when amplified sounds like a dive bomber or motorcycle revving. Symptoms usually start in the first decade, and patients can have a characteristic muscular build. Chloride channel mutations can be both dominantly and recessively inherited and have a characteristic warmup of myotonia with repetition. Sodium channel myotonias typically have more myotonia on eye closure and can demonstrate a paradoxical worsening of myotonia with activity (paramyotonia).

Diagnosis and Differential Diagnosis

Diagnosis is based on family history, myotonia on clinical examination, and electrodiagnostic testing. It is confirmed by genetic testing. The differential diagnosis includes myotonic dystrophy and secondary causes of myotonia (other myopathies and drugs associated with myotonia—e.g., statins, fibric acid derivatives, and colchicine).

Treatment

Treatment for nondystrophic myotonias consists of non-mutation–specific sodium channel blockade: mexiletine, a class IB antiarrhythmic, is the first line therapy but phenytoin, procainamide, and flecainide have also been used. Certain sodium channel myotonias respond to the carbonic anhydrase inhibitor acetazolamide.

Periodic Paralyses

Definition and Epidemiology

The periodic paralyses are disorders due to mutations in the calcium (CACN1AS on chromosome 1), sodium (SCN4A on chromosome 17), and potassium channels (KCNJ2 on chromosome 17) that result in depolarized but inexcitable sarcolemma and episodes of paralysis. Overall prevalence for the primary periodic paralyses is greater than 1 : 100,000 and varies between conditions from 1 : 100,000 to 1 : 1,000,000.

Pathology

Hyperkalemic periodic paralysis is due to sodium mutations that lead to persistent inward sodium current causing both myotonia and paralysis depending on the relationship of depolarization to the sodium channel inactivation potential. Hypokalemic periodic paralysis is due to an anomalous gating pore current that, in low potassium conditions, produces a depolarizing current larger than hyperpolarizing potassium currents. Andersen Tawil syndrome is due to loss of function in a potassium inward rectifier.

Clinical Presentation

Common to all is attacks of flaccid tetraplegia, often brought on by rest after exercise, or in the mornings, and is associated with changes in extracellular potassium. Hyperkalemic periodic paralysis is due to mutations in sodium channels and is associated with either high or normal extracellular potassium. Triggers include potassium-rich foods. In hypokalemic periodic paralysis attacks are associated with low extracellular potassium, and are triggered by carbohydrates, stress, alcohol, or rest after exercise. Andersen-Tawil syndrome is due to mutations in a potassium inward rectifier and is characterized by the clinical triad of attacks of flaccid paralysis, dysmorphic features (wide-set eyes, narrow mandible, low-set ears, bent fifth finger, and common origin for the second and third toes), and polymorphic ventricular tachyarrhythmias.

Diagnosis and Differential Diagnosis

Diagnosis is based in family history and clinical history, supported by electrodiagnostic testing and confirmed by genetic testing.

Treatment

In all of the periodic paralyses disorders mild exercise at onset of weakness can abort attacks of paralysis. Treatment for acute attacks consists of carbohydrates (hyperkalemic periodic paralysis) or potassium supplementation (hypokalemic periodic paralysis). Prophylactic treatment for all the periodic paralyses consists of carbonic anhydrase inhibitor acetazolamide.

ACQUIRED MYOPATHIES

Unlike the inherited myopathies, the acquired myopathies are typically secondary to another process: toxic, inflammatory, or infectious. Pathological changes can be distinctive and are not due to mutations in muscle-related proteins. Clinically, symptoms appear acutely or subacutely. Treatment often includes eliminating the precipitating factor.

Inflammatory Myopathies

The idiopathic inflammatory myopathies can be divided into dermatomyositis/polymyositis and sporadic inclusion body myositis (Table 122-9).

Dermatomyositis/Polymyositis

Definition and Epidemiology

Dermatomyositis/Polymyositis (DM/PM) are acquired idiopathic diseases of muscle characterized by inflammation and variable symmetrical proximal muscle weakness, associated with elevated serum creatine kinase and irritable features on electromyography. The overall annual incidence is approximately 1 in 100,000.

Pathology

Dermatomyositis shows a characteristic pattern on muscle biopsy of perifascicular atrophy with perivascular inflammatory infiltrates and positive pericapillary membrane attack complex staining (Fig. 122-1D). In contrast, polymyositis shows endomyseal inflammatory infiltrates with invasion of non-necrotic fibers, without other pathological changes.

Clinical Presentation

Dermatomyositis has a bimodal age of onset with peaks in childhood and adulthood, with an acute to insidiously progressive onset of painless symmetrical proximal muscle weakness with characteristic skin changes, which include heliotrope rash, shawl sign (maculopapular violaceous rash in v-shape around neck), Gottron's nodules (erythematous papular rash on the extensor surfaces of the hands or fingers), and mechanic's hands (dry, cracked skin on the dorsal or ventral hands). In contrast, Polymyositis is largely a diagnosis of exclusion, occurring in adults and not associated with skin changes. Myalgias are more common in polymyositis. In both DM/PM can be associated with respiratory