temperature) are relatively mild; however, large fiber function (vibration and proprioception) is more severely impaired. Other clinical features include pain (20%), paresthesias (50%), autonomic symptoms (20%), facial weakness (50%), ophthalmoparesis (9%), bulbar weakness, and respiratory failure (25%). Symptoms associated with GBS typically evolve over a 2- to 4-week period, with approximately 90% of patients showing no evidence of progression beyond 4 weeks. For this reason, patients who are seen within several weeks from onset continue to require hospitalization for close observation. Respiratory muscle strength should be monitored with bedside measurements of the forced vital capacity. Intubation should be initiated when the forced vital capacity falls below 15 mL/kg.

Treatment may include either intravenous gammaglobulin (0.4 g/kg/day for 5 days) or plasmapheresis (the exchange of the patient's plasma for albumin) (200 mL/kg over 7 to 10 days). Clinical studies have confirmed equal efficacy between these two therapies, with no additional benefit conferred with combination therapy. Corticosteroids are not effective in GBS. Indications for therapy include inability to ambulate independently, impaired respiratory function, or rapidly progressive weakness.

Clinical features predicting a poor prognosis or prolonged recovery time include rapidly progressive weakness, need for mechanical ventilation, and low-amplitude compound muscle action potentials. The mortality rate remains 5% to 10%, usually because of respiratory complications, cardiac arrhythmia, or pulmonary embolism. With appropriate supportive care and rehabilitation, 80% to 90% of patients recover with little or no disability.

Chronic Inflammatory Demyelinating Polyneuropathy

Chronic inflammatory demyelinating polyneuropathy (CIDP) has been considered the "chronic form" of GBS, because by definition the symptoms must progress for at least 8 weeks. The clinical features include proximal and distal weakness, areflexia, and distal sensory loss. Autonomic dysfunction, respiratory insufficiency, and cranial nerve involvement can occur but are much less common than in GBS. Treatment for CIDP includes the use of oral immunosuppressive agents such as prednisone, cyclosporine, mycophenolate mofetil, and azathioprine. Intravenous immune globulin and plasmapheresis are also indicated for severe or refractory cases.

Diabetic Neuropathy

Diabetes mellitus is the most frequent cause of peripheral neuropathy worldwide. The diabetic neuropathies take many clinical forms, including symmetrical polyneuropathies and a wide variety of individual plexus or nerve disorders.

Diabetes mellitus often causes a slowly progressive, distal, symmetrical sensorimotor polyneuropathy (DSPN). DSPN is uncommon at the time of diagnosis of diabetes, but its prevalence increases with duration of diabetes with a lifetime prevalence of 55% for type 1 and 45% for type 2. The precise pathogenesis is not defined, but, similar to the ocular and renal complications, diabetic neuropathy can be reduced in incidence and in severity by maintaining blood glucose levels close to normal.

Initial symptoms may consist of numbness, tingling, burning, or prickling sensations affecting the feet and toes. Mild distal weakness and gait instability may subsequently develop. The sensory symptoms can then slowly progress to involve a "stocking-glove pattern." The small-fiber dysfunction often produces spontaneous neuropathic pain in which unpleasant sensations can be evoked by normally innocuous stimuli, such as the bed sheets on the toes at night. Continuous burning or throbbing pain may occur, and prolonged walking is often distressing. In severe cases, patients may develop foot ulcers in insensitive areas that necessitate amputation. Autonomic dysfunction is also frequently associated with DSPN including impotence, nocturnal diarrhea, sweating abnormalities, orthostatic hypotension, and gastroparesis.

Other less common neuropathies associated with diabetes include cranial neuropathies (the sixth, third, and rarely fourth nerves), mononeuropathies, mononeuropathy multiplex, radiculopathies, and plexopathies. Diabetic amyotrophy (also known as *diabetic lumbosacral polyradiculopathy*) is a distinctive disorder characterized by severe thigh pain followed by proximal greater than distal lower extremity weakness that progresses over a period of months. The onset is invariably unilateral, but the condition may progress to involve both lower extremities. Physical therapy and effective pain management are essential; treatment with immune modulators is controversial.

Toxic-Induced Neuropathies

Toxic-induced neuropathies constitute a large number of disorders caused by alcohol, drugs, heavy metals, and environmental substances (E-Table 121-3). The majority of toxic neuropathies manifest as a distal sensorimotor axonal neuropathy that chronically progresses over time unless the offending agent is eliminated. Clinical evaluation should focus on the temporal relationship between exposure and the onset of sensory or motor symptoms as well as symptoms of systemic toxicity.

Critical Illness Polyneuropathy

Critical illness polyneuropathy (CIP) is a common cause of failure to wean from a ventilator in a patient with associated sepsis and multi-organ failure. Clinical features include generalized or distal flaccid paralysis, especially involving the lower extremities, depressed or absent reflexes, and distal sensory loss with relative sparing of cranial nerve function. The diagnosis can be confirmed with nerve conduction studies showing evidence of a severe, generalized axonal neuropathy. CSF protein should be normal and, in addition to conduction studies, distinguishes CIP from GBS.

SPECIFIC HEREDITARY POLYNEUROPATHIES

Charcot-Marie-Tooth Disease

The eponym Charcot-Marie-Tooth (CMT) identifies a group of heritable disorders of peripheral nerves that share clinical features but differ in their pathologic mechanisms and the specific genetic abnormalities (E-Table 121-4). CMT is the most common heritable neuromuscular disorder, with an incidence of 17 to 40 cases per 100,000.