TABLE 123-1 DRUGS TO BE AVOIDED OR USED WITH CAUTION IN MYASTHENIA GRAVIS

DRUGS TO BE AVOIDED

- D-penicillamine and α-interferon should not be used in myasthenic patients because they can cause Myasthenia Gravis (MG)
- Botulinum toxin treatment should be avoided as it blocks NMT

DRUGS TO USE ONLY WITH CAUTION AND MONITOR FOR EXACERBATION OF MG SYMPTOMS

- Selected antibiotics, particularly aminoglycosides, telithromycin (Ketek) and ciprofloxacin (many other antibiotics have been reported to increase weakness in occasional patients with MG)
- Magnesium, magnesium salts contained in some laxatives and antacids
- Neuromuscular blocking agents such as succinylcholine and vecuronium should only be used by an anesthesiologist familiar with MG
- Quinine, quinidine or procainamide
- Beta-blockers (propranolol; timolol maleate eyedrops)
- Calcium channel blockers
- Iodinated contrast agents

patients with MG experience refractory symptoms despite optimal treatment. Mortality is currently less than 5%.

LAMBERT-EATON MYASTHENIC SYNDROME (LEMS)

Definition/Epidemiology/Pathology

Lambert-Easton myasthenic syndrome (LEMS) is an acquired, presynaptic neuromuscular transmission disorder caused by antibodies against the P/Q type voltage-gated calcium channel (VGCC). P/Q VGCC antibodies cause reduced Ca^+ influx into the presynaptic nerve terminal resulting in decreased acetylcholine release and neuromuscular transmission failure. LEMS is associated with cancer, usually small cell lung carcinoma, in 60% of cases. LEMS may predate tumor detection by up to 3 years. LEMS is very rare and more common in men (3 : 1).

Clinical Presentation

LEMS should be suspected whenever the triad of muscle weakness, dry mouth, and decreased or absent reflexes is present. Patients have fluctuating weakness and fatigability of proximal limb and trunk muscles, with the lower limbs more severely affected than the upper ones. Difficulty walking is a common symptom. Dysphagia, dysarthria, and ocular symptoms (ptosis, blurred vision, and diplopia) are less common than in MG. Tendon reflexes are hypoactive or absent and may increase following short exercise of the muscle. Autonomic manifestations (dry mouth, impotence, decreased sweating, orthostatic hypotension, and slow pupillary reflexes) occur in 75% of patients.

Diagnosis and Differential Diagnosis

Serum antibodies against P/Q VGCCs are found in nearly all cases of paraneoplastic LEMS, and in about 90% of non-paraneoplastic cases. Electrodiagnostic testing can help confirm the diagnosis by demonstrating reduced CMAP amplitudes in distal hand muscles; CMAP facilitation of at least 100% after 10" maximal voluntary contraction or high frequency RNS (posttetanic facilitation); and CMAP decrement greater than 10% with low frequency RNS. Patients diagnosed with LEMS should be screened and monitored with chest CT for lung cancer, especially if they are smokers and over age 50. LEMS and MG can be differentiated with electrodiagnostic and antibody testing.

Treatment

Symptomatic treatment with 3,4-DAP 5 to 10 mg every 3 to 4 hours and up to a maximum daily dose of 80 to 100 mg is most effective in improving muscle strength in patients with LEMS. Side effects at doses up to 60 mg per day are rare. Acral and perioral paresthesias occur within minutes from a dose and resolve in about 15 minutes. It is contraindicated in patients with seizures. 3,4-DAP is not currently FDA approved in the United States, but it can be obtained in specialized neuromuscular centers. Pyridostigmine 60 mg every 4 hours is also used to improve symptoms. In patients in whom symptoms are not adequately controlled with 3,4-DAP and pyridostigmine, immunomodulation with prednisone, azathioprine, or mycophenolate mofetil is used. Severe weakness is treated with plasmapheresis or IVIG. The underlying cancer should be treated.

Prognosis

In paraneoplastic LEMS the prognosis is determined by the underlying cancer. The presence of LEMS in patients with small cell lung cancer (SCLC) is associated with longer survival from the malignancy. Non-paraneoplastic LEMS, when optimally treated, has an excellent prognosis and normal life expectancy, although patients may continue to experience various degrees of muscle weakness.

BOTULISM

Definition/Epidemiology/Pathology

Botulism is a rare, potentially lethal, paralytic illness caused by the neurotoxin produced by the anaerobic, spore-forming bacterium *Clostridium botulinum*. Botulinum toxin blocks voluntary and autonomic cholinergic neuromuscular junctions by binding irreversibly to the presynaptic nerve endings where it inhibits the release of acetylcholine. Human forms of the disease include foodborne botulism most commonly caused by home-canned food, wound botulism with most cases occurring among "black tar" heroin users, and infant botulism occurring usually in the second month of life due to intestinal colonization. Outbreaks of foodborne botulism occur in prison inmates due to ingestion of pruno, an alcoholic drink made illicitly in prison. About 145 botulism cases are reported each year in the United States; approximately 15% are foodborne, 65% are infant, and 20% are wound botulism.

Clinical Presentation

The disease is characterized by symmetric descending flaccid paralysis starting with blurred or double vision, ptosis, dysphagia, dry mouth, dysarthria, and muscle weakness. Symptoms usually start 18 to 36 hours after ingesting contaminated food.

Botulism should be suspected in any infant with poor feeding and sucking, constipation, dilated pupils, weak cry, poor tone, and respiratory distress. Sensory examination and mental status are normal.