Acquired Myopathy/Dystrophies

Anthony Chiodo, MD

Abstract: Diseases of muscle may be congenital or acquired. They cause muscle weakness without sensory loss. The onset, distribution, and clinical course help to differentiate the type of muscle disorder. The diagnostic workup may include laboratory examination, electrodiagnostic studies, and muscle biopsy. A definitive diagnosis leads to better decision making with regard to treatment, genetic education, prognosis, functional expectations, and the impact of exercise on muscle function.

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INTRODUCTION

Simply put, a myopathy is a muscle disorder. Historically, classification systems relied on classic clinical presentations and, later, relied on muscle biopsy findings. More recently, classification has been refined by genetic analysis and reverse genetics, which allow for identification of the defective gene byproduct and which has led to an understanding of the pathophysiology of specific myopathies. Rapid evolution of the science of myopathies has made classification a continually moving process, but one reasonable example is shown in Table 1.

MUSCULAR DYSTROPHIES

The dystrophinopathies are known historically as Duchenne and Becker muscular dystrophy. Caused by defects at the Xp21 locus, the disease is caused by the lack of or defect in the protein dystrophin. A defect to this critical cell membrane protein causes cell damage during muscle contraction because the relationship between actin and the membrane bound dystrophin-glycoprotein complex is lost. The result is cell necrosis and apoptosis. Other less common genetic defects to components of the dystrophin-glycoprotein complex cause defects that range from minimal deficit to fatal disease [1].

The classic presentation of Duchenne muscular dystrophy is disease recognition between the ages of 3 and 5, with delayed motor development and with cognitive and behavioral impairment. Initial presentation includes hip greater than shoulder girdle weakness with a Gower maneuver present by the age of 5-8. Extensor weakness is greater than flexor, although neck flexor weakness is common. Calf pseudohypertrophy may be present. Achilles tendon and iliotibial band contractures occur by age 6 years, with knee and elbow flexor and wrist extensor contractures occurring later. Boys typically require a wheelchair by the age of 10 years with progressive contractures and scoliosis. Oral prednisone may prolong motor skill ability. Cardiomyopathy is seen with left ventricular ejection fraction deficits and systolic hypertension. Tall right precordial R-waves and deep, narrow Q-waves in left leads is a common electrocardiographic finding. Respiratory failure is universal, with only 25% of patients surviving or being ventilator free by the age of 21 years. However, overall life expectancy has significantly improved in recent decades due to the use of assisted ventilation.

Limb girdle muscular dystrophy (LGMD) is a heterogeneous set of disorders that has a common presentation of axial and proximal limb weakness. Onset can range from late childhood through adulthood, depending on the disorder. Recessive forms have been identified that are related to defects that affect sarcoglycans, calpain 3, and dysferlin. The dysferlinopathies are also known as Miyoshi myopathy and LGMD type 2B, with defects at the 2p13 locus of the human genome. Dysferlin is a protein that is responsible for T-tubule

A.C. Physical Medicine and Rehabilitation, University of Michigan Hospital, 325 E Eisenhower Parkway, Ann Arbor, MI 48118. Address correspondence to: A.C.; e-mail: tchiodo@med.umich.edu

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Table 1. *Myopathies*

Congenital	Acquired
Dystrophies	Inflammatory
Dystrophinopathies	Paraspinous
LGMD	Endocrine
FSH	Toxic
Myotonic	Steroid
OPMD	Statin
EDMD	Sarcopenia
Others	
Congenital myopathies	
Central core	
Nemaline	
Centronuclear	
CFTD	
Metabolic myopathies	
Mitochondrial myopathies	

CFTD = congenital fiber type disproportion; FSH = facioscapulohumeral dystrophy; LGMD = limb girdle muscular dystrophy; OPMD = oculopharyngeal muscular dystrophy; EDMD = Emery-Driefuss muscular dystrophy.

homeostasis and muscle membrane repair. Animal models of this disorder are currently being used to study adeno-associated virus vector transfer therapy [2]. There also are autosomal dominant limb girdle dystrophies, two in particular that affect collagen VI and caveolin-3.

Facioscapulohumeral dystrophy, with an incidence of 1 in 20,000, is characterized by profound scapular, facial, and proximal limb weakness. Hearing loss is common but is not functionally limiting. Cardiac and respiratory dysfunctions are rare. There are 2 types, one due to a deletion at 4q35, whereas type 2 results in a methylation defect. Myotonic dystrophy is now classified into 2 types, the first characterized by a CTG repeat expansion 30 of DMPK, and type 2 which is a CTG repeat expansion in CNBP. These expansions alter the processing of certain messenger RNAs, which lead to cell dysfunction. In the myotonic dystrophies, alternative splicing at exon 29 affects Ca(V)1.1, a calcium channel responsible for controlling excitation-contraction coupling. The degree of the skipping correlates with the degree of muscle weakness [3]. The disorder has multiorgan involvement, including ocular, endocrine, cardiac, reproductive, gastrointestinal, and skin. Muscle weakness is most prominent in the face, neck, and distal extremities. Male frontal balding and mental retardation are characteristic.

Oculopharyngeal muscular dystrophy results from GCG expansions in PABPN1, a nuclear protein involved in the polyadenylation of messenger RNA. It presents with ptosis and dysphagia. Emery-Driefuss muscular dystrophy has 2 forms, autosomal dominant due to lamin A/C defect and X-linked due to a defect in the protein emerin. Muscle involvement includes the cervical spine and distal lower extremities. Cardiac involvement is common, and sudden death can occur. Congenital muscular dystrophy can be caused by gene defects to a number of gene products, including merosin, fukutin, FKRP, and a-7 integrin.

The FHL1 muscular dystrophies are associated with defects at Xq26.3 and can present with multiple phenotypes, including scapuloperoneal dystrophy, bent spine syndrome, and reducing body myopathy. The case can be made that these myofibrillar myopathies, characterized by Z-line disintegration, are characteristic, given the common lower leg and axial weakness and atrophy seen. However, the degree of weakness is highly variable, and the onset has been seen anywhere between the ages of 6 years and 75 years [4]. Defects in collagen VI can result in a number of neuromuscular disorders, including Ullrich congenital muscular dystrophy, Bethlem myopathy, and intermediate phenotypes, depending on the severity of the gene defect [5].

CONGENITAL MYOPATHIES

Congenital myopathies have historically been categorized and named based on their biopsy appearance. A common theme in the congenital myopathies is disruption of excitation-contraction coupling in skeletal muscle [6]. Nemaline myopathy is due to defects in contractile filaments; nemaline rods are Z-disk–derived material. Their accumulation can give rise to many defects, including α-actin (autosomal dominant with variable penetrance), nebulin (autosomal recessive), or other thin filament–associated proteins such as tropomyosin 2 and 3, troponin T2, or cofilin. Nemaline myopathies can have onset throughout life, with variable severity, although a common pattern includes involvement of proximal and facial muscles and respiratory insufficiency, without ophthalmoplegia.

The other congenital myopathies are due to disruption of calcium homeostasis at the level of the T-tubule and sarcoplasmic reticulum. In central core disease, there is an absence of mitochondria, with central cores that run the length of the myofiber. The gene defect is RYR1, the ryanodine receptor responsible for calcium homeostasis on the sarcoplastic reticulum. The autosomal dominant form is a central core disease, characterized by proximal weakness and less facial involvement. The autosomal recessive form is minicore myopathy. The SEPN-1 defect results in multiminicores, with the mutation found at 1p36-13. The gene product, selenoprotein N1, is responsible for calcium homeostasis and protects the cell against redox-related cellular damage. This phenotype presents with slowly progressive proximal weakness, axial weakness and deformities, and progressive respiratory failure [7].

Centronuclear myopathy is an X-linked disorder due to mutations in the MTM1 gene for myotubulin, which is a phosphoinositide phosphatase protein. There also is an autosomal dominant form that results in a defect in the DNM2 gene. This causes a defect in the protein dynamin-2, a GTPase responsible for endocytosis and interactions between actin and the microtubule network in the muscle.

The operational definition of congenital fiber type disproportion (CFTD) is that type 1 fibers are consistently smaller

Table 2. *Proposed classification of inflammatory myopathies*

Entity	Pathology	Clinical
Immune myopathy with perimysial pathology	Perimysial inflammation, perivascular B cells; muscle necrosis, regeneration	Polymyositis, dermatomyositis, fasciitis; anti-Jo-1 and others; also elas high
Myovasculopathy	Intermediate and capillary vessel damage	Dermatomyositis, childhood and adult
Immune polymyopathy	Muscle necrosis	Paraneoplastic; anti-SRP and HMG-CoAR
Immune myopathy with endomysial pathology		Brachiocervical inflammatory myopathy
Histiocytic inflammatory myopathy	Histiocytes predominate	Sarcoid, immunizations
Inflammatory myopathy with vacuoles, aggregates and mitochondrial pathology	As stated	Inclusion body myositis

than type 2 fibers by at least 35%-40%. For this diagnosis, it is necessary that no other histologic finding is seen on biopsy because small type 1 fibers are common in other conditions, such as the congenital myopathies, spinal muscular atrophy, myotonic dystrophy, and Ullrich muscular dystrophy. Multiple gene defects have been implicated in CFTD. Scores of autosomal dominant defects in TPM3 have been implicated in this disorder, yet they all result in similar clinical features of mild to moderate weakness, with progressive respiratory decline. Defects in p.R168H, p.R168C, and RYR1 result in highly variable phenotypes [8].

METABOLIC MYOPATHIES

Defects in fat oxidation can lead to myopathy. The classic is carnitine palmitoyl transferase 2 deficiency, although other disorders exist, including trifunctional protein deficiency and very-long-chain acetyl-CoA dehydrogenase deficiency. Glycogen storage disorders also cause myopathy. The most well characterized is McArdle disease, due to myophosphorylase deficiency at genetic site 11q13. Tarui disease due to phosphofructokinase deficiency has also been extensively studied.

Abnormal serum lactate accumulation in aerobic exercise testing can be more helpful than baseline serum lactate levels in patients with mitochondrial myopathies. This test is specific but not highly sensitive. Myophosphorylase deficiency or McArdle disease (1/100,000 incidence) can be evaluated with the ischemic forearm test, in which a lack of rise of lactate with exercise is indicative of a glycolytic pathway defect. Normal or exaggerated rises in ammonia serum concentrations are seen. Myoadenylate deaminase deficiency, the most common metabolic pathway defect in skeletal muscle (1 in 100) will result in normal or decreased lactate with decreased ammonia concentration [9].

Pompe disease, or acid maltase deficiency, is an autosomal recessive disorder caused by the deficiency of the lysosomal enzyme acid α-glucosidase and results in cellular lysosomal and cytoplasmic glycogen accumulation. The severity of disease, depending on the extent of the mutation, can vary from severe hypotonia and cardiac hypertrophy in the first few months of life to adult-onset disease. Patients typically have proximal weakness as in the limb girdle dystrophies, but the incidence of respiratory weakness in higher in Pompe disease. There currently is available enzyme replacement therapy for this disorder, which does result in glycogen depletion in cardiac and skeletal muscle. However, it does not correct glycogen deposition in other cells, especially in neural cells. Therefore, adeno-associated virus-mediated gene therapy is being explored in animal models of this disease. An additional downside of enzyme therapy is that it leads to anti-GAA antibodies; tolerance strategies need to be developed around infusions [10].

Mitochondrial myopathies include chronic progressive external ophthalmoplegia, mitochondrial encephalopathy, lactic acidosis and stroke-like episodes, and myoclonic epilepsy with ragged red fibers. Electrodiagnostic studies are commonly abnormal but not pathognomonic (see below). Coenzyme Q supplementation is recommended for patients with this disorder [11].

ACQUIRED INFLAMMATORY MYOPATHIES

Inflammatory muscle disorders include dermatomyositis, polymyositis, inclusion body myositis (IBM), skeletal muscle vasculitis in rheumatologic disorders (systemic sclerosis, rheumatoid arthritis, systemic lupus erythematosus, and Sjogren syndrome), and sarcoid myopathy [12-14]. Inflammatory myopathies have an incidence of 2-8 per million adults with the adult peak between 45 and 55 years of age; women predominate 3 to 2. A pathologic classification of immune and inflammatory myopathies has been proposed, as associated with typical muscle biopsy, clinical, and laboratory features [15], which is summarized in Table 2.

IBM has an incidence of 2-5 per million adults with a peak at 50-70 years old and male predominance. IBM is considered the most prevalent idiopathic inflammatory myopathy in the geriatric population, although cancer-related dermatomyositis is more common. Patients with cancer-related muscle disease may be undetected clinically, as evidenced by

a muscle biopsy study of older persons with cancer. Cancers associated with dermatomyositis in this population include lung, ovarian, pancreatic, stomach, colorectal, and non-Hodgkin lymphoma. Ongoing cancer screening should continue for 5 years after the diagnosis of dermatomyositis in the elderly because several years may elapse between the onset of muscle disease and detection of the precipitating cancer.

Genetic associations with polymyositis and dermatomyositis in HLA class I and II genes have been identified. A genetic relationship to IBM is less established, although gene studies have shown that there may be susceptibility in IBM, but further characterization is required [16]. Autoantibodies unique to the inflammatory myopathies are seen in fewer than 50% of patients. Anti-Jo 1 is found in polymyositis and dermatomyositis, whereas anti Mi-2 is seen in dermatomyositis. Rituximab has been found to decrease disease activity by depleting B cells. Antimitochondrial antibodies have also been identified in slightly more than 11% of patients [17]. One-third of these patients had primary biliary cirrhosis, one-third had cardiac involvement (arrhythmias or decreased ejection fraction), and one-third had decreased respiratory function, occasionally to the point of requiring ventilation.

An important mimic for myopathy in the elderly population is polymyalgia rheumatica (PMR). Rapid onset of shoulder pain and stiffness is a hallmark of PMR, although neck and pelvic muscle pain is common. Systemic signs such as low-grade fever, anorexia, fatigue, and weight loss can be seen in up to 40% of patients. Sedimentation rate is elevated in inflammatory myopathies but a high sedimentation rate, higher than 40 mm/h, is the sole abnormality in PMR [22]. Distinguishing among these disorders is important for directing treatment. Polymyositis and dermatomyositis are treated with prednisone and IVIG. Steroid-sparing strategies include cyclosporine and tacrolimus. Hydroxychloroquine is used for the skin manifestations of dermatomyositis. No effective treatment strategy has been identified for IBM.

TOXIC MYOPATHIES

The sheer number of people who take statins (more than 10 million Americans) would seem to magnify the importance of this disorder. However, significant statin-induced myopathy affects fewer than 5%, with rhabdomyolysis in fewer than 0.1% [18]. Patho-anatomy and physiology of statin myopathies start with their metabolism by the cytochrome P-P450 3A4 system; with competition by concomitant drug intake, there is an resultant increased risk of myopathy. Common comedications are clarithromycin, mibefradil, verapamil, nefazodone, cyclosporine, diltiazem, and itraconazole. Fluvastatin and pravastatin use a different metabolic pathway, which alleviates this drug-drug interaction concern. The lipophilic cerivastatin, lovastatin, and simvastatin are more myotoxic. Gemfibrozil is a lower-risk additive agent for cho-

lesterol control than fenofibrate. Vitamin D deficiency may have an additive effect such that vitamin replacement results in relative muscle protection and improvement. The mechanism of the myopathy is not clear.

However, it is now clear that genetic variants and mutations in the SLCO1B1, cytochrome P-P450, and COQ2 genes may determine individual susceptibility to statin myopathy. Statins may also initiate immune-mediated forms of necrotizing and inflammatory myopathy that are unmasked during statin therapy. The unmasking or aggravating of various metabolic myopathies and other neuromuscular disorders has been characterized in persons who are using statins, including hypokalemic and mitochondrial myopathies. The same is true of McArdle disease and postsynaptic neuromuscular junction disorders. Drug-induced lysosomal (chloroquine and amiodarone), antimicrotubular (colchicine and vinca alkaloids), and myofibrillar (emetine, ipecac) myopathies have also been reported during statin use [19].

High-dose statin treatment can result in as much as a 10-fold increase in the risk for myopathy. Medication cessation is the only known antidote to this myopathy. However, once patients have recovered muscle function, they can sometimes be effectively treated with every-other-day dosing with minimal adverse effects and relatively effective low-density lipoprotein cholesterol management [20]. Muscle biopsy is useful in distinguishing among inflammatory muscle disease, dystrophies, vasculitis, and mitochondrial disorders. Statin-related myopathies show nonspecific changes consistent with mitochondrial respiratory chain dysfunction (ragged red fibers, increased lipid, cytochrome-oxidase negative fibers). However, granuloma formation has also been seen in patients with statin myopathy and elevated CPK levels.

Steroid myopathy is due to the muscle proteolysis effect of steroids. Steroids also slow down the rate of protein synthesis in muscle and facilitate amino acid mobilization from muscle. The steroid effect on muscle is dose dependent, increasing significantly at a dose of 30 mg of prednisone daily. Exercise mitigates these effects, and every-other-day dosing may help as well.

SARCOPENIA

Sarcopenia is seen in 20% of all persons over the age of 70 years and may be due to malnutrition, hormone deficiency, inactivity, or chronic disease (chronic obstructive pulmonary disease, renal disease, liver disease, rheumatoid arthritis, cancer, congestive heart failure, Crohn disease). Evaluation of sarcopenia should include thyroid function, vitamin D level, growth hormone, and, in men, serum testosterone [21]. Vitamin D therapy is controversial from the standpoint of how effective it is in improving sarcopenia. Testosterone replacement in men shows a definite improvement in muscle mass and strength. Growth hormone replacement increases

muscle mass but not strength. This finding and the adverse effects seen in older persons leave questions regarding its relative benefit-to-risk ratio.

ELECTROMYOGRAPHY IN MYOPATHY

Electromyography (EMG) is helpful in identifying the presence of a myopathy by evaluating motor units and their recruitment as well as identifying likely muscle necrosis and inflammation as inferred by the presence of abnormal spontaneous activity. Electrodiagnosis is also important in ruling out other disorders that may mimic a myopathy by evaluating the pattern of involvement and by directing the choice of location for a muscle biopsy. It may also be used to evaluate response to treatment.

Nerve conduction studies (NCS) are typically normal in myopathies; however, low compound muscle action potential amplitudes may be present if the myopathy is severe and/or affects distal musculature because distal muscles are most typically used in NCS. Sensory responses are expected to be normal, except in disorders that cause both a myopathy and neuropathy, for example, critical illness neuromyopathy or amyloid. Typically, at least 1 motor and 1 sensory NCS is performed in the arm and in the leg, and the study expanded, depending on those findings. EMG and/or NCS also allows differentiation between muscle disease and defects of neuromuscular transmission (both pre- and postsynaptic disorders). If diffusely low compound muscle action potentials are present, then Lambert-Eaton Myasthenic syndrome should be considered.

EMG examination should include proximal and distal muscles, and should include clinically weak muscles. Prolonged insertional activity and abnormal spontaneous activity may be identified, depending on the type of myopathy. Myotonic potentials may be seen with channelopathies and specific toxic myopathies (see Table 3). Complex repetitive discharges, although more common in chronic neurogenic disorders, may also be encountered in myopathies. Spontaneous activity is greatest in proximal muscles in polymyositis

Table 3. *Spontaneous activity in myopathies*

Myopathies With Fibrillation Potentials	Myopathies With Myotonia
Polymyositis/dermatomyositis	Myotonic dystrophy
Inclusion body myositis	Myotonia congenital
Sarcoid myopathy	Paramyotonia congenital
Progressive muscular dystrophies	Hyperkalemic periodic paralysis
Centronuclear myopathy	Centronuclear myopathy
Acid maltase deficiency	Acid maltase deficiency
Carnitine deficiency	Colchicine myopathy
Colchicine myopathy	Chloroquine myopathy
Chloroquine myopathy	
Critical illness myopathy	
Infectious myopathies	

and/or dermatomyositis, with the thoracic paraspinal muscles targeted because they are unlikely to be abnormal due to degenerative spine disease. Classic changes include low amplitude, short duration, polyphasic motor unit potentials. An early recruitment pattern may be seen because a great number of motor units are needed to generate a low force level. In the presence of a chronic myopathy, such as inclusion body myositis, a mixture of both long- and short-duration motor units may be present. EMG is typically normal in PMR and sarcopenia.

EMG is effective in evaluating patients with suspected congenital myopathy. In a study of 62 young patients, 55 had EMG evidence of myopathy, 2 had evidence of neurogenic disorder, and 5 were normal. Routine muscle biopsy specimens in these patients showed 50 with myopathy and 5 with nonspecific findings. A final diagnosis in these patients was DMD (n = 27), Becker muscular dystrophy (1), congenital muscular dystrophy (9), dermatomyositis (4), limb-girdle muscular dystrophy (6), unidentified muscle disease (4), neurogenic disorder (4), and nonspecific findings (8). The sensitivity of EMG was more than 95% in identifying a myopathy in this group of patients; sensitivity improved minimally but significantly by adding turns and amplitudes analysis [24].

EMG has been studied in a population of patients with mitochondrial myopathies. NCS were abnormal in 36.4% of cases, with the finding of an associated sensorimotor axonal multifocal neuropathy affecting the lower more than the upper extremities. Needle examination was abnormal in 54.5% of patients, with myopathic motor unit changes seen in proximal lower more than the upper limb muscles. The proportion of patients with abnormalities did not differ among the different mitochondrial myopathies [25].

SKELETAL DEFORMITY IN MYOPATHY

A common cause for physiatric evaluation of these patients is the presence of skeletal deformity. An excellent review is provided by Finsterer and Strobl [26]. Spine deformities are a common feature in the muscular dystrophies and certain inherited myopathies. Scoliosis is seen in 90% of patients with dystrophinopathy. However, it is also commonly seen in FSH, collagen VI myopathies, laminopathies, CFTD (SEFN-1), central core, and multicore myopathies. Bent spine syndrome, or camptocormia, is commonly associated with gluteal weakness and increases with standing. It is commonly seen in dysferlinopathies, nemaline myopathy, and myotonic dystrophy types 1 and 2. A differential diagnosis includes dermatomyositis, polymyositis, CIDP, inclusion body myositis, motor neuron disease, and postsynaptic neuromuscular junction disorders. Dropped head syndrome is most common with facioscapulohumeral dystrophy but can be seen in laminopathies, nemaline myopathies, myotonic dystrophies type 1 and 2, mitochondrial myopathy, and acid maltase deficiency. Differential diagnosis

considerations include motor neuron disease and postsynaptic neuromuscular junction disorders. Hyperlordosis can be seen in dystrophinopathies, LGMD, FSH dystrophy, and laminopathies. Hyperkyphosis is seen in dystrophinopathies and laminoplasties. Rigid spine is seen in laminopathies, EDMD, Ullrich, multicore, and multiminicore myopathies.

Other skeletal anomalies include scapular, pelvic, and chest wall changes. Scapula winging is universally seen in facioscapulohumeral dystrophy. However, it also can be seen in many of the limb girdle dystrophies, EDMD, laminopathies, and acid maltase deficiency. Pectus excavatum, pectus carinatum, and anteroposterior flattening of the chest can be seen in any of the congenital myopathies as well as the dystrophinopathies. Pelvic obliquities are found in DMD, laminopathies, and congenital MP with type 1 predominance.

Joint contractures are also commonly seen in specific myopathies. In the dystrophinopathies, contractures of the iliotibial band, hip flexors, knees, and ankles are seen. In EDMD, knee, elbow, Achilles, and cervical spine contractures are seen. Laminopathies and Ullrich myopathy result in proximal contractures, whereas Bethlem myopathy leads to distal contractures. Limb girdle MD 2a (calpain) and 2b (dysferlinopathy) are associated with ankle contractures. Central cord patients frequently have contractures, and patients with myotonic dystrophy commonly have hip abduction and knee flexion contractures.

Myopathies can also be associated with joint hypermobility, hyperlaxity, subluxation, or dislocation. Common associations in dystrophinopathies include hip subluxation in mitochondrial myopathies and hip dislocations in central core myopathy. Generalized joint laxity is seen in the collagen VI myopathies, LGMD 2E (β-sarcoglycan), multiminicore disease, CMP, merosin-+, and CMD.

Toe walking is seen in dystrophinopathies, laminopathies, EDMD, and dysferlinopathies. Not surprisingly, equinovarus contractures can be seen in these disorders, particularly in dystrophinopathies and laminopathies. Club foot is found in central core and multicore disease. Arthrogryposis can have any foot deformity as can collagen VI myopathies, centronuclear myopathy, CFTD, and Emery-Dreifuss muscular dystrophy.

EXERCISE IN MYOPATHY

Overall, the limited body of literature on exercise in myopathies is favorable in this regard. In McArdle disease, exercise training improved cardiac output, work capacity, and oxidative capacity as measured by increased mitochondrial enzyme concentrations [27]. In inflammatory myopathies, nonresistive exercise improves aerobic capacity, endurance, and fatigue. There is evidence that messenger RNA expression is influenced by exercise, with a decrease in proinflammatory and profibrotic expression, which influences the course of

the disease [28]. Of 12 studies completed on exercise in inflammatory myopathies, none saw an increase in disease activity or pain. Strength was not influenced by the exercise regimen. In patients with chronic inflammatory myopathies, resistive training, aerobic exercise, and home exercise improve strength and function [29]. Resistance training 3 times per week in sarcopenia is effective in improving strength, muscle mass, and associated mobility deficits. Adding creatine to the exercise regimen provides further benefit. A high protein diet or supplements are not effective without exercise and provide no additive advantage [21].

Creatine has a role in anaerobic muscle energy delivery and is important in mitochondrial respiration function. It is postulated that supplementation would have an effect on muscle performance in patients with myopathy. This has been shown to be the case in the muscular dystrophies and in mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes, whereas the effect in myotonic dystrophy and McArdle disease was not demonstrated [30]. The addition of creatine does increase muscle mass and function in patients with chronic inflammatory myopathy who are undergoing a resistance and aerobic exercise program [29].

CLINICAL PEARLS

- Many myopathies can now be classified by genetic analysis, which allows for identification of the defective gene by-product. So-called congenital myopathies have historically been categorized and named based on their biopsy appearance.
- In DMD, oral prednisone may prolong motor skill ability. Overall life expectancy has significantly improved in recent decades due to the use of assisted ventilation.
- Along with muscle weakness, most prominently in the face, neck, and distal extremities, individuals with myotonic myopathy may have characteristic male frontal balding.
- Mitochondrial myopathies, such as chronic progressive external ophthalmoplegia; mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes, and myoclonic epilepsy with ragged red fibers, may benefit from coenzyme Q supplementation.
- IBM is considered the most prevalent idiopathic inflammatory myopathy in the geriatric population, although cancer-related dermatomyositis is more common. In fact, in the elderly, ongoing cancer screening should continue for 5 years after the diagnosis of dermatomyositis. To date, no effective treatment has been identified for IBM.
- Polymyositis and dermatomyositis are treated with prednisone and IVIG. Steroid-sparing strategies include cyclosporine and tacrolimus. Hydroxychloroquine is used for the skin manifestations of dermatomyositis.
- The steroid effect on muscle is dose dependent, increasing significantly at a dose of 30 mg of prednisone daily. The

effect of steroid myopathy may be lessened with exercise and with reducing steroid dosing (such as every other day dosing) when tolerable.

- In addition to exercise, creatine supplementation is postulated to improve muscle performance in patients with myopathy due to its role in anaerobic muscle energy delivery and mitochondrial respiration.
- In patients with suspected inflammatory myopathy, sampling the thoracic paraspinal muscles may be useful in detecting spontaneous activity in a region unlikely to be affected by confounding degenerative spine disease. Proximal and distal limb musculature should be sampled with needle EMG to characterize myopathy.

FURTHER READING

This section consists of references that are included in the reference list but are not cited in the article text [23].

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