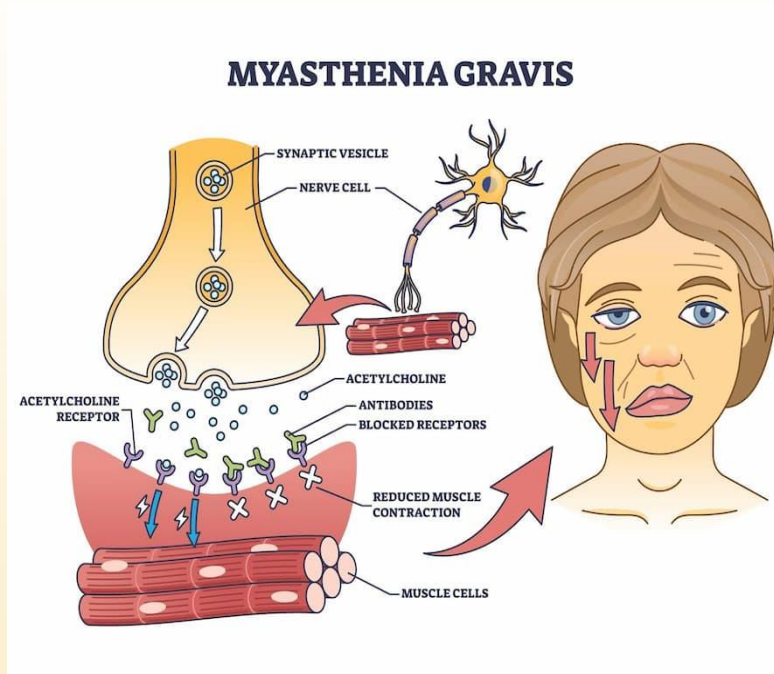
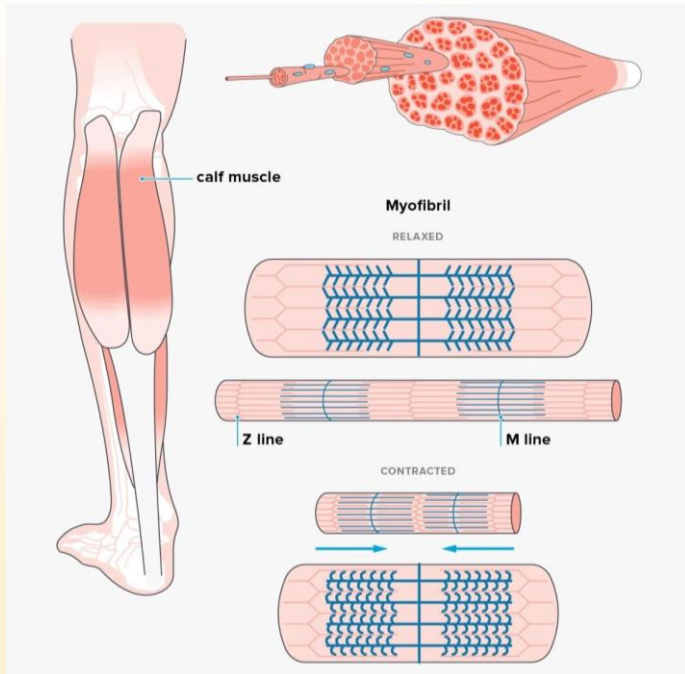


DISORDERS OF MUSCLE



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Myasthenia gravis

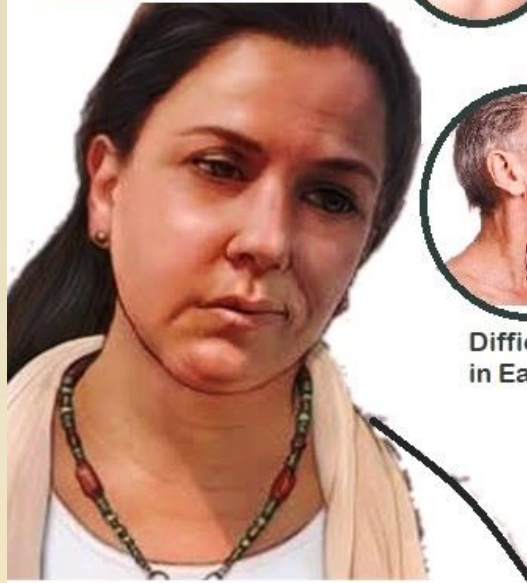
- This autoimmune condition of unknown origin affects more women than men, usually aged between 20 and 40 years.
- Antibodies are produced that bind to and block the acetylcholine receptors of the neuromuscular junction.
- The transmission of nerve impulses to muscle fibers is therefore blocked.
- This causes progressive and extensive muscle weakness, although the muscles themselves are normal.
- Extrinsic and eyelid muscles are affected first, causing *ptosis* (drooping of the eyelid) or *diplopia* (double vision), followed by those of the neck (possibly affecting chewing, swallowing and speech) and limbs.
- There are periods of remission, relapses being precipitated by, for example, strenuous exercise, infections or pregnancy.

DO YOU HAVE MYASTHENIA GRAVIS WITHOUT THYMOMA?

Myasthenia gravis is a rare autoimmune neuromuscular disease



These individuals experience weakness of the muscles of the eye, neck, jaw, limb and in severe cases, the muscles of respiration



Difficulty in Eating



Facial Paralysis



Difficulty in walking



Fatigue



Difficulty in breathing



Left, three different serial pictures to demonstrate fatigue of eyelid muscles as the patient keeps looking up.



Left, after a few minutes of rest, the eyelids have returned to near-normal position.

WHO IS AT RISK?



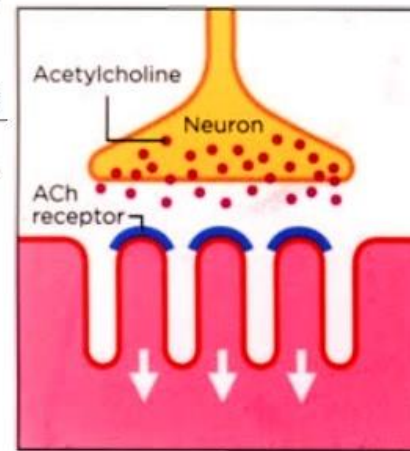
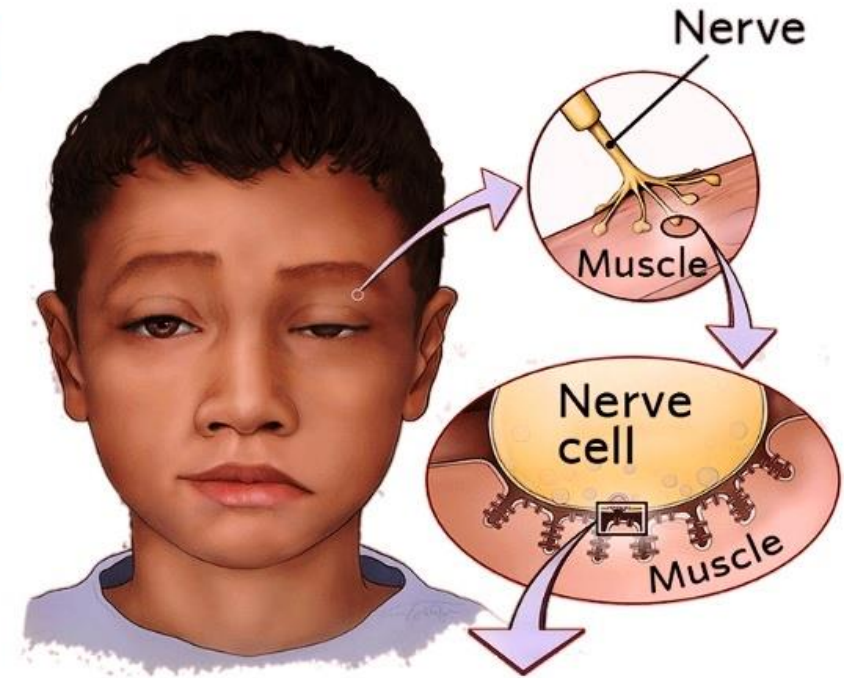
Mothers in postpartum were found to be at increased risk



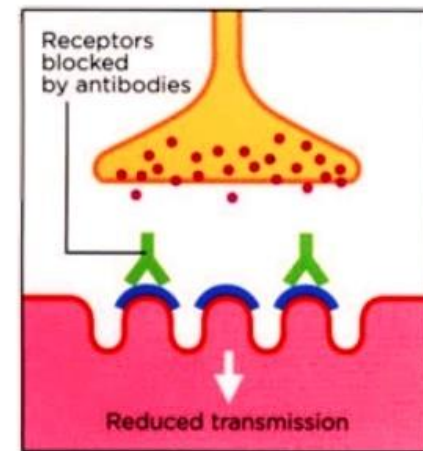
Age of onset peaks at 20-30 for females and 60-68 for males



10-15% of cases in North America are autoimmune juvenile myasthenia



Normal neuromuscular junction



Neuromuscular junction in myasthenia gravis

- Myasthenia gravis is an autoimmune disease that causes chronic, progressive damage of the neuromuscular junction.
- The immune system inappropriately produces antibodies that bind to and block some ACh receptors, thereby decreasing the number of functional ACh receptors at the motor end plates of skeletal muscles.
- Because 75% of patients with myasthenia gravis have hyperplasia or tumors of the thymus, it is thought that thymic abnormalities cause the disorder.
- As the disease progresses, more ACh receptors are lost. Thus, muscles become increasingly weaker, fatigue more easily, and may eventually cease to function.
- Myasthenia gravis occurs in about 1 in 10,000 people and is more common in women, typically ages 20 to 40 at onset; men usually are ages 50 to 60 at onset.
- The muscles of the face and neck are most often affected.

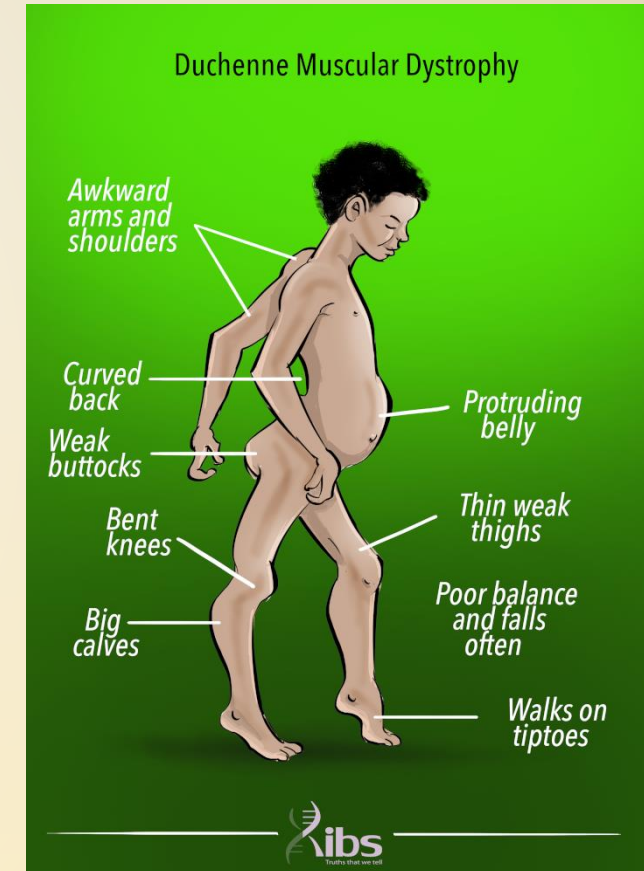
- Initial symptoms include weakness of the eye muscles, which may produce double vision, and weakness of the throat muscles that may produce difficulty in swallowing.
- Later, the person has difficulty chewing and talking.
- Eventually the muscles of the limbs may become involved.
- Death may result from paralysis of the respiratory muscles, but often the disorder does not progress to that stage.
- Anticholinesterase drugs such as pyridostigmine or neostigmine, the first line of treatment, act as inhibitors of acetyl cholinesterase, the enzyme that breaks down ACh.
- Thus, the inhibitors raise the level of ACh that is available to bind with still-functional receptors.
- More recently, steroid drugs such as prednisone have been used with success to reduce antibody levels.
- Another treatment is plasmapheresis, a procedure that removes the antibodies from the blood.
- Often, surgical removal of the thymus (thymectomy) is helpful.

Muscular dystrophies

- In this group of inherited diseases there is progressive degeneration of groups of muscles.
- The main differences in the types are age of onset, rate of progression and groups of muscles involved.

Duchenne muscular dystrophy

- Inheritance of this condition is sex linked. Because the mutated gene is on the X chromosome, and because males have only one X chromosome,
- DMD strikes boys almost exclusively.
- Worldwide, about 1 in every 3500 male babies—about 21,000 in all—are born with DMD each year.
- The disorder usually becomes apparent between the ages of 2 and 5, when parents notice the child falls often and has difficulty running, jumping, and hopping.
- Wasting and weakness begin in muscles of the lower limbs then spread to the upper limbs, progressing rapidly without remission.
- Death usually occurs in adolescence, often from respiratory failure, cardiac arrhythmias or cardiomyopathy.



Facioscapulohumeral dystrophy

- This disease affects both sexes.
- It usually begins in adolescence and the younger the age of onset the more rapidly it progresses.
- Muscles of the face and shoulders are affected first.
- This is a chronic condition that usually progresses slowly and may not cause complete disability.
- Life expectancy is normal.



FIG 2. Patient 2.A 14-year-old boy who first presented with symptoms of facioscapulohumeral muscular dystrophy type I from age 11 years. Clinical photographs showing (a) asymmetrical facial weakness more on the left side, and (b, c) marked winging of scapula

Myotonic dystrophy

- This disease usually begins in adult life and affects both genders.
- Muscles contract and relax slowly, often seen as difficulty in releasing an object held in the hand.
- Muscles of the tongue and the face are first affected, then muscles of the limbs.
- Systemic conditions associated with myotonic dystrophy include:
 1. Cataracts
 2. Atrophy of the gonads
 3. Cardiomyopathy
 4. Glucose intolerance.
- The disease progresses without remission and with increasing disability. Death usually occurs in middle age from respiratory or cardiac failure.

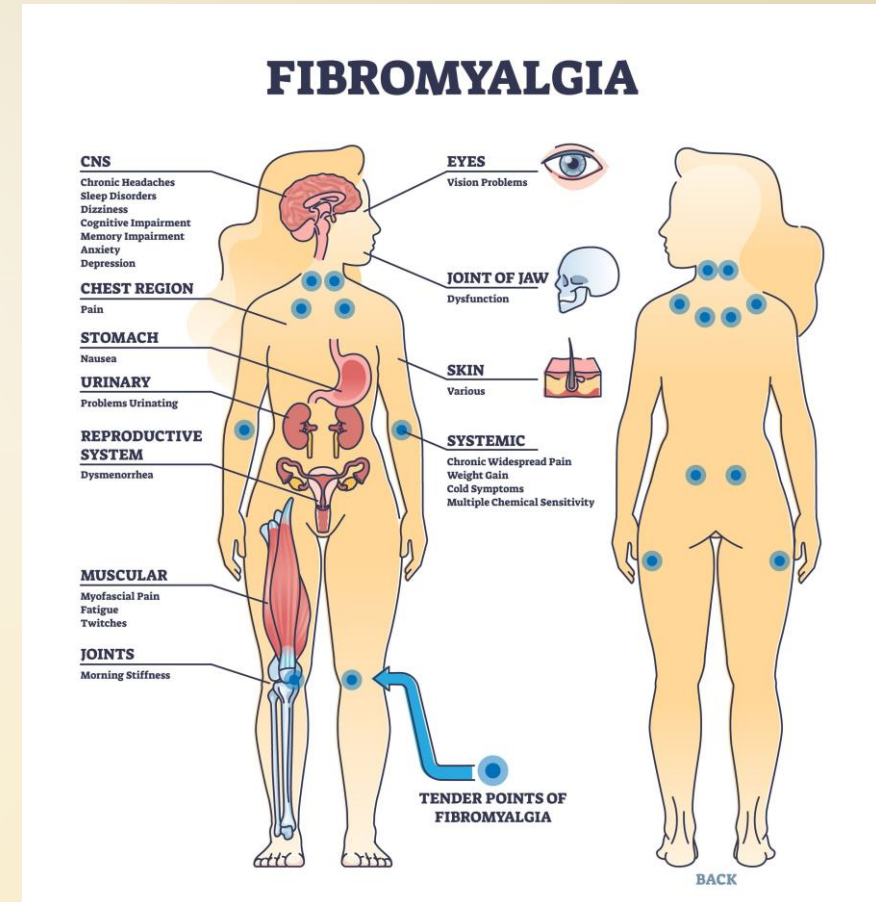
Abnormal Contractions of Skeletal Muscle

Type of Abnormal Contraction	Description	Causes / Notes
Spasm	Sudden, involuntary contraction of a single muscle in a large group	General muscle response; can be non-painful
Cramp	Painful spasmodic contraction	Caused by inadequate blood flow, overuse, dehydration, injury, prolonged positioning, low electrolyte levels (e.g., potassium)
Tic	Involuntary spasmodic twitching of muscles usually under voluntary control	Common in eyelid and facial muscles

Tremor	Rhythmic, involuntary, purposeless contraction causing quivering or shaking	Common in neurological disorders
Fasciculation	Involuntary brief twitch of an entire motor unit, visible under the skin	Occurs irregularly, not associated with movement; seen in multiple sclerosis and ALS
Fibrillation	Spontaneous contraction of a single muscle fiber, not visible under the skin but detectable by electromyography	May indicate motor neuron destruction

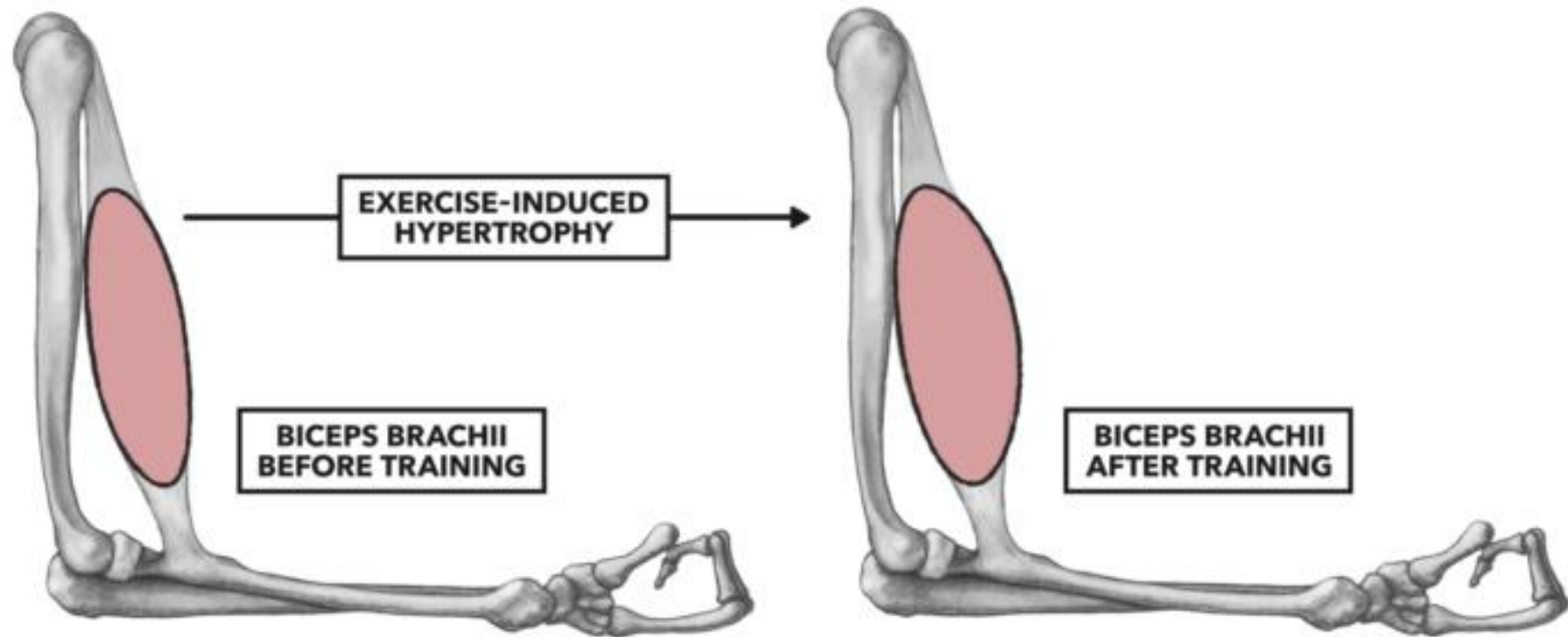
Fibromyalgia

- **Fibromyalgia** is a chronic, painful, non-articular rheumatic disorder that affects the fibrous connective tissue components of muscles, tendons, and ligaments.
- A striking sign is pain that results from gentle pressure at specific “tender points.”
- Even without pressure, there is pain, tenderness, and stiffness of muscles, tendons, and surrounding soft tissues.
- Besides muscle pain, those with fibromyalgia report severe fatigue, poor sleep, headaches, depression, irritable bowel syndrome, and inability to carry out their daily activities.
- There is no specific identifiable cause.
- Treatment consists of stress reduction, regular exercise, application of heat, gentle massage, physical therapy, medication for pain, and a low-dose antidepressant to help improve sleep.



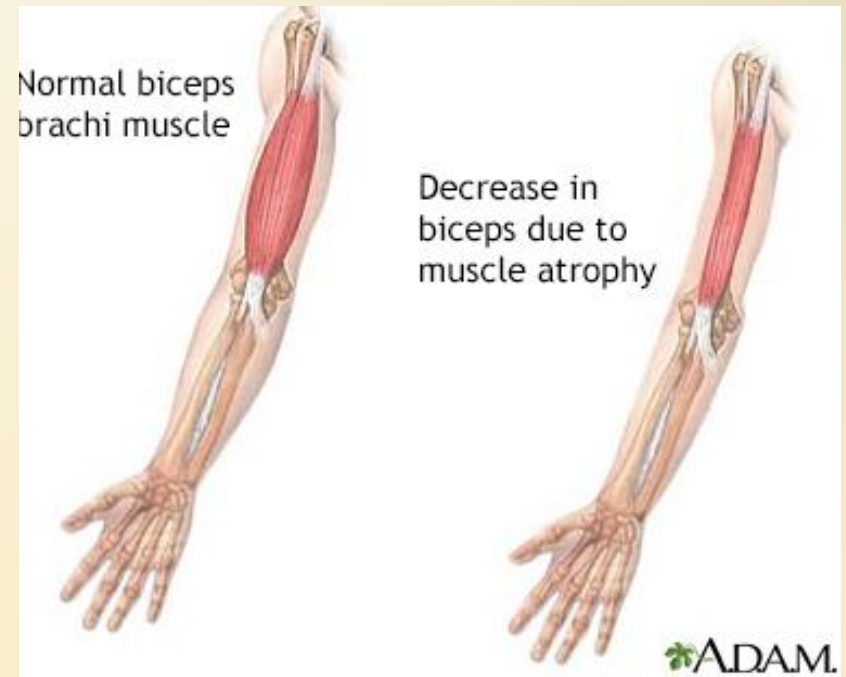
Muscular Hypertrophy & Fibrosis

- The muscle growth that occurs after birth occurs by enlargement of existing muscle fibers, called **muscular hypertrophy**.
- Muscular hypertrophy is due to increased production of myofibrils, mitochondria, sarcoplasmic reticulum, and other organelles.
- It results from very forceful, repetitive muscular activity, such as strength training. Because hypertrophied muscles contain more myofibrils, they are capable of more forceful contractions.
- During childhood, human growth hormone and other hormones stimulate an increase in the size of skeletal muscle fibers.
- The hormone testosterone promotes further enlargement of muscle fibers.
- A few myoblasts do persist in mature skeletal muscle as *satellite cells*.
- Satellite cells retain the capacity to fuse with one another or with damaged muscle fibers to regenerate functional muscle fibers.
- However, when the number of new skeletal muscle fibers that can be formed by satellite cells is not enough to compensate for significant skeletal muscle damage or degeneration, the muscular tissue undergoes **fibrosis**, the replacement of muscle fibers by fibrous scar tissue.



Muscular Atrophy

- **Muscular atrophy** is a decrease in size of individual muscle fibers as a result of progressive loss of myofibrils.
- Atrophy that occurs because muscles are not used is termed *disuse atrophy*.
- Bedridden individuals and people with casts experience disuse atrophy because the flow of nerve impulses to inactive skeletal muscle is greatly reduced, but the condition is reversible.
- If instead its nerve supply is disrupted or cut, the muscle undergoes *denervation atrophy*.
- Over a period of 6 months to 2 years, the muscle shrinks to about one fourth its original size, and its fibers are irreversibly replaced by fibrous connective tissue.



Crush syndrome

- Sustained pressure, on the trunk or a limb, causes ischemia resulting in massive muscle necrosis.
- When pressure is relieved and circulation restored, myoglobin and other necrotic products are released from damaged muscle and enter the blood.
- This material is highly toxic to the kidneys and acute renal failure may develop.
- A common complication is infection, especially by anaerobic microbes, e.g. *Clostridium perfringens*, causing *gas gangrene*.

Crush Syndrome

Myoglobin toxicity



Clostridium Perfringens (Gas gangrene)



By Dr. Rakesh Prasad Sah
Associate Professor, Microbiology

Exercise-induced Muscle Damage

- Comparison of electron micrographs of muscle tissue taken from athletes before and after intense exercise reveals considerable **exercise induced muscle damage**, including torn sarcolemma's in some muscle fibers, damaged myofibrils, and disrupted Z discs.
- Microscopic muscle damage after exercise also is indicated by increases in blood levels of proteins, such as myoglobin and the enzyme creatine kinase, which are normally confined within muscle fibers.
- From 12 to 48 hours after a period of strenuous exercise, skeletal muscles often become sore.
- Such **delayed onset muscle soreness (DOMS)** is accompanied by stiffness, tenderness, and swelling.
- In response to exercise-induced muscle damage, muscle fibers undergo repair: new regions of sarcolemma are formed to replace torn sarcolemma's, and more muscle proteins (including those of the myofibrils) are synthesized in the sarcoplasm of the muscle fibers.



Medical Terminology

Myalgia (mī-AL-jē-a; *-algia* = painful condition) Pain in or associated with muscles.

Myoma (mī-Ō-ma; *-oma* = tumor) A tumor consisting of muscle tissue.

Myomalacia (mī'-ō-ma-LĀ-shē-a; *-malacia* = soft) Pathological softening of muscle tissue.

Myositis (mī'-ō-SĪ-tis; *-itis* = inflammation of) Inflammation of muscle fibers (cells).

Myotonia (mī'-ō-TO-nē-a; *-tonia* = tension) Increased muscular excitability and contractility, with decreased power of relaxation; tonic spasm of the muscle.

Volkmann's contracture (FÖLK-manz kon-TRAK-chur; *contra-* = against) Permanent shortening (contracture) of a muscle due to replacement of destroyed muscle fibers by fibrous connective tissue, which lacks extensibility. Typically occurs in forearm flexor muscles. Destruction of muscle fibers may occur from interference with circulation caused by a tight bandage, a piece of elastic, or a cast.