Forearm Exercise Test In myopathies with intermittent symptoms, and especially those associated with myoglobinuria, there may be a defect in glycolysis. Many variations of the forearm exercise test exist. For safety, the test should not be performed under ischemic conditions to avoid an unnecessary insult to the muscle, causing rhabdomyolysis. The test is performed by placing a small indwelling catheter into an antecubital vein. A baseline blood sample is obtained for lactic acid and ammonia. The forearm muscles are exercised by asking the patient to vigorously open and close the hand for 1 min. Blood is then obtained at intervals of 1, 2, 4, 6, and 10 min for comparison with the baseline sample. A three- to fourfold rise of lactic acid is typical. The simultaneous measurement of ammonia serves as a control, because it should also rise with exercise. In patients with myophosphorylase deficiency or other glycolytic defects, the lactic acid rise will be absent or below normal, while the rise in ammonia will reach control values. If there is lack of effort, neither lactic acid nor ammonia will rise. Patients with selective failure to increase ammonia may have myoadenylate deaminase deficiency. This condition has been reported to be a cause of myoglobinuria, but deficiency of this enzyme in asymptomatic individuals makes interpretation controversial.

Muscle Biopsy Muscle biopsy is an important step in establishing the diagnosis of a suspected myopathy. The biopsy is usually obtained from a quadriceps or biceps brachii muscle, less commonly from a deltoid muscle. Evaluation includes a combination of techniques—light microscopy, histochemistry, immunocytochemistry with a battery of antibodies, and electron microscopy. Not all techniques are needed for every case. A specific diagnosis can be established in many disorders. Endomysial inflammatory cells surrounding and invading muscle fibers are seen in polymyositis; similar endomysial infiltrates associated with muscle fibers containing rimmed vacuoles and amyloid deposits consisting of SMI-31-, p62-, and TDP-43-positive inclusions within fibers are characteristic of inclusion body myositis; and perivascular, perimysial inflammation associated with perifascicular atrophy is a feature of dermatomyositis. In addition, the congenital myopathies have distinctive light and electron microscopy features essential for diagnosis. Mitochondrial and metabolic (e.g., glycogen and lipid storage diseases) myopathies also demonstrate distinctive histochemical and electron-microscopic profiles. Biopsied muscle tissue can be sent for metabolic enzyme or mitochondrial DNA analyses. A battery of antibodies is available for the identification of abnormal proteins to help diagnose specific types of muscular dystrophies. Western blot analysis on muscle specimens can be performed to determine whether specific muscle proteins are reduced in quantity or are of abnormal size.

HEREDITARY MYOPATHIES

Muscular dystrophy refers to a group of hereditary progressive diseases each with unique phenotypic and genetic features **(Tables 462e-5, 462e-6, and 462e-7)**.

DUCHENNE MUSCULAR DYSTROPHY

This X-linked recessive disorder, sometimes also called *pseudohypertrophic muscular dystrophy*, has an incidence of ~1 per 5200 live-born males.

Clinical Features Duchenne dystrophy is present at birth, but the disorder usually becomes apparent between ages 3 and 5 years. The boys fall frequently and have difficulty keeping up with friends when

TABLE 462e-5 PROGRESSIVE MUSCULAR DYSTROPHIES

Type	Inheritance	Defective Gene/ Protein	Onset Age	Clinical Features	Other Organ Systems Involved
Duchenne	XR	Dystrophin	Before 5 years	Progressive weakness of girdle muscles Unable to walk after age 12 Progressive kyphoscoliosis Respiratory failure in second or third decade	Cardiomyopathy Mental impairment
Becker	XR	Dystrophin	Early childhood to adult	Progressive weakness of girdle muscles Able to walk after age 15 Respiratory failure may develop by fourth decade	Cardiomyopathy
Limb-girdle	AD/AR	Several (Tables 462e-6, 462e-7)	Early childhood to early adult	Slow progressive weakness of shoulder and hip girdle muscles	± Cardiomyopathy
Emery-Dreifuss	XR/AD	Emerin, lamin A/C Nesprin-1, nesprin-2, *TMEM43*	Childhood to adult	Elbow/knee/ankle contractures, humeral and peroneal weakness	Cardiomyopathy
Congenital	AR	Several	At birth or within first few months	Hypotonia, contractures, delayed milestones Progression to respiratory failure in some; static course in others	CNS abnormalities (hypomyelination, malformation) Eye abnormalities
Myotonic[a] (DM1, DM2)	AD	DM1: Expansion CTG repeat DM2: Expansion CCTG repeat	Childhood to adult; possibly infancy if mother affected (DM1 only)	Slowly progressive weakness of face, shoulder girdle, and foot dorsiflexion Preferential proximal weakness in DM2	Cardiac conduction defects Mental impairment Cataracts Frontal baldness Gonadal atrophy
FSHD1	AD	*DUX4* 4q	Childhood to adult	Slowly progressive weakness of face, shoulder girdle, and foot dorsiflexion	Deafness
FSHD2	AD	*SMCHD1*			Coats' (eye) disease
Oculopharyngeal	AD	Expansion, poly-A RNA binding protein	Fifth to sixth decade	Slowly progressive weakness of extraocular, pharyngeal, and limb muscles	—

[a]Two forms of myotonic dystrophy, DM1 and DM2, have been identified. Many features overlap (see text).

Abbreviations: AD, autosomal dominant; AR, autosomal recessive; CNS, central nervous system; XR, X-linked recessive.