Muscle Diseases

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INTRODUCTION

Skeletal muscle fibers are the effector cells of the nervous system, turn thoughts into actions, and are the means by which we interact with our environment. Myopathies are primary diseases of the muscle and can be both inherited and acquired (Table 122-1). Myopathies can result in weakness and muscle wasting, myalgias, cramps, muscle breakdown, or contractures. Inherited disorders affect muscle proteins involved in transmission of signals from the neuromuscular junction, proteins involved in energy production or metabolism, or structural proteins that anchor and transmit force from the contractile apparatus to the extracellular matrix. Acquired myopathies are caused by external factors and can be due to metabolic derangements, toxic exposures or drugs, infections, or autoimmune dysfunction causing inflammation in the muscle. Acquired myopathies often improve with treatments geared towards eliminating or ameliorating the precipitating factors. To date, there have not been specific treatments for most inherited disorders of muscle, but as our understanding of the molecular pathological mechanisms of these disorders advances, new disease-directed therapies are entering clinical trials.

ORGANIZATION AND STRUCTURE OF MUSCLE

Each muscle is enclosed in a connective tissue sheath made up of collagen and extracellular matrix proteins called the epimyseum, which merges at either end to form the tendons, which attach muscle to bone. The epimyseum divides internally into the perimysium, which separates the muscle into individual bundles of muscle fibers called fascicles. The endomyseum surrounds and provides support for the individual fibers. Each muscle fiber is a single multi-nucleated syncytial cell and can be as long as 10 cm. On cross section, muscle fibers appear polygonal in shape and in adults range from 40 to 80 micrometers in diameter. Medium size arterioles and veins run in the perimysium, with capillaries between the individual muscle fibers. On hematoxylin and eosin stains, cytoplasm appears pink and the nuclei blue, with a thin rim of white, the epimyseum, between fibers (Fig. 122-1A). Each individual muscle fiber has multiple nuclei, which are found beneath the sarcolemma membrane on the periphery of the cell. The amount of connective tissue between fibers, the position and number of myonuclei, and the amount and distribution of mitochondria can all be indicators of disease.

The plasma membrane around the muscle fiber is called the sarcolemma, and inside there are a large number of myofibrils made of thick (myosin) and thin (actin) filaments, which make up 70% to 80% of the volume of the cell, and when activated, create force. Electrochemical signals carry the signal from the nerve, through the neuromuscular junction, into the muscle fiber along the sarcolemma and t-tubule system. Muscle ion channels line this network and carry electrochemical signals. Mitochondria and enzymes involved in glycolysis and fatty acid metabolism provide energy for muscle. A network of proteins, the dystrophin-glycoprotein complex (DGC), anchors the myofibrils to the subsarcolema cytoskeleton and connects to the extracellular matrix (Fig. 122-2). Many inherited myopathies are due to mutations in these ion channels, metabolic enzymes, or structural anchoring proteins.

TABLE 122-1 OVERVIEW OF MYOPATHIES

HEREDITARY MYOPATHIES	ACQUIRED MYOPATHIES
Muscular dystrophies	Inflammatory myopathies
Congenital myopathies	Endocrine myopathies
Metabolic/Mitochondrial myopathies	Systemic illness/infectious myopathies
Channelopathies	Toxic/Drug-induced myopathies

ASSESSMENT

The work-up of a patient with a suspected myopathy is a staged process and involves a history and physical examination, followed by laboratory studies, electrodiagnostic testing, muscle biopsy, and genetic testing (Table 122-2). The family history is important because muscle disease can run in the family and may not have been previously diagnosed. Questions about whether family members require assistive devices to walk or wheelchairs, and concerning common extra muscular manifestation of muscular dystrophies can be useful. The genetic myopathies can be inherited in an autosomal dominant or recessive fashion, be X-linked, show maternal inheritance, or be sporadic (Table 122-3).

The most common symptom of a patient with muscle disease is a loss of function caused by weakness (see Table 122-2). Other common symptoms, like fatigue or myalgias (muscle pain), are less specific than muscle weakness. Muscle cramping is most often benign, and can be secondary to neuropathic changes. Muscle contractures are sustained contractions that are distinguished from cramping on electrodiagnostic testing, where contractures are electrically silent. Tendon contractures, on the other hand, are a fixed shortening of the tendon, and associated with long-standing disuse.

EXAMINATION

The physical examination uses a standard modified Medical Research Council scale of motor strength to determine the