Neuromuscular diseases often affect the respiratory muscles. When they do, they characteristically cause hypercapnic respiratory failure that is often associated with hypoxemia. This article presents an anatomic approach to the diagnosis of these diseases. It then describes common representative diseases within this anatomic format. The article concludes with a discussion of the intensive care unit (ICU) management of respiratory failure caused by neuromuscular disease.

THE NEUROANATOMY OF RESPIRATION

The brain stem is the primary center for the central control of respiration. This control occurs at a subconscious level and results in the rhythmic contraction and relaxation of the respiratory muscles. This automatic state can be temporarily overridden by voluntary mechanisms or by reflex actions such as coughing or sneezing. These voluntary mechanisms are essential for speech and phonation. The cortical centers for the voluntary control of respiration are presently not well localized.

Like other central nervous system control systems, the brain-stem respiratory center receives afferent information (in this instance concerning respiration), integrates this afferent information with data from other sources, sends out efferent signals to its target organ (in this case the respiratory muscles), and is modified by input from other areas of the brain, brain stem, and spinal cord.

The afferent information comes from several sources. These include the central chemoreceptors located in the anterolateral surface of the medulla, the carotid and aortic bodies, and the various stretch receptors in the lungs. The respiratory center in the medulla is composed of several nuclear groups that integrate the afferent information and possess the primary efferent neurons that control respiration. These efferent neurons send axons down the ventrolateral spinal cord that synapse on the anterior horn cells that go to the respiratory muscles. Other regions in the brain stem such as the pneumotaxic center modify the output of the respiratory center.

For the central commands controlling respiration to have their desired effect, the motor units of the respiratory muscles must be functioning properly. A motor unit consists of an anterior horn cell, its peripheral nerve axon (with its myelin sheath), the neuromuscular junction, and the muscle fibers it innervates. Under normal circumstances, when an anterior horn cell fires, an electrical impulse is conveyed through the peripheral nerve causing release of acetylcholine (Ach) at the terminal axon. The Ach diffuses across the neuromuscular junction where it binds to receptors on the postjunctional membrane (also called the motor end plate) and opens channels for the passage of calcium and sodium ions. The ion influx depolarizes the muscle membrane that in turn triggers contraction of the myofibrils. The Ach is then inactivated by lysis to acetic acid and choline by the enzyme acetylcholinesterase, located in the subneural cleft. The postjunctional membrane then is repolarized by the reestablishment of its normal ion gradients through active ion pumps, thereby returning the muscle to its resting condition.

The muscles of respiration consist of four groups: the diaphragm, the chest wall muscles, the abdominal muscles, and the muscles of the upper airway. The muscles of the upper airway include the muscles of the mouth (innervated by cranial nerves IX and X), uvula and palate (XI), tongue (IX and XII), and larynx (C1). While these muscles do not have a direct action on the thorax, they are essential for keeping the upper airway open and because they affect airway resistance and airflow, may impact on lung volume.
The diaphragm is the principal muscle of inspiration. It is innervated by the lower motor neurons of the phrenic nerve that originate at the C3 to C5 spinal cord level. Clinically, weakness of the diaphragm and other inspiratory muscles is manifested by a decrease in the vital capacity (VC) and total lung capacity (TLC), a reduction in the maximum inspiratory pressure (Pimax), and by abdominal paradox, in which the abdomen moves inward during inspiration.10

The chest wall muscles consist of the internal and external intercostals (T1-T12), the parasternal intercostals (T1-T12), the scalenes (C4-C8) and the accessory muscles (the sternocleidomastoids [XI, C1-C2], trapezoids [XI, C2-C3], and pectoralis major [C5-C7]). Recent data suggest that during normal respiration, the most important muscles for breathing apart from the diaphragm are the parasternal intercostals and the scalenes. The external and internal intercostals as well as the accessory muscles are primarily postural muscles and only have significant effects on breathing at high rates of ventilation.9

The abdominal respiratory muscles include the rectus and transverse abdominis and the external and internal obliques. These muscles are innervated at the T7-L1 levels. They generally are regarded as expiratory muscles, although they also enhance the mechanical advantage of the diaphragm. The abdominal muscles are not used during quiet exhalation to functional residual capacity (FRC), which is accomplished through passive recoil of the lungs. However, they are called on during forceful exhalation that allows lung deflation to residual volume (RV). Weakness of the expiratory muscles is evident clinically by a reduction in the maximum expiratory pressure (PEmax) and an inability to exhale forcefully or cough.

AN ANATOMIC APPROACH TO THE DIAGNOSIS OF NEUROMUSCULAR DISEASES

Figure 1 demonstrates the neuroanatomy of the respiratory muscles. Only lesions along the pathways demonstrated in this figure can produce weakness of the respiratory muscles. Diagnosis of the cause of neuromuscular dysfunction is best made by anatomically localizing the site of the lesion by history and physical examination. Once the anatomic site (ie, myoneural junction, spinal cord) is determined, the correct diagnosis can be confirmed by associated
nonneurologic symptoms and other tests.

Lesions above the foramen magnum typically produce unilateral weakness on the side opposite the lesion, referred to as hemiplegia. Lesions in the cortex or subcortical areas are often associated with disturbances of speech or other cortical functions. Disorders in the brain stem usually affect cranial nerve function ipsilateral to the lesion in addition to causing a contralateral hemiplegia. Abnormalities in the spinal cord typically cause bilateral weakness because of the close proximity of the descending tracts. Any lesion in the cortex, brain stem, or spinal cord is said to be an upper motor neuron lesion and is accompanied by an increase in muscle tone (spasticity), an increase in reflex activity, and the reemergence of primitive reflexes such as the extensor plantar response (sign of Babinski).

The lower motor neuron system begins at the anterior horn cell and includes the peripheral nerve, neuromuscular junction, and muscle. Classic signs of disorders of lower motor neurons include flaccidity, depressed reflexes, fasciculations, and atrophy. Again, the distribution and character of the weakness are important in identifying the exact site of the lesion.

Anterior horn cell diseases typically cause patchy, distal weakness unaccompanied by sensory symptoms because the sensory neurons are spared. Peripheral nerve disorders are almost always accompanied by prominent sensory loss secondary to the involvement of sensory nerves, have profound hyporeflexia, and usually have predominantly distal weakness. Peripheral nerve weakness can result from damage to either the core axon (axonal neuropathies) or the myelin sheath that coats the nerve (demyelinating neuropathies).

Disorders of the myoneural junction are characterized by weakness that fluctuates over time and often has a predilection for the extraocular and bulbar muscles. Pain is usually absent and sensory symptoms are lacking.

Muscle disorders usually present with proximal weakness manifested by inability to rise from a chair or to comb the hair. Dull, aching pain is often prominent, sensory symptoms are absent, and reflexes are normal. Frequently, serum levels of creatine kinase (CK) values are elevated in muscle diseases. In some cases, a family history of muscle disorders is also found. Table 1 summarizes the clinical characteristics.

<table>
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<th>Level</th>
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<td>Myoneuronal junction</td>
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<td>Acid maltase deficiency</td>
<td>No sensory or autonomic changes</td>
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<td>Carnitine palmityl transferase deficiency</td>
<td>Often have pain</td>
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of lesions at various levels in the neural axis and lists common disorders that cause respiratory weakness at these levels.

Upper motor neuron disorders can further be identified and differentiated by lumbar puncture and by imaging techniques such as computerized tomography (CT), magnetic resonance imaging (MRI), and myelography. Lower motor neuron diseases can best be evaluated by electrical testing of the peripheral nervous system, which is referred to as electromyography (EMG). EMG can be used to differentiate between anterior horn cell disorders, various peripheral neuropathies, myoneural junction disorders, and muscle diseases.

**Specific Neuromuscular Diseases Affecting Respiration**

**Central Disorders**

_Stroke_ is a common cause of upper motor neuron respiratory dysfunction. Strokes occur most frequently in the middle cerebral artery distribution and affect the voluntary system of respiration. Strokes can alter respiratory function in several ways. First, they often affect the muscles that protect the upper airway and maintain its patency. Horner et al. found that among 47 patients with stroke, one half showed signs of aspiration. Although patients with brain-stem strokes with resultant bilateral cranial nerve palsies were at greatest risk, aspiration occurred frequently in patients with unilateral symptoms.

As expected, patients with hemiplegia exhibit decreased voluntary muscle activity in their diaphragm and parasternal intercostals as documented by ENMG on their weak side. Additionally, the hemidiaphragm on the side of the hemiplegia is typically elevated. Despite these findings, cortical strokes usually do not have a major impact on respiratory function, in part because the automatic system in the brain stem is rarely affected by supratentorial disorders.

*Extrapyramidal disorders* can also affect respiration. Vincker and associates studied patients with parkinsonism and essential tremor and found that many had either rhythmic or irregular involuntary movements of their glottic and supraglottic structures during respiration. In more than one third of their patients, these abnormal movements resulted in upper airway obstruction due to intermittent closure of the upper airway.

The automatic system of respiration can also be affected by diseases. Poliomyelitis often involves the primary ventilatory nuclei in the brain stem, and temporary or permanent sleep apnea is a frequent consequence of this disease. Severinghaus and Mitchell reported the cases of three patients who had normal voluntary ventilation, but would become apneic when they fell asleep. All three patients had undergone surgery involving the high spinal cord or brain stem. The investigators termed this syndrome *Ondine's Curse* after the German legend about the water nymph, Ondine, who, having been jilted by her mortal husband, took him all automatic functions, requiring him to remember to breathe. A similar syndrome has been reported following medullary infarction involving the ventilatory nuclei or their descending tracts.

Central respiratory drive is often depressed by drugs. Narcotics, sedatives, and hypnotics all impair respiratory drive and are by far the most common cause of life-threatening central alveolar hypoventilation.

**Spinal Cord Injuries**

_Quadriplegia_ resulting from acute cervical spinal cord trauma, spinal artery infarction, or compression by tumor is often associated with profound respiratory compromise. Injuries at or above the cord segments C3 to C5 involve the phrenic nerves and cause partial or complete bilateral hemidiaphragmatic paralysis. In addition, intercostal muscle paralysis caudal to the lesion limits the normal outward expansion of the middle and upper rib cage, further compromising inspiration.Expiration is also greatly reduced because of paralysis of the abdominal and other expiratory muscles. Sternocleidomastoid, scalene, and trapezoid activity persists in high cord injuries; however, their efficiency is greatly reduced.

Because of their extensive respiratory muscle dysfunction, high cervical quadriplegics are unable to generate an adequate VC because of reduced inspiratory and expiratory function. Hypoxemia is common and results both from hypoventilation and microatelectasis.

Quadriplegic patients with lesions in the lower cervical cord, whose phrenic nerve nuclei are completely or partially intact, can contract their diaphragms to a variable extent. Nevertheless, they lack the intercostal muscle activity necessary to stabilize the rib cage so the hemidiaphragms can function properly; as a result, their inspiratory function is compromised. Like higher level quadriplegics, these patients also have lost the use of their abdominal and other expiratory muscles. This combination of expiratory and inspiratory weakness prevents them from coughing and clearing secretions, placing them at high risk of respiratory tract infections.

As is evident from the previous discussion, a large percentage of patients with acute spinal cord injuries will require ventilatory support. VC is commonly between 1.2 and 1.5 L following these injuries and is accompanied by reductions in Pmax and, to a greater extent, PEmax. Obviously, the higher the level of the spinal cord lesion, the more profound the respiratory
failure. Fortunately, however, the need for ventilatory support is often temporary. As the initial phase of spinal shock passes, chest wall flaccidity is replaced with spasticity and pulmonary function significantly improves as the more rigid chest wall resists collapse. Ledsome and Sharp\textsuperscript{22} reported an increase in the VC of a group of quadriplegics from 1.5 L at the time of hospital admission to 2.7 L 18 weeks later. Overall, approximately 80 percent of patients with injuries at or below the C4 level can eventually be safely weaned from mechanical ventilation.

**Anterior Horn Cell Disorders**

*Paralytic poliomyelitis*, a communicable disease caused by a picorna virus, was at one time the most common cause of lower motor neuron disease in the United States. Polio begins as a minor illness, with fever and other minor symptoms such as myalgias in adults or upper respiratory tract infection in children. These symptoms disappear in several days, but reappear five to ten days later associated with meningeal irritation and the onset of paralysis. The gray matter of the brain stem and spinal cord can be affected resulting in a flaccid paralysis that is usually asymmetric, may be widely distributed, and tends to involve the lower extremities and trunk.

Respiratory function can be affected in several ways. The respiratory motor nuclei can be directly involved resulting in diaphragmatic or other respiratory muscle dysfunction. Additionally, the lower cranial nerve nuclei can be involved resulting in upper airway obstruction, pooling of secretions, and aspiration. Finally, the medullary cardiorespiratory centers can be directly infected resulting in irregular respirations, apnea, and other dysautonomies.

The diagnosis of poliomyelitis is based on clinical presentation, cerebrospinal fluid (CSF) analysis showing a pleocytosis associated with a mild protein elevation, and an ENMG that demonstrates patchy, widespread denervation with normal sensory nerve studies.

Although overall mortality from polio is only 5 to 7 percent, patients with bulbar involvement have a much higher mortality. Many of these patients require aggressive ventilatory and hemodynamic support during the acute phase of their illness. Most patients show substantial muscle recovery over time, although some are left with significant residual weakness. The recovery seen in polio patients is due to the reinnervation of damaged muscle fibers by the sprouting of new nerve twigs from the remaining viable motor neurons.

Recently, a syndrome of recurrent muscle weakness occurring 20 to 40 years after the initial bout of polio has been reported and termed the *postpolio syndrome*.\textsuperscript{23,24} This syndrome has caused much anxiety among the estimated 300,000 survivors of polio in the United States. It is due to the abiotrophy of the extra neuronal sprouts formed during the original recovery period from polio. Fortunately, this weakness tends to progress slowly with an average decline in muscle strength of 1 percent per year.\textsuperscript{24} Although some patients have developed progressive respiratory failure, it remains to be seen how frequently respiratory function will be significantly affected in this cohort of patients.

*Amyotrophic lateral sclerosis* (ALS) is now the most common lower motor neuron disorder in developed countries. ALS is classified as a disorder of lower motor neurons because it damages the anterior horn cells of the spinal cord and brain stem. Nevertheless, the disease may also affect upper motor neurons.

Although the clinical course of ALS varies, the disease most frequently presents as progressive distal muscle weakness and wasting in an older adult. Involvement of the bulbar muscles may occur and lead to impairment of the gag reflex, laryngeal dysfunction, and aspiration. Signs of upper motor neuron involvement such as spasticity and hyperreflexia are usually present on neurologic examination. The coexistence of upper and lower motor signs should strongly suggest the diagnosis of ALS. ENMG will reveal changes of muscle denervation with normal motor velocities until axonal dropout is sufficiently severe to cause mild slowing. Results of sensory nerve studies are normal.

Despite intensive investigations, the cause of ALS is unknown.\textsuperscript{25} Specific therapy is not available, and the prognosis of ALS is generally poor. More than 50 percent of patients die of complications such as aspiration and pneumonia within three years of diagnosis. Serial pulmonary function testing in such patients reveals a progressive decline in VC and TLC and an increase in RV caused by the widespread loss of respiratory muscle function that will eventually lead to respiratory failure.\textsuperscript{26}

**Disorders of the Peripheral Nerves**

*Peripheral neuropathies* can affect either the nerve axon or the myelin sheath, as previously stated. Although greater than 100 types of peripheral neuropathies exist, few cause respiratory dysfunction.

*Acute idiopathic polyradiculoneuritis*, also known as the Landry-Guillain-Barré syndrome (LGBS), is the most common peripheral neuropathy causing respiratory failure. It is a monophasic illness with an annual incidence of 0.6 to 1.9 cases per 100,000 and is probably of autoimmune origin. Approximately 50 percent of patients will have an antecedent upper respiratory tract or gastrointestinal infection within four weeks of the onset of symptoms. In addition, there seems to be an increased association of LGBS with a variety of diseases, including lymphoma, car-
cinoma, herpes zoster infection, mononucleosis, and human immunodeficiency virus (HIV) seroconversion. \(^{27-30}\) LGBS most commonly presents with subacutely evolving painless muscle paralysis and subjective distal paresthesias. It has been classically termed “ascending paralysis” because the weakness most commonly begins in the lower extremities before spreading to the trunk and upper extremities. The disease rapidly progresses; 50 percent of patients reach their nadir by two weeks and 90 percent reach it by four weeks.

Approximately 20 percent of patients with LGBS will eventually require ventilatory support. Daily bedside evaluation of VC and respiratory muscle strength is essential. Patients should be electively intubated when signs of respiratory distress occur, when they lose their ability to protect their airway, or when their VC falls to a critical level. Although ventilatory failure does not generally occur until VC deteriorates to approximately 10 ml/kg, because of bulbar involvement and the inability to handle secretions, a large percentage of LGBS patients will eventually aspirate and develop pneumonia if this criterion is used. \(^{30}\) Earlier intubation (ie, at a VC around 20 to 25 ml/kg) appears to reduce the risk of pneumonia and should be considered in a patient with rapidly deteriorating respiratory function or worsening bulbar symptoms.

Most patients with LGBS recover without sequelae. However, approximately 15 percent will be left with residual weakness and an additional 5 percent will have relapsing episodes of demyelination and a chronic course and fall into the disease spectrum called chronic relapsing dysimmune polyneuropathy. These patients have relapsing bouts of demyelination that tends to affect the limbs more than the trunk, although occasionally respiratory failure does occur.

At present, no therapy has been shown to affect the eventual outcome of patients with LGBS. Plasmapheresis, however, has been shown to markedly shorten the duration of the hospital and ICU stay in patients who become nonambulatory if it is begun within 14 days of onset of symptoms. \(^{31}\) Because of the psychological and economic consequences of prolonged ventilation and hospitalization, plasmapheresis is indicated in all patients with severe LGBS of recent onset.

Although LGBS is the most common cause of neuromuscular respiratory failure seen in the United States, other diseases can cause respiratory failure and need to be excluded; these are summarized in Table 1. Among the peripheral neuropathies leading to respiratory failure, Lyme disease can present with a syndrome identical to the LGBS except that a moderate CSF pleocytosis is usually found. \(^{32}\) In endemic areas, serologic testing for Lyme disease is therefore indicated. Acute intermittent porphyria (AIP) can cause a neuropathy severe enough to cause respiratory failure. Diphtheric polyneuropathy, toxic neuropathies (thallium, triorthocresyl phosphate [TOCP], and lead), paralytic shellfish (Saxitoxin) poisoning, and the polyneuropathies associated with systemic lupus erythematosus and polyarteritis nodosa also can cause ventilatory failure.

All of the neuromuscular diseases previously discussed will usually be present prior to admission to the ICU. Of equal importance, however, is a recently described syndrome of an acquired peripheral neuropathy occurring as a complication of sepsis and multiple organ failure. \(^{33}\) Termed critical illness polyneuropathy, this syndrome is characterized by failure to wean from mechanical ventilation, muscle atrophy, and diminished reflexes. It is caused by peripheral nerve dysfunction and is present to varying degrees in a high percentage of patients who are in the ICU for more than two weeks. ENMG shows an axonal sensorimotor neuropathy. Although the cause of this polyneuropathy is unclear, prognosis for recovery is good if the underlying disease can be successfully treated.

A variety of drugs can affect peripheral nerve function. The effect is usually mild and subclinical, but it may be significant in patients who have underlying neuromuscular defects. Drugs clearly associated with motor neuropathies include vincristine, amiodarone, dapsone, and phenytoin. \(^{34}\)

**Disorders of the Neuromuscular Junction**

*Myasthenia gravis* is the most common disorder of the neuromuscular junction. It affects any age group, although clusters of cases are found in young women and older men. Myasthenia is characterized by weakness that has a predilection for the ocular and bulbar muscles and fluctuates over time. It is an immunologic disorder due to circulating antibodies directed against the postsynaptic Ach receptor. These anti-Ach receptor antibodies can be detected in the serum of 90 percent of patients with generalized myasthenia gravis. \(^{35}\) Diagnosis is confirmed by demonstrating fluctuating weakness that improves after the injection of acetylcholinesterase inhibitors such as edrophonium (Tensilon) and by the finding of a decremental response of the amplitude of the motor response to repetitive nerve stimulation. Associated thymic disorder (benign hyperplasia or thymoma) occurs in 80 to 90 percent of myasthenics, as well as a higher than normal incidence of other autoimmune diseases.

Involvement of the respiratory muscles occurs in approximately 10 percent of myasthenics and was once a fairly common cause for ICU admission. However, with recent improvements in the care of these patients, respiratory failure requiring mechanical ventilation is now infrequent. \(^{36}\) Nevertheless, respiratory failure can be precipitated by concurrent infection, surgical
stress, or drugs known to affect myasthenia gravis. Therapy during these acute attacks involves mechanical ventilation in combination with plasmapheresis, steroids, acetylcholinesterase inhibitors, and immunosuppressive agents. Thymectomy eventually is recommended in most patients with generalized myasthenia gravis and results in improvement or remission in 80 percent of patients who have no evidence of thymoma.

Botulism is a disorder of the neuromuscular junction caused by the binding of one of eight neurotoxins (labeled A through G) elaborated by the bacterium Clostridium botulinum. The toxin prevents the release of Ach from the presynaptic terminal and affects both nicotinic and muscarinic synapses. Botulism occurs in three forms: food-borne botulism, in which preformed toxin is ingested in nonacidic home-canned or factory-canned vegetables or meat; infant botulism in which the organism and its spores are ingested in honey or other foods or from the environment; and wound botulism, in which C botulinum and its spores contaminate traumatic or surgical wounds.

All forms of botulism have the same clinical findings. These include blurred vision, pupillary paralysis, ileus, dry mouth, and a descending paralysis that begins with the extracocular and bulbar muscles and frequently progresses to the respiratory muscles. Diagnosis is supported by repetitive nerve stimulation showing small amplitude motor responses that increase in amplitude at high rates of stimulation similar to that seen in other presynaptic disorders such as Eaton-Lambert syndrome and aminoglycoside toxicity. Botulism is verified by demonstrating neurotoxin in the serum, stool, or contaminated food. Treatment involves the elimination of unabsorbed neurotoxin from the gut by means of enemas and gastric lavage, administration of trivalent antitoxin (against neurotoxins A, B, and E) to neutralize circulating neurotoxin in the serum, the administration of high-dose penicillin to kill C botulinum organisms if present, and surgical debridement of offending wounds. Mechanical ventilation is frequently required, and pneumonia is a common complication and a major cause of death. Although severely affected patients may require ventilation for several months, prognosis is good for recovery.

The neurotoxin produced by the Rocky Mountain wood tick Dermacentor andersoni can produce a rapidly progressive ascending paralysis that can cause respiratory failure and death. Tick paralysis usually begins about five to six days after the insect has embedded itself into the skin, usually along the hairline. Although the toxin had been thought to act by inhibiting the release of Ach from the presynaptic nerve terminal, recent evidence suggests that the major affect is to prevent depolarization in the terminal portion of the motor nerve.

The neuromuscular junction is perhaps the most common site adversely affected by drugs. Of particular interest is the effect of overdoses of acetylcholinesterase inhibitors given to myasthenics. At high doses, these drugs can produce neuromuscular blockade and cause respiratory weakness. This phenomenon is termed cholinergic crisis and is usually associated with nausea, diarrhea, and excessive salivation.

At least 50 other drugs have been reported to produce or potentiate unwanted neuromuscular blockade. They include the aminoglycosides, polymyxin antibiotics, calcium channel blockers, quinidine, procainamide, lithium, and corticosteroids. Finally, D-penicillamine, procainamide, and trimethadione have been reported to cause a drug-induced syndrome similar to myasthenia gravis.

Disorders of Muscles

The final component of the lower motor neuron unit is the muscle itself. Disorder of muscles are called myopathies. Most myopathies do not cause clinically significant respiratory dysfunction. However, respiratory failure is a common cause of death in several of the muscular dystrophies, and respiratory failure can be the presenting feature of a few unusual myopathic disorders.

Muscular dystrophies are a subgroup of myopathies with three characteristics: hereditary transmission, progressive weakness, and biopsy evidence of muscle degeneration without evidence of stored material or structural abnormality. The most common of these is Duchenne muscular dystrophy (DMD), an X-linked disorder that produces progressive muscle weakness starting in childhood. Children with DMD often develop significant kyphoscoliosis that combines with respiratory muscle weakness to cause severe respiratory failure. Respiratory tract infections become common, and patients usually die of respiratory failure in the third decade of life.

The diagnosis of DMD is confirmed by ENMG, an elevated CK level, and muscle biopsy. Affected male siblings of patients with DMD can be identified in the neonatal period because their CK levels are always markedly elevated. One third of cases, however, arise as a spontaneous mutation. There is no specific treatment except for physical therapy, splints, corrective orthopedic surgery, and mechanical ventilation, if desired.

Dermatomyositis, an inflammatory disorder of muscles, can affect respiratory and bulbar muscles in severe cases. This is particularly true in childhood dermatomyositis where severe respiratory failure requiring mechanical ventilation has occurred.

Glucocorticoids are a common and significant cause of muscle weakness. They can affect the respiratory
muscles, although the constant activity of the diaphragm and other inspiratory muscles may provide a measure of protection against the deleterious effects of steroids. Chloroquine, amiodarone, β-adrenergic agonists, clofibrate, and epsilonaminocaproic acid also can cause muscle injury that is usually reversible on withdrawal of treatment with the offending drug.

**MANAGEMENT IN THE INTENSIVE CARE UNIT**

**Precipitating Factors**

Precipitating factors are often the immediate cause for ICU admission of patients with neuromuscular disease. The identification of such factors is essential because they may be more amenable to therapy than the neuromuscular disease itself. Upper airway obstruction and aspiration should be suspected in patients with bulbar dysfunction, whereas microatelectasis and lower respiratory tract infections are common among all patients with generalized weakness. Pulmonary hypertension and right-sided heart failure should be anticipated in patients who are chronically hypoxemic. Intercurrent illnesses such as urinary tract sepsis or pulmonary embolism may occur and prompt admission to the ICU.

Additionally, electrolyte and endocrinologic disorders may exacerbate respiratory dysfunction. Phosphate, potassium, magnesium, and calcium are all important for healthy neuromuscular function and should be kept within the normal range. Thyroid and growth hormone disorders should be corrected, and acid-base balance should be optimized.

**Evaluation of the Need for Respiratory Support**

The need for respiratory support should be assessed in patients with neuromuscular disease as early as possible. The finding of severe hypoxemia, hypercapnia, and acidemia on arterial blood gas analysis may not occur until respiratory failure is profound. Although it cannot be diagnosed solely on physical examination, respiratory failure is suggested by a rapid, shallow breathing pattern and by the presence of abdominal paradox.

Determination of Pimax and PEmax is the most sensitive way to quantitate respiratory muscle weakness. In one study, Pimax was found to be less than 80 percent of predicted in 87 percent of patients with generalized neuromuscular disease and less than 50 percent of predicted in 66 percent of patients. By contrast, Pimax exceeded 80 percent of predicted in 83 percent of patients. The PEmax averages 100 cm H₂O in normal adults, whereas a pressure of less than 40 cm H₂O precludes effective coughing. The average Pimax is −70 cm H₂O, whereas a normal PaCO₂ cannot be maintained if the pressure is less negative than −20 cm H₂O.

In lieu of determining maximum pressures, VC may be measured by spirometry. The VC averages approximately 50 ml/kg in normal adults. Impaired secretion clearance occurs at a VC of less than 30 ml/kg, and ventilatory failure occurs at a VC of approximately 10 ml/kg. Spirometry and pulmonary function tests also may be performed before and after therapeutic interventions such as inhaled β-adrenergic agonists or in various postures to help determine in which positions patients will breathe most effectively.

If muscle relaxation is required for intubation, depolarizing agents such as succinylcholine should generally be avoided, since massive release of potassium is occasionally induced by this drug in patients with neuromuscular diseases.

As part of the initial assessment, the decision to initiate or withhold mechanical ventilation should be made by the patient and the physician after a thorough discussion of the prognosis and the implications of this type of care.

**Providing Ventilatory Support**

The preferred mode of mechanical ventilation for patients with neuromuscular diseases is controversial and a discussion of the various modes of positive pressure ventilation is beyond the scope of this article. However, assist-control (AMV) and mechanical (mandatory) ventilation (IMV) can be used only in those patients who can generate substantial respiratory efforts. Therefore, most patients with severe weakness or paralysis are ventilated, at least initially, in the controlled mode (CMV).

Patients with neuromuscular disorders and reactive airway disease should be treated with aerosolized β-adrenergic agonists, systemic corticosteroids, and other drugs as indicated. The role of theophylline as a bronchodilator is controversial, but theophylline has been reported to improve contractility of the diaphragm and other respiratory muscles. Nevertheless, the effects of theophylline on diaphragmatic contractility are not well defined. Furthermore, no one has demonstrated that theophylline can reduce ventilator dependence or facilitate weaning of patients with neuromuscular disease. If theophylline is administered empirically in such patients in hope of strengthening the respiratory muscles, drug levels should be followed closely to reduce potential toxicity.

Patients with neuromuscular disorders require meticulous nursing care to avoid secondary nerve pressure palsies (especially involving the ulnar and peroneal nerves) and bed sores. Patients should be turned frequently and may benefit from insulating pads or flotation beds. Footboards and wrist splints should be provided to prevent contractures. Physical therapy may prevent disuse (but not denervation) atrophy, maintain venous tone, and improve patient morale. Nutrition also should be provided by the enteral route.
whenever possible, although aspiration must be avoided. Oral feedings can occasionally be used in patients who have a tracheostomy and can swallow. Nasointestinal feedings are desirable for patients who cannot swallow but are likely to regain neuromuscular function, whereas feeding jejunostomies may be more appropriate for those who are permanently weak or paralyzed. Low-dose subcutaneous heparin or pneumatic leg compression devices are indicated to prevent deep venous thrombosis and pulmonary embolism.

Autonomic dysfunction in patients with LGIBS and other neuromuscular diseases is a major cause of mortality. Involvement of both the sympathetic and parasympathetic systems can result in wide fluctuations in pulse and blood pressure, as well as a wide variety of atrial and ventricular arrhythmias. Treatment consists of maintaining adequate hydration, avoiding sudden changes in position, using stool softeners, and treating dysrhythmias with specific agents. Extremes of blood pressure should be treated with short-acting, titratable agents to avoid overshooting, if therapy is necessary. The hypotension that accompanies cervical cord injury and other conditions may be treated with intravenous fluids or short-acting α-adrenergic agonists, whereas bradycardia is treated with atropine. Patients with profound vagal tone in whom bradycardia occasionally progresses to asystole may require ventricular pacing.

Finally, patients receiving mechanical ventilation on a short-term basis require enormous emotional support. Patients should be constantly spoken to and reassured that their needs will be met. They should also be closely evaluated for signs of pain or discomfort and given adequate amounts of analgesics and sedatives. Methods of communication should be assured for patients who are unable to speak or move their extremities. The issue of providing long-term ventilatory support is beyond the limits of this review but is discussed elsewhere.

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