

A very simplified introduction to neuromuscular illnesses (NMIs) with a particular focus on the muscular dystrophies.

Bill Tillier
Calgary Alberta
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Available on-line at:

Terminology.

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- Myo = relating to muscle.
- Neuro = relating to nerves.
- Dystrophy = a general wasting away or degeneration.
- Muscular dystrophy (MD) = a group of disorders that, in one way or another, impair muscle function and lead to muscle weakness.
- Neuromuscular = relating to muscles and/or to their control by nerves.
- Atrophy = a general shrinkage or wasting away
- - pathy = a suffix that means disease, for example, a neuropathy is a pathology (disease) of the nerves.
- - itis = a suffix indicating inflammation: myositis is an inflammation of muscle.

Terminology.

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- Neuron = an individual nerve cell.
- Neurological = relating to the nervous system.
- Sclerosis = a hardening or scarring of tissue.
- Many disorders are named after the doctor who discovered them, for example, Duchenne muscular dystrophy, named after a French neurologist.
- Some disorders are named after the primary areas they affect, for example, FacioScapuloHumeral MD, a disorder affecting the muscles of the face and the muscles attaching to the scapula & humerus bones.
- Some disorders are named after their action, for example, myotonic dystrophy: myotonia involves an unusually long muscle contraction or inability to relax.

Classification.

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- Illnesses are often classified based on their primary impact: disorders affecting the nervous system are usually put under the neurological umbrella – for example, multiple sclerosis.
- The muscular dystrophies and neuromuscular disorders primarily impact the nerves supplying muscle, the junction of the nerve and muscle, or the muscle itself.
- Classification is somewhat arbitrary and there is often overlap in how a disorder could be classified.

Three components of MD disorders.

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- Muscles must be stimulated by electrical signals originating in the brain & carried to muscles by nerves.
- Muscular dystrophy disorders usually impact one of three major components:
 - The nerves delivering messages to the muscle,
 - the junction where the nerve meets the muscle,
 - the muscles themselves.
- Problems primarily in the brain or in the nerves will be mentioned here but usually fall under the umbrella of neurological disorders.

Nerves carry electrical signals.

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- The nervous system: the brain, spinal cord and a complex series of nerves that run throughout the body.
- Nerves carry electrical signals – we can measure these as brain waves using an EEG machine and we can test the signals using nerve conduction studies.
- The electrical signals are created by chemical reactions within the nerves, sort of like how the chemicals in a battery produce an electrical charge.
- To work correctly, all of the chemicals must be at the proper levels, the brain must be working correctly and the nerves must be able to carry and transmit the signals properly.

Neurons - 1.

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- Neuron: a special type of cell that creates electrical signals (nerve impulses or “action potentials”).
- Nerves are made up of millions & millions of neurons.
- Neurons have three parts:
 - Cell body: like that found in any cell.
 - Axon {AXE-on}: a long “cord” that carries the signal.
 - Dendrites {DEN-drites}: branch-like projections that transmit the signals from one neuron to the next.
- Myelin {MY-Lynn} = A fat covering & insulating axons:
 - Needed to maintain the strength & speed of the electrical signals as they travel down the axon.

Neurons - 2.

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- There are three main types of nerves (neurons):
 - 1A). Receptors: special cells in the outer parts of the body (e. g. skin) that sense the environment and send information back to sensory neurons.
 - 1B). Sensory neurons: carry information from receptors back to the spinal cord and then up to the brain for processing.
 - 2). Interneurons: a sort of internal communication or bridge system within the nervous system.
 - 3). Motor neurons: neurons that transmit signals from the brain down the spinal column and out to the muscles, organs & glands in the body.

Problems in nerve transmission.

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- Any disruption in the transmission of signals in the brain or spinal column will affect subsequent function.
- Some conditions affect sensation, some affect muscle strength, some affect both sensation and strength.
- Non-functional muscle & nerves deteriorate over time.
- Again, there is considerable overlap – there are many disorders that impact muscle function.
- Some disorders are situated in the brain, for example, Alzheimer's disease and Parkinson's disease.
- Some disorders affect the brain and spinal cord, for example, multiple sclerosis.
- Spinal cord injuries are a major cause of impairment.

A few nerve transmission disorders.

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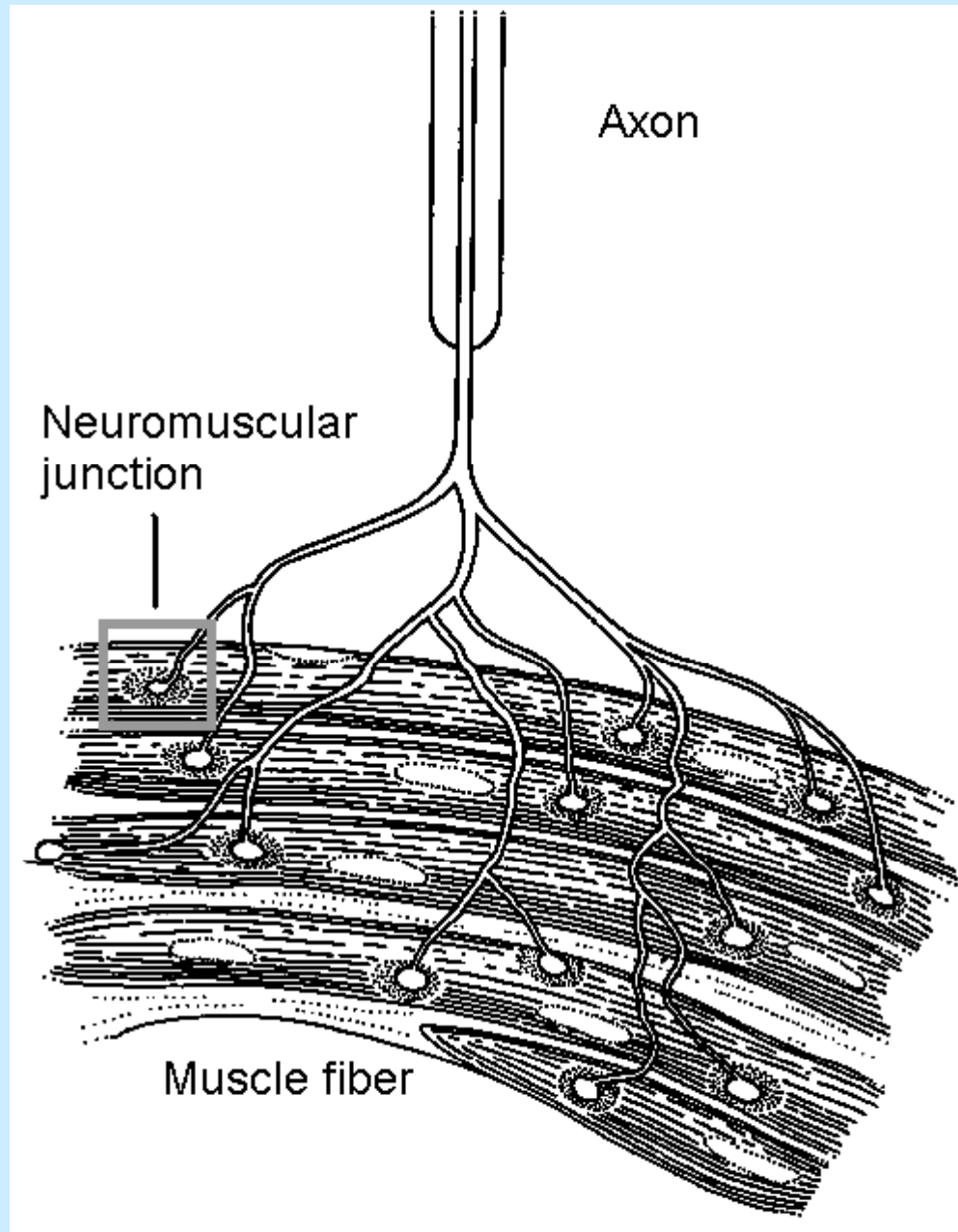
- Multiple sclerosis attacks the myelin of the nerve leading to impaired signal transmission.
- A number of different disorders affect motor neurons:
 - Amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease).
 - Cerebral palsy.
 - Poliomyelitis (polio).
 - Spinal muscular atrophy.

Problems in the nerve / muscle junction. 11

- Neuromuscular junction: The junction between the end of a motor neuron and a muscle fibre:
 - The ends of motor neurons contain thousands of “containers” filled with a chemical called acetylcholine {ah-SEAT-toe-coe-line} (ACh).
 - When a nerve impulse reaches the axon’s end, hundreds of these containers discharge their ACh.
 - ACh fills up special ACh receptors in the muscle fibre, when enough are full, the muscle contracts.
 - After a muscle contraction, an enzyme called acetylcholinesterase “cleans out” the ACh. This allows the muscle to immediately return to normal (relax) and get ready for the next signal.

The neuromuscular junction.

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Nerve / muscle junction disorders.

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- The most common disorder in this category is myasthenia gravis – a disorder that blocks the receptors for acetylcholine preventing proper signaling from reaching the muscle.
- Eaton-Lambert syndrome affects the amount of acetylcholine available.
- Various other conditions attack the neuromuscular junction, for example, botulism and the venom of the black widow spider.

Problems within the muscle.

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- Muscles are made up out of proteins:
 - There are a few large proteins & many small ones:
 - All of the proteins must fit together and work as a team, like the gears and levers in an old clock.
 - As muscles work, some muscle protein wears down and is damaged and must be recycled while new protein must be created to replace it.
 - The ongoing production of new protein is governed by genetics and genetic mutations are a common cause of protein abnormalities that affect the proper function of the muscle.
 - As well, some muscle disorders are acquired, for example, the myositis disorders.

Some basic muscle disorders.

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- There are a number of genetically based disorders that impair normal muscle protein production, for example, Duchenne and Becker muscular dystrophy affect a protein called dystrophin.
- Limb-girdle muscular dystrophy includes a number of disorders, each affecting different muscle proteins.
- Facioscapulohumeral (FSH) is another dystrophy leading to muscle wasting and weakness.
- Myotonic dystrophy is a genetic disorder that impairs the normal relaxation of muscle after contraction.
- Myositis disorders involve inflammation of the muscle.
- There are many other rare disorders affecting muscle.

Metabolic muscle problems.

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- Muscles also need power – fuel: created by a complex biochemical reaction: part of our basic metabolism.
- There are several types of muscular dystrophies that arise because of problems in the creation of muscle energy– metabolic muscle disorders.
- These disorders involve the “engine” of the cell – mitochondria. Many of these disorders impair the fuel reaching mitochondria and in turn, the muscle cannot get enough energy to operate properly.
- There are many metabolic muscle disorders, for example, acid maltase deficiency (Pompe's disease).

Synopsis of the muscular dystrophies. 17

- Muscular dystrophy is a broad term encompassing many different disorders, affecting different parts of the nerve or muscle, all ultimately lead to muscle impairment and a wasting and weakening of muscle.
- To date, more than 250 specific disorders have been described that fall under the muscular dystrophy umbrella.
- The wide variety of disorders and the different mechanisms involved pose a significant challenge for researchers.
- Great progress has been made in describing and understanding these complex conditions and research continues toward developing effective treatments.