TABLE 122-5 CHARACTERISTIC PATTERNS OF MUSCLE WEAKNESS AND ASSOCIATED MYOPATHIES

PATTERN	WEAKNESS	DISEASES
Proximal limb-girdle	Symmetrical, pelvic and shoulder girdle muscles. Distal muscles to lesser extent. ± Neck flexor/extensor.	Nonspecific: Duchenne muscular dystrophy; limb-girdle muscular dystrophy; inflammatory myopathies; certain autoimmune neuropathies
Distal	Symmetrical, distal upper or lower extremity. Proximal muscles to lesser degree.	Nonspecific: Miyoshi myopathy (calves); Welander myopathy (wrist and finger extensors); Nonaka and Markesbery/Udd myopathy (tibialis anterior); rule out neuropathy
Proximal arm/distal leg	Scapuloperoneal distribution: periscapular muscles (proximal arm) and anterior compartment distal leg (tibialis anterior). Scapular winging. Can be asymmetrical.	When face involved highly suggestive of facioscapulohumeral muscular dystrophy; with elbow contractures Emory-Dreifuss dystrophy; scapuloperoneal dystrophies; certain limb-girdle dystrophies; congenital myopathies
Distal arm/proximal leg	Distal forearm muscles (distal finger flexors) and proximal leg (quadriceps). Other muscles variable. Often asymmetrical.	Highly suggestive of sporadic inclusion body myositis; also consider myotonic dystrophy
Ptosis ± ophthalmoparesis	Ocular weakness at presentation. Restriction of eye movements often without diplopia. Occasionally followed by pharyngeal weakness. Variable extremity weakness	Ocular and pharyngeal weakness highly suggestive of oculopharyngeal muscular dystrophy; ptosis and ophthalmoplegia without pharyngeal involvement mitochondrial myopathies
Neck extensor weakness	Neck extensors, "dropped head syndrome." Variable neck flexor. ± extremity weakness.	In isolation consider isolated neck extensor myopathy; rule out amyotrophic lateral sclerosis and myasthenia gravis
Bulbar weakness	Tongue and pharyngeal weakness	Certain myopathies (e.g., oculopharyngeal muscular dystrophy); significant overlap with neuromuscular junction and motor neuron disease
Episodic pain, weakness, and myoglobinuria	May be triggered by exercise or metabolic stress	Metabolic myopathies; may also occur in deconditioning
Episodic weakness delayed or unrelated to exercise	May be triggered by food, stress, rest after exercise	Characteristic of periodic paralyses
Stiffness and decreased ability to relax	May be episodic, triggered by cold	Characteristic of myotonic disorders; but may be seen in other myopathies; acquired conditions (e.g. stiff person syndrome)

Modified from Jackson CE, Barohn RJ: A pattern recognition approach to myopathy, Continuum (Minneap Minn) 19(6 Muscle Diseases):1674-1697, 2013.

TABLE 122-6 CAUSES FOR ELEVATED SERUM CK

MYOPATHIES	MEDICATIONS
Muscular dystrophies/carrier state Congenital myopathies Metabolic myopathies Inflammatory myopathies	Statins Fibric acid derivatives Chloroquin Colchicine
CHANNELOPATHIES	ENDOCRINE ABNORMALITIES (THYROID/PARATHYROID)
MOTOR NEURON DISEASE (ALS, SMA)	SURGERY
NEUROPATHIES (GBS, CIDP)	TRAUMA
VIRAL ILLNESS	STRENUOUS EXERCISE
	INCREASED MUSCLE MASS
	IDIOPATHIC

INHERITED MYOPATHIES

Muscular Dystrophies

The muscular dystrophies are inherited myopathies characterized by progressive weakness and mutations in genes coding for structural and other muscle proteins. Typically the muscular dystrophies are divided into the dystrophinopathies, the myotonic dystrophies, facioscapulohumeral muscular dystrophy, Emery-Dreifuss muscular dystrophy, and the limb-girdle dystrophies (Tables 122-7, 122-8, and E-Table 122-1). The limb-girdle muscular dystrophies (LGMD) are a diverse group of diseases due to mutations in more than 20 genes. The LBMDs are inherited in either autosomal dominant or recessive fashion, and present anywhere from childhood to later in life, having as the name implies, a limb-girdle pattern of weakness (E-Table 122-1). Another group of patients who have dystrophic changes in the muscle from birth, often with accompanying changes in the brain on MRI, include congenital muscular dystrophies (see Table 122-8; not discussed in text). The traditional distinction between dystrophies and other inherited myopathies is becoming blurred as our genetic understanding advances because mutations for different diseases are often allelic.

Dystrophinopathies

Definition and Epidemiology

Dystrophinopathies are X-linked recessive disorders resulting from mutations of the large dystrophin gene located at Xp21. The incidence of Duchenne muscular dystrophy is 1 in 5300 male births; one third of the cases result from a new mutation. Becker muscular dystrophy is a milder form of dystrophinopathy and is less common than the Duchenne form, with an incidence of 5 per 100,000.

Pathology

Dystrophin is a large subsarcolemmal cytoskeletal protein that, along with the other components of the dystrophin-glycoprotein complex, provides support to the muscle membrane during contraction. Muscle biopsies are typically not required for diagnosis but show variability in fiber size; active and chronic changes, including necrotic and regenerating fibers; and, later in the disease, increased connective tissue and deposition of fat (Fig. 122-1B).

Clinical Presentation

Mutations in dystrophin result in a spectrum of disorders reflecting variations in the amount of functional dystrophin still expressed—from Duchenne muscular dystrophy and Becker's on the severe end, to isolated quadriceps weakness and isolated cardiomyopathy in the middle, and to cramps and myalgias with