Muscle Physiology and the
Pathology of Muscular Dystrophy

Angela Tompkins

February 23, 2010

Everglades University

Biology
Muscle Physiology and the Pathology of Muscular Dystrophy

Humans are able to freely move their bodies about which is a precious, complex physiology that should not be taken for granted. There are different types of muscles in the human body like voluntary and involuntary muscles and smooth and striated muscle fibers that all function in a tight realm with the nervous system and different chemical reactions. Here is a brief explanation of what happens within the skeletal muscles:

Muscles are composed mostly of protein in a highly organized system from large groups to small fibers. Muscle units are separated from other muscle groups by plasma membranes called the sarcolemma and the cytoplasm within is called the sarcoplasm. Within the sarcoplasm are multiple long protein bundles called myofibrils, and many ATP producing mitochondria, as well as glycogen (a form of stored glucose for energy) and myoglobin (oxygen stored in blood for the break down of glycogen). Bundles of parallel myofilaments make up the myofibrils which is where most of the action takes place. In the myofilaments are contractile proteins called myosin (thick filaments), and actin (thin filaments). When signaled, the actin and myosin interlock and slide over each other to stretch or slide into one another to contraction. They are signaled from the nervous system followed by a series of chemical reactions involving ATP, calcium, sodium and potassium ions.
There are many other proteins involved in the process. Aside from the contractile proteins, there are regulatory proteins called tropomyosin and troponin which act like a switch to determine when to contract and when to relax. On the muscle fiber the ‘I band’ is the space between the myosin (thick) filaments, where lies only the thin filaments. In the middle of each ‘I band’ is a dark disc called the ‘Z disc’ made of titan, (elastic filament), which is connected to the sarcolemma by the cytoskeleton. The space between each Z disc, where these filaments interact, is called the sarcomere. As the muscle contracts the ‘I band” shrinks and the sarcomere shortens and as the Z disc’s come closer together pulling on the sarcolemma shortening the cell. This is how the muscle contracts.

One of the most clinically important accessory proteins here is dystrophin which is located just under the sarcolemma in the cytoplasm in the area of the ‘I band’. It is produced by specific genes and links the actin filaments to the protein extracellular matrix in the membrane known as the dystrophin-associated protein complex. Elements of the dystrophin gene and the protein structure have been identified, yet the exact functional role is still a bit unclear. However as research continues it is thought that its primary function is to provide mechanical reinforcement to the structure of the sarcolemma and thereby protecting the membrane from the stress or
tearing during contraction. If dystrophin is defective or absent, the membrane breaks down which then substances and molecules like proteins and enzymes leak out of the fiber into circulation. These enzymes and chemicals that leak out are responsible for certain chemical reactions and necessary for energy production for muscle contraction. At the same time the extracellular substances leak into the fiber through the broken down membrane damaging the fiber and disrupting the process of muscle contraction and may cause irreparable damage.

The absence or abnormality of dystrophin results in a condition known as Muscular Dystrophy. Muscular Dystrophy is a crippling disease resulting from mutated genes which slowly wastes away muscle tissue. Without dystrophin to help protect the fiber membrane keeping it intact, and assisting to create energy, the muscles begin to degenerate and atrophy, being replaced by fat and fibrous scar tissue creating fascia adhesions throughout the body. It is thought that the major determinate of the membrane damage would be the level of stress associated with contraction rather than the number of muscle activations, according to Petrof, Shrager, Stedman, Kelly, & Sweeney, 1993, which would explain why it primarily affects the peripheral limbs. Muscular dystrophies most commonly involve a genetic mutation in the dystrophin genes preventing the production of dystrophin or limiting the amount in subnormal levels. Generally in muscle tissue it’s normal for small tares on the sarcolemma to occur as the muscle undergoes excessive strain and there are small molecules that enhance the natural repair process. However in the absence of dystrophin, the sarcolemma (the membrane) is left unprotected tearing more frequently and more easily therefore muscle degeneration
greatly outweighs muscle regeneration eventually leading to death and adhesion of the tissue.

There are nine known different types of Muscular dystrophy which are classified depending on distribution of affected muscle groups, severity and prognosis, genetic defects and the means of inheritance. Duchenne muscular dystrophy (DMD) is the most common and most severe as it affects not just all the voluntary muscles but also the heart and respiratory muscles as well shortening ones life span drastically. It’s caused by a genetic mutation on the 23rd chromosome, the sex determining chromosome, being an X-linked recessive or sex-linked recessive trait. Therefore males are primarily affected from the gene passed down by their mother who most likely was only a carrier. Other types of MD that were inherited through the X-linked recessive trait are Becker and Emery-Dreifuss Muscular Dystrophy. Becker MD is a different mutated gene but located on the same gene locus as Duchenne MD. Coincidently being very much alike Duchenne MD, Becker MD often affects the heart tissue but in general is less severe and has a longer life expectancy.

Other dystrophies are inherited through autosomal dominate traits, meaning the mutated gene is dominate in one of the 22 chromosomes (excluding the 23rd sex chromosome), equally affecting both males and females. The dystrophies inherited in this manner include facioscapulohumeral, distal, and oculopharyngeal muscular dystrophies as well as myotonic dystrophy. Facioscapulohumeral Muscular Dystrophy (FSHD) is caused by a missing piece of DNA on chromosome 4. FSHD primarily affects the face, shoulders and upper arms but later affects certain muscles of the legs, the abdominals and the pelvic girdle leading to extreme lordosis which may eventually require a wheelchair.
However this type rarely affects the heart and respiratory muscles therefore not shortening the life span. The onset of FSHD usually begins in the age of the 20’s being a slow process spanning over decades with occasional rapid bursts of muscle deterioration.

The other means of inheritance are by autosomal recessive traits, autosomal again meaning they come from a mutation in one of the first 22 sets of chromosomes, yet being recessive decreases the chance of being affected, due to the dominance of the normal genes on that same locus (particular location on the chromosome). However that person will still be a carrier. This is very rare for a person to be affected by these dystrophies because their genotype for this degenerative trait must be homozygous. This means that both parents must carry the same rare mutated gene and still if both parents are heterozygous there is still a 25% chance the child won’t receive the gene at all. These particular types of dystrophies include the limb girdle dystrophy of early childhood and congenital muscular dystrophy.

As of now there is not yet a cure for Muscular Dystrophy. However there are exciting new ideas and discoveries on the horizon as scientists and medical professionals are working hard to find a treatment and a cure. Nutritional therapy may have a very powerful effect. Also according to (Saul), science has known for decades that many specific birth defects are a direct result of a specific vitamin deficiency. This may be a reflection of the depletion of our food of our essentials by the food industries. The interrelationship between food and genes is known as the genetotrophic concept. Muscular dystrophy may be a good example of that, therefore high dosage nutritional therapy, including CoQ10, Vitamin E, Selenium, and Lecithin and others may be extremely beneficial. It has been shown that these particular nutrients are severely
decreased in MD. Also on the horizon is research on stem cell therapy. Researchers in France have recently discovered a stem cell protein in between the muscle fibers of baby mice that may be capable of generating and repairing muscle tissue, as well as replicating itself. They call this protein PIC standing for proteins interstitial cells, ("Mda.org," 2010). This was just posted last month, January 2010. There is also research on gene therapy for Muscular Dystrophy that’s transported through the body via a viral shell. So although there is presently no cure or specific therapy now, it wasn’t long ago that Muscular Dystrophy was a complete mystery and in such a short time science and health professionals have come a long way in understanding the pathophysiology of the disorder and discovering new interventions.
References


http://www.duchenne-information.eu/complex.gif (picture)

http://legacy.owensboro.kctcs.edu/gcaplan/anat/images/Image286.gif (picture)