elevated serum CK on the mild end. Duchenne muscular dystrophy manifests as early as age 2 to 3 years with delays in motor milestones and difficulty running. Patients can have marked pseudo-hypertrophy of the calf muscles. And when asked to get up from the floor, boys use a Gower's maneuver (use hands to push up). The average age of diagnosis is around 4 years of age. The proximal muscles are the most severely affected, and the course is relentlessly progressive. Patients begin to fall frequently by age 5 to 6, have difficulty climbing stairs by age 8 years, and are usually confined to a wheelchair in their early teens. The smooth muscle of the gastrointestinal tract is involved and may cause intestinal pseudo-obstruction. The average IQ of boys with Duchenne muscular dystrophy is low, reflecting central nervous system involvement.

Diagnosis and Differential Diganosis

Diagnosis is based on clinical history, physical examination, serum CK, and is confirmed by genetic testing. The majority of patients have deletions or duplications in the dystrophin gene. In the remaining patients, mutations can be small insertions or deletions, point mutations, or splicing errors. Other differential considerations are congenital myopathies and muscular dystrophies, and limb-girdle muscular dystrophies.

Treatment

Duchenne muscular dystrophy is a combination of surveillance for respiratory, orthopedic, and cardiac involvement, and the use of prednisone. Prednisone and deflazacort (a synthetic derivative of prednisolone available in other countries) improve strength and motor function in boys with Duchenne muscular dystrophy. Cardiac evaluation should begin at the time of diagnosis and, if cardiac involvement is found, afterload reduction is recommended (ACE inhibitor, β-blocker). Respiratory function should be monitored beginning prior to wheelchair use or when the forced vital capacity drops below 80%. Regular orthopedic screening for scoliosis and bone health is recommended. New investigational strategies for treatment include gene therapy, exon skipping strategies, and readthrough of premature stop mutations, all of which are designed to make the cell produce some form of dystrophin. There are no guidelines for the treatment of Becker muscular dystrophy and clinical presentation is highly variable, but monitoring for cardiac and respiratory involvement is warranted. Some female carriers of dystrophin mutations may become symptomatic later in life, and may have severe cardiomyopathy.

Prognosis

Patients with Duchenne muscular dystrophy die of respiratory complications in their 20s unless they are provided with respiratory support. Congestive heart failure and arrhythmias can occur late in the disease. The disease course for other dystrophinopathies is highly variable.

Myotonic Dystrophy

Definition and Epidemiology

Myotonic dystrophies are autosomal dominant diseases characterized by muscle wasting and myotonia. There are two types and both are due to expanded DNA repeats: type 1 (DM-1) due to CTG expansion on chromosome 19; and type 2 (DM-2) to CCGT expansion on chromosome 3. DM-1 is the most prevalent adult muscular dystrophy, with an incidence of 13.5 per 100,000 live births.

Pathology

In both myotonic dystrophy types 1 and 2, accumulation of aberrant RNA in the nucleus binds regulatory proteins and causes aberrant splicing of a variety of proteins. Both disorders are multisystem diseases, affecting skeletal, cardiac, smooth muscle, and other organs, including the eyes, the endocrine system, and the brain. Muscle biopsies are not required for diagnosis but characteristic findings include rows of internal nuclei (boxcar appearance), ring fibers, type 1 fiber predominance, and later, fibrosis and fatty infiltration.

Clinical Presentation

DM-1 can present at any age, with the usual onset of symptoms in the late second or third decade. However, some affected individuals may remain symptom-free their entire lives. A severe form of DM-1 with onset in infancy is known as congenital myotonic dystrophy. The severity of DM-1 generally worsens from one generation to the next (anticipation). Typical patients exhibit facial weakness with temporalis muscle wasting, frontal balding, ptosis, and neck flexor weakness. Extremity weakness usually begins distally and progresses slowly to affect the proximal limb-girdle muscles. Percussion myotonia can be elicited on examination in most patients, especially in thenar and wrist extensor muscles. DM-2 is typically milder but can present in an identical fashion to DM-1; however, some patients can only have a mild proximal limb-girdle pattern of weakness. Associated manifestations in the myotonic dystrophies include cataracts, testicular atrophy and impotence, intellectual impairment, and hypersomnia associated with both central and obstructive sleep apnea.

Diagnosis and Differential Diagnosis

The diagnosis is based on clinical examination, demonstration of myotonia on electromyography, and is confirmed by genetic testing. Myotonic dystrophy needs to be distinguished from other adult onset muscular dystrophies and non-dystrophic myotonic disorders.

Treatment

Yearly surveillance for cardiac and respiratory involvement is recommended. Mexiletine, a type IB anti-arrhythmic medication, can be used for symptomatic myotonia. There is currently no treatment to halt disease progression but many therapies targeting the interaction between RNA accumulations and regulatory proteins, or RNA accumulations themselves, are under investigation.

Prognosis

Respiratory muscle weakness may be severe, with impairment of ventilatory drive. Chronic hypoxia can lead to cor pulmonale. Cardiac conduction defects are common and can produce sudden death. Pacemakers may be necessary.