbness, pain in the palmar aspect of the 1st, 2nd, 3rd, and radial aspect of the 4th finger</td>
<td>Tinel sign: symptoms with tapping on the palmar aspect of the wrist Phalen sign: symptoms when the wrists is held in flexion for 60 seconds</td>
</tr>
<tr>
<td>Ulnar</td>
<td>Cubital tunnel</td>
<td>Cubital tunnel: behind the medial epicondyle</td>
<td>Repetitive use, trauma</td>
<td>Tingling of the 5th and lateral aspect of the 4th fingers; weakness of intrinsic muscles of the hand</td>
<td>Tinel sign: symptoms with tapping on the elbow at the cubital tunnel Elbow flexion sign: symptoms when the elbow is flexed and the wrist is extended for 3 min Froment sign: the thumb interphalangeal joint flexes when attempting to hold a card between the 1st and 2nd digits</td>
</tr>
<tr>
<td>Guyon’s canal, handlebar palsy</td>
<td>At the Guyon canal at the wrist, bounded by the pisiform and hamate bones</td>
<td>Repetitive use, trauma</td>
<td>Weakness of the intrinsic muscles of the hand</td>
<td>Unable to abduct the fingers</td>
<td></td>
</tr>
<tr>
<td>Radial</td>
<td>Saturday night palsy</td>
<td>Upper part of the arm at the spiral groove</td>
<td>Compression injury or midshaft humeral fracture</td>
<td>Wristdrop, dorsal sensory loss in the hand</td>
<td></td>
</tr>
<tr>
<td>Radial tunnel syndrome</td>
<td>Sensory branch at the elbow</td>
<td>Repetitive motion</td>
<td>Forearm pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>—</td>
<td>Motor branch at the elbow</td>
<td>Radial fracture, elbow fracture or dislocation</td>
<td>Extensor muscles of the hand more than the wrist</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peroneal</td>
<td>—</td>
<td>Below the fibular head</td>
<td>Compression (crossing the legs, rapid weight loss, casting, any source of direct pressure on the fibular head, fracture, knee dislocation)</td>
<td>Footdrop, steppage gait</td>
<td></td>
</tr>
<tr>
<td>Lateral cutaneous femoral</td>
<td>Meralgia paresthetica</td>
<td>Compression (inguinal ligament, seat belt, tight pants, pregnancy)</td>
<td>Anterolateral thigh pain, paresthesias, numbness; no motor component</td>
<td>Worsening pain with hip extension, pain with palpation of the inguinal ligament</td>
<td></td>
</tr>
</tbody>
</table>
behavioral modification. In patients with a systemic disease, the primary process should be treated. Diuretics may be given if edema is believed to be contributing significantly to the patient’s symptoms. More invasive procedures, such as local nerve block for meralgia paresthetica or surgical decompression for carpal tunnel syndrome, are reserved for severe cases.

**Autoimmune Disorders**

**GUILLAIN-BARRÉ SYNDROME**

**EPIDEMIOLOGY**

Guillain-Barré syndrome (GBS) is also known as acute inflammatory demyelinating polyradiculopathy or Landry-Guillain-Barré syndrome. Its worldwide incidence is 0.6 to 4 per 100,000 individuals annually.\(^\text{14}\)

**PATHOPHYSIOLOGY**

GBS is characterized by immune-mediated destruction of the myelin sheath of peripheral nerves. Biopsy frequently reveals a mononuclear inflammatory infiltrate. Although its exact etiology remains unknown, two thirds of cases are preceded by an infection. Associations have been made with viral or febrile illness, Campylobacter jejuni infection, vaccinations, and even surgery or trauma. GBS is a monophasic illness with progressive symptoms that reach a nadir in 2 to 4 weeks. Recovery can vary from weeks to a year. Mortality has been reported in 4% to 15% of patients, whereas another 10% to 20% have significant residual motor dysfunction.

**PRESENTING SIGNS AND SYMPTOMS**

**CLASSIC GUILLAIN-BARRÉ SYNDROME**

Classic GBS is preceded by a viral prodrome and followed by acute or subacute ascending symmetric weakness or paralysis and loss of the deep tendon reflexes. Paralysis may ascend to the diaphragm and compromise respiratory function to the extent that mechanical ventilation is required. One third of patients will require intubation and 15% will experience dysautonomia. Specific findings are strongly suggestive of this diagnosis (**Box 97.2**).

**VARIANTS OF GUILLAIN-BARRÉ SYNDROME**

**Acute Motor Axonal Neuropathy**

This purely motor form of GBS is associated with *C. jejuni* infection and is more often preceded by diarrhea than by a viral prodrome. It results in axonal injury rather than demyelination.

**Acute Motor and Sensory Axonal Neuropathy**

This variant involves loss of both motor and sensory function. As with acute motor axonal neuropathy, electrodiagnostic testing reveals axonal degeneration.

**Miller-Fisher Syndrome**

Identified in 1956, Miller-Fisher syndrome is characterized by ophthalmoplegia, ataxia, and decreased or absent reflexes. Patients have significantly less weakness and a milder course than do those with classic GBS.

**DIAGNOSTIC TESTING**

It is critical that respiratory function be assessed early and often because maintenance of airway protection well in advance of respiratory compromise decreases the incidence of aspiration and other complications of emergency intubation (**Box 97.3**). The most studied monitoring parameter is vital capacity (VC), with normal values ranging from 60 to 70 mL/kg. However, a simple bedside assessment of respiratory status can be obtained by having the patient count from 1 to 25 with a single breath and trending the values over time.

If the patient’s condition does not initially meet the criteria for intubation, VC should be monitored closely—every hour for the first 4 hours and then every 4 hours.\(^\text{15}\)

Lumbar puncture often reveals the classic “albuminocytologic dissociation” in which cerebrospinal fluid (CSF) protein is high without pleocytosis. The protein level is greater than 45 mg/dL. Cell counts are typically below 10/mL and usually

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**BOX 97.2 Findings Suggesting Guillain-Barré Syndrome**

Relative symmetry of symptoms  
Mild sensory signs and symptoms  
Cranial nerve involvement  
Autonomic dysfunction  
Absence of fever at onset  
Cytoalbuminologic dissociation of cerebrospinal fluid  
Typical electrodiagnostic findings  
Progression over days to weeks  
Recovery beginning 2 to 4 weeks after cessation of progression

**BOX 97.3 Indications for Intubation in Patients with Guillain-Barré Syndrome**

Rapid progression of respiratory compromise  
Vital capacity less than 20 mL/kg  
Negative inspiratory force less than −30 cm H\(_2\)O  
Greater than a 30% decrease in either vital capacity or negative inspiratory force in the first 24 hours  
Autonomic instability
Myasthenia gravis has a prevalence of 50 to 125 individuals per million. The age at onset is bimodal: the first peak involves persons in their 20s to 30s, with women being affected more than men, and the second peak occurs during the sixth and seventh decades, with men being affected more than women.

**Pathophysiology**

Myasthenia gravis has many causes, but they all lead to the formation of autoantibodies directed against nicotinic acetylcholine receptors (AChRs) at the NMJ ([Fig. 97.3](#)). This results in autoimmune destruction of AChRs through complement-mediated destruction, as well as increased endocytosis by muscle cells. The autoantibodies further compete with acetylcholine (ACh) for binding at the remaining receptors. Thus with repeated stimulation of the same muscle, fewer and fewer sites are available and fatigue develops.

**Presenting Signs and Symptoms**

**New Onset**

Muscular weakness and fatigability are the hallmarks of myasthenia gravis. When patients are seen in the emergency department (ED) with an initial manifestation of the disease, the symptoms usually consist of mononeuropathy involving the ocular or bulbar muscles. The typical finding is ptosis, diplopia, or blurred vision. Ocular muscle weakness may be the first sign in up to 40% of patients, although it will develop in 85% in due course. When present, ptosis is often worse toward the end of the day. When the bulbar muscles are involved, dysarthria or dysphagia occurs. Respiratory failure is a rare initial sign. Nevertheless, up to 17% of patients may have weakness of the muscles of respiration.
ACUTE MYASTHENIC CRISIS

Acute myasthenic crisis is defined as respiratory failure eventually requiring mechanical ventilation. It occurs in 15% to 20% of patients, generally within the first 2 years of the disease. With the use of better and more aggressive techniques in the intensive care unit, mortality has declined tremendously.

Underlying infection, aspiration, and changes in medications most often trigger myasthenic crisis, but the precipitant may not be found in up to 30% of cases (Box 97.4).

Some patients experience an increase in weakness when starting chronic steroid therapy. Other precipitants include surgery and pregnancy.

As with GBS, the initial step in managing patients in myasthenic crisis is assessing respiratory status and securing the airway, if necessary. A patient who is complaining of shortness of breath or difficulty breathing should have VC measured frequently. In contrast to the steady deterioration associated with GBS, patients in myasthenic crisis may have fluctuating weakness. In these patients a lower VC of 15 mL/kg is considered an indication for intubation, but the trend of their respiratory function is more useful than a single measurement.


CONGENITAL MYASTHENIA GRAVIS

Approximately 12% of pregnant women with myasthenia gravis will give birth to symptomatic infants because of placental transfer of autoantibodies. An infant’s symptoms develop within 2 days of life and include impaired sucking, weak cry, limp limbs, and rarely, respiratory insufficiency. The symptoms disappear within days or weeks as antibody titers in the infant decline. In severe cases of respiratory failure, intubation is necessary, and exchange transfusion should be considered.

DIAGNOSTIC TESTING

The diagnosis is based on clinical findings, bedside testing, and serologic studies.

BEDSIDE TESTING

The edrophonium test is a pharmacologic test involving the use of a short-acting acetylcholinesterase (AChE)-blocking agent that can be done at the patient’s bedside. The test confirms the diagnosis of myasthenia if the ptosis improves after the intravenous administration of edrophonium. An initial dose of 1 mg is given and the patient is observed for an adverse reaction or improvement in the symptoms of ptosis, medial rectus weakness, or dysphonia. If unimproved in 30 to 90 seconds, a second dose of 3 mg is given. Another 3-mg dose of edrophonium is administered if no response is seen after 30 to 60 seconds. If there is still no response, a final dose of 3 mg is given, for a total maximum dosage of 10 mg. Edrophonium may result in a severe anticholinergic reaction, especially in the elderly, cardiac disease patients, those with chronic obstructive pulmonary disease, or asthmatics. Symptoms include salivation and gastrointestinal cramping but may be more severe, such as bradycardia, bronchorrhea, bronchospasm, and worsening weakness. Because of the potential for bradycardia, atropine should be at the bedside during edrophonium testing.

The ice test is another bedside test that can be used to quickly confirm the diagnosis. Cooling decreases the symptoms of myasthenia gravis, whereas heat exacerbates them. In this test the distance between the upper and lower lids is measured before the application of an ice pack for 2 to 3 minutes to the most severely affected eye.

SEROLOGIC TESTING

Receptor antibody testing is positive in 80% to 90% of patients. Many patients found to be seronegative nonetheless respond to traditional therapy aimed at lowering levels of circulating antibodies, thus suggesting that antibodies are present but not detected.

TREATMENT

ACETYLCOLINESTERASE INHIBITORS

AChE inhibitors such as pyridostigmine and neostigmine are the backbone of outpatient chronic therapy and provide symptomatic improvement. This class of drugs inhibits the hydrolysis of ACh, which leads to an increased circulating concentration of ACh to compete with the antibody for AChR binding sites. The most common side effects are those of excessive cholinergic stimulation as mentioned earlier. These drugs are not directed at the underlying immunologic basis of the disease and are often used as adjunctive therapy to control symptoms while allowing time for other therapy to take effect, after which they are discontinued.

The use of intravenous pyridostigmine in the setting of acute exacerbation of myasthenia gravis is controversial. Some evidence indicates that its use may complicate ventilation by worsening pulmonary secretions. Consequently, cholinergic drug therapy should be discontinued during a myasthenic crisis. In addition, a cholinergic crisis characterized by acute decompensation and excessive muscarinic stimulation may be caused by excessive medication with AChE inhibitors. Cholinergic crisis should be distinguished from an exacerbation of the disease by muscarinic findings on physical examination: excessive sweating, salivation, lacrimation, miosis, tachycardia, and gastrointestinal hyperactivity.

IMMUNOSUPPRESSION

Immunosuppressant drugs are often used for chronic control of the symptoms of myasthenia gravis. They have no role in the acute management of myasthenic crisis, although they may be started before extubation of patients recovering from
a crisis. Corticosteroids, azathioprine, and cyclosporine have all been used.

**THYMECTOMY**

Thymectomy in otherwise well patients between adolescence and 60 years of age results in remission or improvement in up to 50% of cases. However, the onset of improvement after thymectomy is often delayed for 2 to 5 years.

**IMMUNOMODULATORY THERAPY**

Plasmapheresis and IVIG are reserved for patients with severe exacerbations or are administered preoperatively to patients with stable myasthenia gravis. Of patients treated with IVIG, 50% to 90% have some improvement following infusion. These treatment modalities should be administered in conjunction with a neurologist.

**LAMBERT-EATON MYASTHENIC SYNDROME**

**EPIDEMIOLOGY**

Lambert-Eaton myasthenic syndrome (LEMS) is relatively uncommon, with a prevalence of 1 in 100,000 individuals. The disease occurs predominantly in those older than 50 years, with both genders affected equally.

**PATHOPHYSIOLOGY**

In healthy presynaptic neurons, depolarization opens channels that allow calcium to enter. This results in ACh-filled vesicles fusing with the presynaptic membrane and release of ACh into the synapse. ACh then stimulates the postsynaptic neuron, which results in transmission of the impulse from one neuron to the next.

LEMS is an autoimmune presynaptic disorder of the NMJ. IgG autoantibodies bind to the presynaptic calcium channels, thereby inhibiting entry of calcium into the cell during depolarization. The net effect is decreased release of ACh and absent or diminished transduction of signal to the postsynaptic membrane. This disease affects not only the NMJ but also muscarinic receptors and results in autonomic dysfunction.

Frequently, this disease is associated with other pathology. Malignancies are often seen with LEMS, with upward of 70% of cases having a concomitant malignancy. The most common association is with small cell lung cancer: 62% of cases have this link. Diagnosis of the malignancy may come after the diagnosis of LEMS. Because LEMS is an autoimmune disorder, it is also associated with other autoimmune disorders, including hypothyroidism, pernicious anemia, and celiac disease.

**PRESENTING SIGNS AND SYMPTOMS**

The typical symptoms involve weakness of the proximal muscles, with the lower extremities being affected more than the upper ones, and decreased or absent reflexes. Bulbar symptoms may be present, though with significantly less frequency and severity than in myasthenia gravis. Autonomic symptoms are reported in 75% of patients; symptoms include dry eyes and mouth, impotence, constipation, and orthostatic hypotension.

Patients often have symptoms of weakness with minimal associated disability; the symptoms frequently improve with repetitive use because calcium is able to accumulate in the presynaptic neuron. This is demonstrated with the Lambert sign, in which there is a progressive increase in grip when maintained over a few seconds. It can also be seen in reflexes, which improve after exercising the muscle.

**DIAGNOSTIC TESTING**

Testing specific to this disease is typically not conducted in the ED, and a neurologist should be consulted for evaluation. Antibody testing is positive in 85% of patients. LEMS may develop up to 2 years before the diagnosis of a malignancy, and therefore patients should be evaluated for malignancy.

**TREATMENT**

The most effective treatment of LEMS involves treatment of the primary malignancy if present. Other treatments have been used over the years, including immunosuppressants such as prednisone, pyridostigmine (AChE inhibitor), plasma exchange, IVIG, and 3,4-diaminopyridine (3,4-DAP). 3,4-DAP is an oral medication that blocks potassium channels and prevents repolarization and removal of calcium from the cell. Evidence for the efficacy of these therapies is limited because the disease itself is uncommon, although randomized controlled trials have found improvement with IVIG and 3,4-DAP.

**BOTULISM**

**EPIDEMIOLOGY**

Botulism is a toxin-mediated illness that can cause acute weakness leading to respiratory failure. In 2009, the Centers for Disease Control and Prevention reported 121 cases of botulism: 69% were categorized as infantile, 19% as wound, and 9% as food-borne botulism. In 2009, of the 23 cases of wound botulism, 21 resulted from injection drug use.

**PATHOPHYSIOLOGY**

*Clostridium botulinum*, the causative organism, is an anaerobic spore-forming bacterium. Three of eight known toxins...
produced by \textit{C. botulinum} cause human disease: toxin types A, B, and E. Most cases of botulism are isolated events associated with improperly preserved canned foods, although the incidence of botulism from wound infections has recently increased. Toxin type E is associated with preserved or fermented fish and marine mammals. These are the most important sources of botulism in Alaska, Japan, Russia, and Scandinavia.\textsuperscript{26}

The botulinum toxin binds irreversibly to the presynaptic membrane of peripheral and cranial nerves and inhibits release of ACh at the peripheral nerve synapse. As new receptors are generated, patients improve.

\section*{PRESENTING SIGNS AND SYMPTOMS}

\subsection*{CLASSIC BOTULISM}

The disorder occurs at the NMJ, so neither sensory deficit nor pain occurs. Symptoms begin 6 to 48 hours after ingestion of the tainted food. The classic finding is a descending, symmetric paralysis. The nerves and muscles often affected first are the cranial nerves and bulbar muscles, which results in diplopia, dysarthria, dysphagia, and blurry vision. The deep tendon reflexes are normal or diminished. Signs and symptoms consistent with gastroenteritis may develop: nausea, vomiting, abdominal cramps, diarrhea, and constipation.

Because the toxins cause decreased cholinergic output, anticholinergic signs may be seen in the form of constipation, urinary retention, dry skin and eyes, and increased temperature. Pupils are often dilated and not reactive to light—an important point of differentiation from myasthenia gravis.

\subsection*{INFANTILE BOTULISM}

Infantile botulism occurs as a result of the ingestion of \textit{C. botulinum} spores that are able to germinate and produce toxin in the high pH of the gastrointestinal tract of infants (the same spores are not active in the gut of adults because of the lower pH). It occurs in infants between the age of 1 week and 11 months and has been implicated as a cause of sudden infant death syndrome. Clinical findings include constipation, poor feeding, lethargy, and weak cry; consequently, this diagnosis must be included in the differential diagnosis of a “floppy” infant.

\section*{DIAGNOSTIC TESTING}

The diagnosis is based on clinical findings and exclusion of other processes. The toxin can be identified in both serum and stool, but the assay is not commonly available in most hospitals and thus requires a prolonged turnaround time. If the suspected food source is available, it should also be tested for the toxin.

\section*{TREATMENT}

Treatment is initially focused on evaluating respiratory effort and securing the airway if respiratory compromise has occurred. The course of the disease can be shortened by administering botulinum antitoxin. A trivalent equine antitoxin is available from the Centers for Disease Control and Prevention, as well as from local poison control centers. Skin testing to assess for horse serum sensitivity should be carried out before administration.

\section*{DIABETIC PERIPHERAL NEUROPATHY}

\subsection*{EPIDEMIOLOGY}

A common complication of diabetes, diabetic peripheral neuropathy has a varied prevalence ranging from 34\% to 60\%, although higher rates often include asymptomatic neuropathies. It is a highly variable entity that is composed of several subsets. Of the various subsets of diabetic neuropathy, distal symmetric polyneuropathy is the most common, with up to 54\% of patients with diabetic neuropathy having this variant. It is seen in patients with type 1 diabetes after 5 years and early in the course of type 2 diabetes.\textsuperscript{27,28}

\subsection*{PATHOPHYSIOLOGY}

Diabetic peripheral neuropathy encompasses any neuropathy in a diabetic patient not attributable to other causes. Although the most common form is distal symmetric polyneuropathy, diabetes also leads to focal and autonomic neuropathies. It is accompanied by significant morbidity: the most common cause of nontraumatic amputation is injury resulting from the impaired sensation associated with diabetic peripheral neuropathy that fails to heal because of the impaired blood flow in patients with diabetic vasculopathy.

Hyperglycemia affects the peripheral nerves by several proposed mechanisms:

1. Oxidative stress
2. Glycosylation of nerve proteins
3. Changes in the diabetic vasculature resulting in increased resistance and decreased flow to the peripheral nerves

Motor, sensory, and small and large fibers can all be involved. Diabetic peripheral neuropathy is an example of a distal axonopathy resulting in length-dependent “dying back” of the affected nerves. This dying-back phenomenon produces the typical stocking-and-glove distribution of diabetic neuropathy.\textsuperscript{29}

\section*{PRESENTING SIGNS AND SYMPTOMS}

Several neuropathic syndromes can be found in diabetic patients and are often present concurrently (Table 97.3). For example, patients may have a sensorimotor polyneuropathy with subsequent development of a mononeuropathy of the upper extremity.\textsuperscript{30}

\section*{TREATMENT}

Disease modification has the greatest effect on the progression of diabetic neuropathy; although the cause is multifactorial, a clear relationship between glycemic control and neuropathy exists. The Diabetes Control and Complications Trial showed
a 60% reduction in risk for the development of neuropathy with tight glycemic control.\(^{31}\)

Foot care should be stressed to the patient because neuropathy-associated anesthesia may result in inadvertent trauma. These injuries, coupled with impaired healing from diabetic vasculopathy, can result in ulcers, cellulitis, and even amputation.

Management of symptoms is the patient’s most immediate concern. NSAIDs may alleviate discomfort but are relatively contraindicated in diabetic patients. Narcotics carry addictive potential. Off-label use of tricyclics, antidepressants, anticonvulsants, and topical capsaicin have all proved beneficial (Table 97.4).\(^ {32,33}\)

### HUMAN IMMUNODEFICIENCY VIRUS–ASSOCIATED PERIPHERAL NEUROPATHY

#### EPIDEMIOLOGY

Peripheral nervous system disease associated with HIV infection most commonly takes the form of a distal sensory polyneuropathy. The prevalence of symptomatic patients is 35%, although an additional 20% of asymptomatic patients have electrophysiologic evidence of disease.\(^ {34}\)

#### PATHOPHYSIOLOGY

The distal peripheral neuropathy associated with HIV disease has two causes. There does not appear to be direct nervous
invasion by HIV, although proteins produced by the virus may have associated neurotoxicity. The resultant inflammatory mediators, including macrophages and cytokines, probably play a role as well. Since the introduction of highly active antiretroviral therapy (HAART), a second proposed mechanism has implicated mitochondrial toxicity because of the medications themselves. Both causes primarily affect small unmyelinated fibers and may progress to involve larger myelinated fibers. The neuropathy demonstrates a dying-back axonal pattern with distal axonal degeneration.35

PRESENTING SIGNS AND SYMPTOMS

The initial signs and symptoms may be similar to those found with diabetic peripheral neuropathy, thus making it difficult to distinguish between them. Patients typically have the symptom of painful feet, usually without associated weakness. Physical examination will probably demonstrate decreased sensation distally, as well as diminished deep tendon reflexes.

DIAGNOSTIC TESTING

Before HIV-associated peripheral neuropathy is diagnosed, other causes such as diabetes, vitamin B12 deficiency, or other neurotoxic drugs must be ruled out. The history and physical examination largely drive the diagnosis of HIV-associated peripheral neuropathy. HAART-associated and non–HAART-associated neuropathy can be very difficult to distinguish clinically. Some patients with antiretroviral toxicity may have a more rapidly progressive course, at times temporally linked to the initiation of medication. The most effective diagnostic strategy is cessation of the suspected medication, which may result in improvement or resolution of the symptoms over a period of several weeks.

TREATMENT

The goals of treatment are similar to those for diabetic peripheral neuropathy: control of the primary disease process is important. Potential toxic drugs should be discontinued if appropriate. Painful neuropathy may be managed with NSAIDs, topical analgesics such as lidocaine patches, anticonvulsants, antidepressants, or narcotic analgesics.36 Randomized controlled trials have demonstrated the effectiveness of pain control over placebo along with the use of specific antiepileptics such as gabapentin and lamotrigine.35,37

Follow-up, Next Steps in Care, and Patient Education

Most patients with peripheral nerve disease can be treated on an outpatient basis. For patients with radiculopathy, compression mononeuropathy, or plexopathy, conservative treatment with analgesics and physical therapy is appropriate initially. This conservative treatment may take several weeks to reach maximal effect, which is important to convey to patients to improve compliance. Diabetics in particular may also benefit from referral to podiatry to prevent the complications of diabetic peripheral neuropathy. Patients with persistent symptoms despite a trial of conservative care may require referral for diagnostic testing with MRI or electrophysiologies, pain management, or surgical evaluation.38 Patients with acute injury, such as fracture or dislocation, will require either immediate consultation by or follow-up with an orthopedist or hand specialist.

For patients with GBS, myasthenia gravis, LEMS, or botulism in whom respiratory compromise or aspiration is a concern, close monitoring as an inpatient is required, usually in an intensive care setting. If these patients are being discharged, the effect of changing or initiating pharmacologic therapy should be considered because a number of medications can exacerbate the underlying disease (notably amino-glycosides and immunosuppressants, including prednisone).

SUGGESTED READINGS


REFERENCES

References can be found on Expert Consult @ www.expertconsult.com.
REFERENCES


