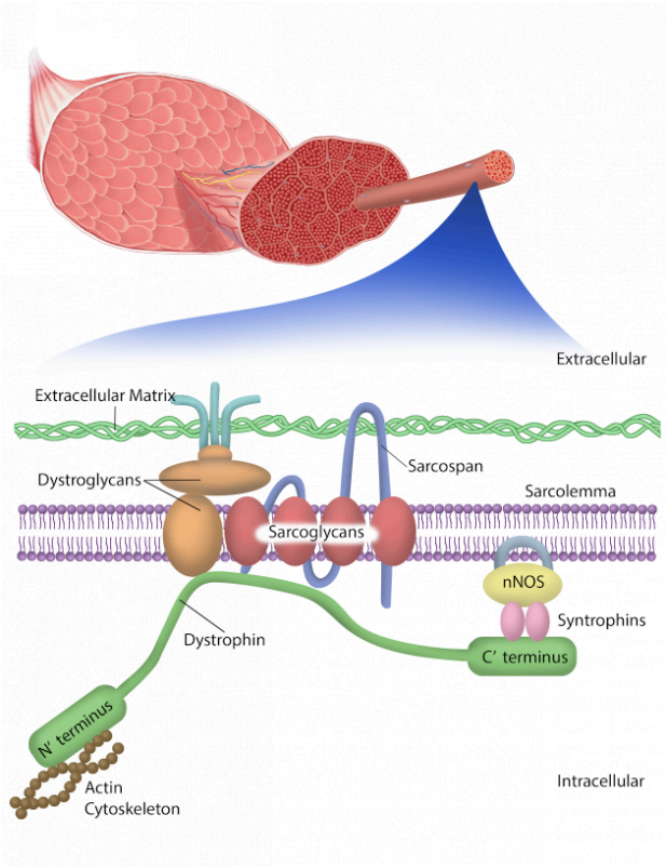
6.1.1

Muscular Dystrophy

Muscular dystrophy is a disorder of the muscles rather than the nervous system, but we will discuss it here. Muscular dystrophy is normally caused by a mutation in the **dystrophin** gene. Dystrophin is a massive gene located on the X chromosome with two million base pairs that codes for the dystrophin protein. Muscular dystrophy is an X-linked recessive disorder, which means it is more common in men because they only have one X chromosome. There are two main types of muscular dystrophy. The first, **Duchenne muscular dystrophy (DMD)**, is more severe and is characterized by an absent or severely dysfunctional dystrophin protein caused by a mutation in the dystrophin gene. Frequent falls and symptoms show by age 5. A common orthopedic test that is observed for diagnosis of DMD is the **Gower's sign**, which is when a child uses their arms to help them get up to a standing position because of weakness in their leg muscles. The second type of muscular dystrophy, **Becker muscular dystrophy (BMD)**, is also caused by a dysfunctional dystrophin gene but is not as severe as DMD. Symptoms of BMD start later in life and are not as debilitating. Muscular dystrophy usually leads to a shorter lifespan because of effects on cardiac and respiratory muscles. Individuals with DMD usually live less than 30 years while individuals with BMD usually live until their mid-40s.



Dystrophin-Associated Protein Complex of Skeletal Muscle *Image by Becky T. BYU-I F19*

The dystrophin protein is a rod-shaped protein that is associated with a larger protein complex in the muscle cell. The role of dystrophin is to link the sarcomere elements to proteins in the sarcolemma (muscle cell membrane). The sarcolemma is linked to the connective tissue of the endomysium which is a linkage to the tendon itself. It is thought that the dystrophin protein is involved in linking the mechanical force of sarcomere shortening with the stability and health of the muscle cell membrane. Those that have muscular dystrophy lack the dystrophin protein. Without dystrophin, the pulling force of sarcomeres on the endomysium and ultimately the tendon is greatly compromised, causing muscle weakness.

Without functional dystrophin protein, the sarcolemma becomes unstable. Over time, cellular proteins like **creatine kinase (CK)** escape the muscle cell, the cell loses energy, and calcium entering the cell leads to cell death. Overall, muscles degenerate and weaken. Creatine kinase catalyzes the reversible reaction that converts creatine into phosphocreatine. Under conditions when additional energy is required by the muscle, the phosphate preloaded on creatine (i.e. phosphocreatine) can quickly be added to an ADP molecule by CK to form ATP. Because the damage of myocytes that occurs in muscular dystrophy leads to CK leaking into the blood, a test measuring CK levels in the blood is part of the diagnosis for MD. Pseudohypertrophy, which is muscular enlargement through deposition of fat rather than muscle fibers, is another common manifestation of muscular dystrophy. It usually occurs in the calf muscles. A muscle biopsy for diagnosis may be obtained by way of a small lateral incision to access the vastus lateralis. Observance of the characteristic histological changes consistent with DMD like increased fat and scar tissue replacing degenerating muscle cells is considered a positive result. With the advent of new molecular techniques, biopsy is no longer necessary for definitive diagnosis of the disease, but is still used in some cases. Tests can be done to monitor muscular dystrophy as well. Ultrasonography can be used to monitor changes in the muscles over time. Electrocardiography (ECG) and pulmonary function tests (PFTs) are used to assess effects on the heart and lungs respectively.

Physical therapy plays an important role in the management of muscular dystrophy because it works to prevent contractures and slow down weakness, especially in the respiratory muscles. Glucocorticoids may be used to slow the decline in muscle strength for those with DMD by suppressing the activity of cytotoxic T-cells in damaged muscles. Another potential treatment may be creatine monohydrate supplementation, which may be useful for increasing muscle strength. Myostatin is a protein produced by skeletal myocytes that prevents muscle cell growth. Follistatin is a protein produced by muscle cells that enhances muscle growth. Treatments with myostatin blockers or overexpressing follistatin genes in mice has been shown to result in much larger and stronger muscles, providing evidence for potential new treatments for muscular dystrophy.