Duchenne muscular dystrophy

Duchenne muscular dystrophy (DMD) is the most severe dystrophy, affecting 1 in 3500 live male births worldwide. It is caused by a mutation in the dystrophin gene, affecting the excitable tissues (skeletal muscle, cardiac muscle and brain). It results in severe muscle wasting, reduced cognitive capacity, loss of mobility and death usually in the third decade of life. It is a x-linked recessive disease, meaning it is usually inherited from the mother who is not showing symptoms of the disease. This is because females have two x chromosomes and males have one. The mother will have one normal dystrophin gene and one mutated one. When the mutated one is passed to a son, there is no normal dystophin gene inherited because a y chromosome has been passed from the father to the son, determining the sex as male, but also leaving the son without the ability to generate the protein dystrophin that is required in muscle, heart and brain.

A child born with DMD is not physically distinguishable from any other baby in regards to their ability to move at this very early age. However with the increasing mobility of the growing child, delays in movement milestones such as crawling and walking are noticeable. The disease progression through the first decade of life is a very severe one, where the child loses normal posture and the use of limbs, resulting in confinement to a wheelchair. The DMD patient continues to decline physically through the second and third decade of life and usually succumbs to respiratory or cardiac failure in this time.

As the underlying mutation in the dystrophin gene causing the protein of the same name to always be absent from the muscles of the DMD patient, the progression of the disease must be associated with ongoing processes triggered by the absence of dystrophin as the person ages. This progression is believed to be induced by the increased mobility of the child with age, causing frequent contraction-induced damage to the muscle that cannot be repaired fully by the normal processes in the body. Normal muscle tissue that is used to generate force is replaced by scar tissue that does not have such an ability and the muscles weaken as a result. The effect is cumulative and so the disease shows progression with age.

Underlying this damage is the entry of calcium into the muscle that most likely activates degenerative pathways that digest important components of the muscle, reducing normal function.

In the bodily fluids, calcium is dissolved at very high concentrations normally and has many important roles in the healthy body. Inside muscle (and all other tissues and organs) it is present at very low concentrations when the muscle is in a rested state (not contracting). The high calcium concentrations in the bodily fluids around the muscle immediately adjacent to the low calcium concentration inside the muscle creates a force that drives calcium into the muscle. This is normal and well tolerated in a healthy muscle. In DMD too much calcium enters the muscle from that in the bodily fluids, upsetting the normal levels of calcium inside the muscle. This is triggering a series of events that leads to muscle damage.

This is exacerbated by types of contractions that cause damage to muscles. These are called eccentric or lengthening contractions. Typically this is when a muscle is contracting (being shortened) but there is also a stretching of the muscle in the opposite direction (the lengthening) that increase the stress on the muscle. This is a normal type of contraction. It commonly occurs as one is walking down a steep hill and the quadriceps (front of the thigh) undergo this contraction. The muscles may be sore a day or so after the exercise in a healthy person and recovery occurs but in DMD recovery does not occur and damage to the muscle is sustained. The damaged incurred to the surface of the muscle of the DMD patient becomes a major way for excessive calcium to enter the muscle and initiate damage to normal tissue.