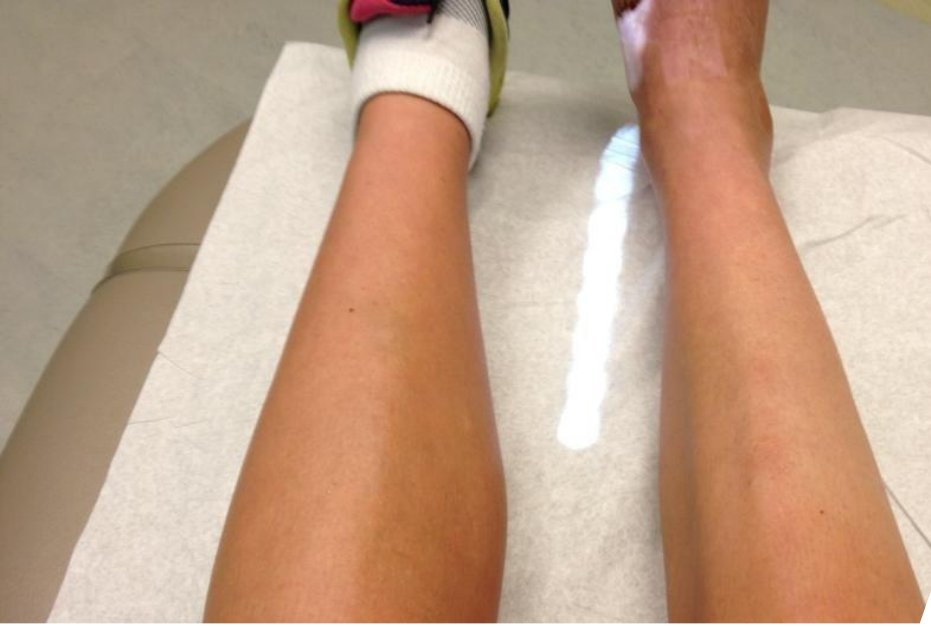
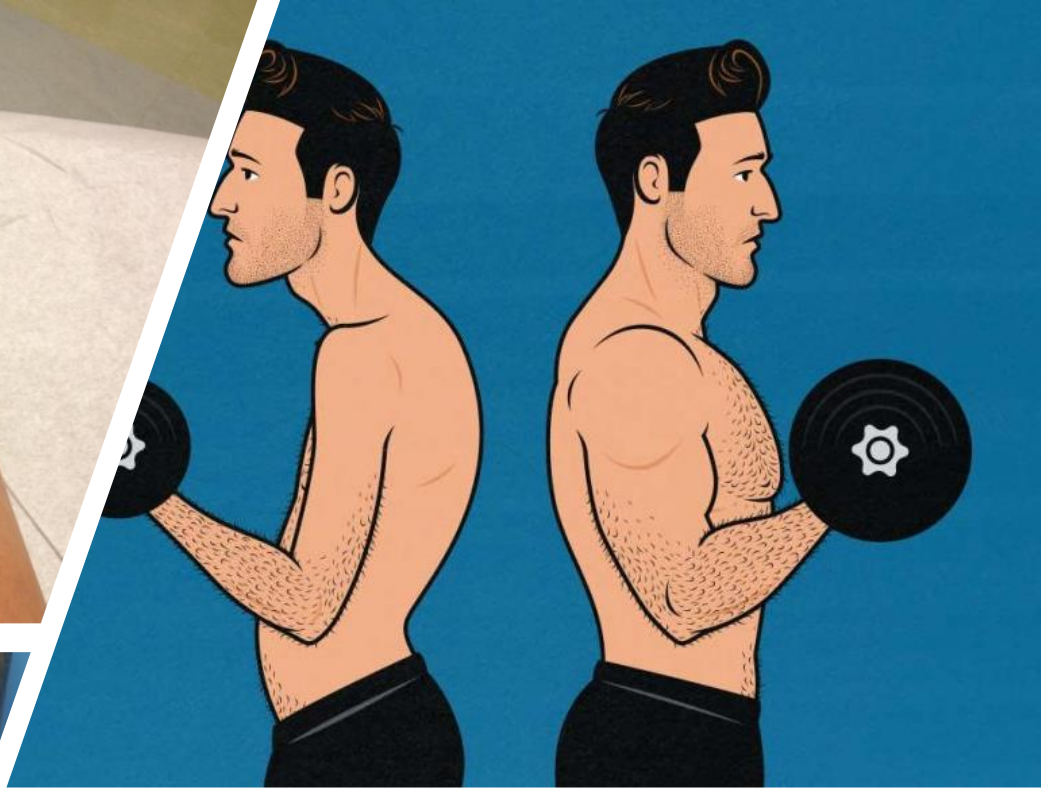
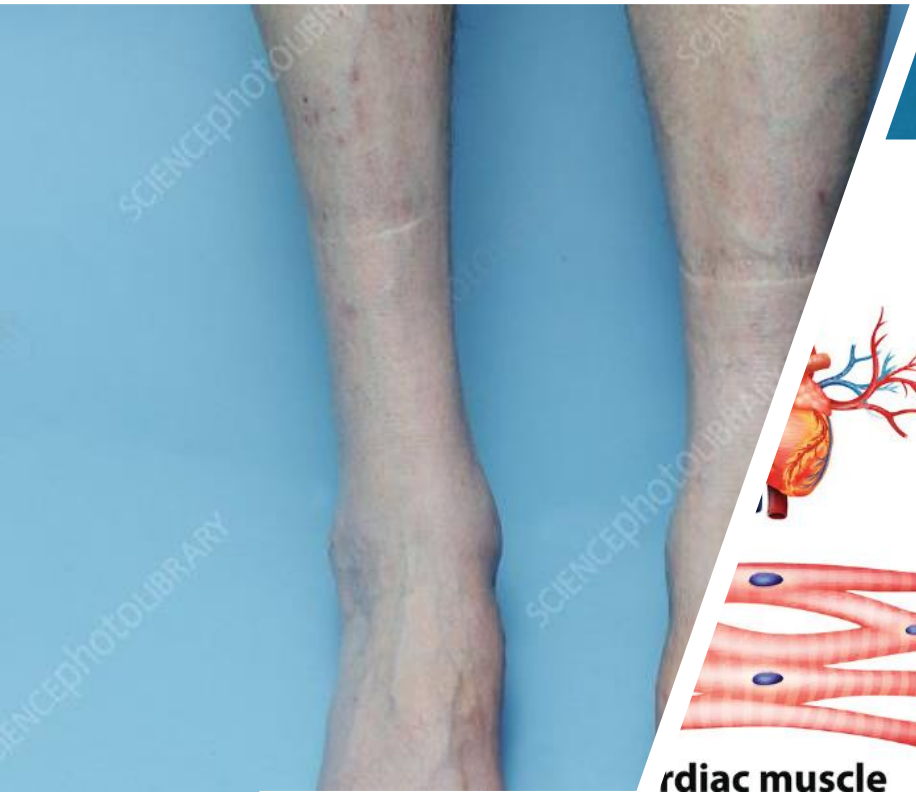
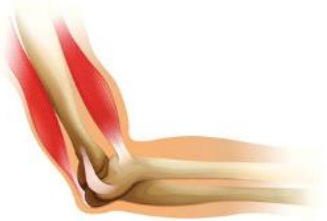


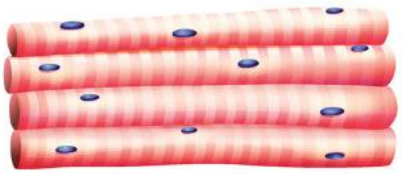




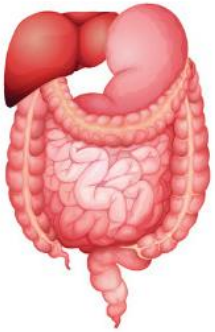
Types of Muscle

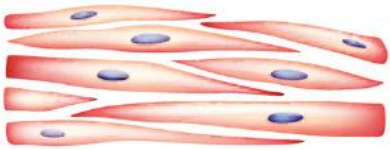
rdiac muscle



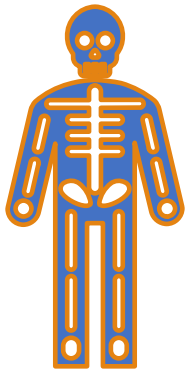


Skeletal muscle





Smooth muscle



Smooth Muscle Contraction

DR AFSHEEN MAHMOOD NOOR
FCPS (MEDICINE) MPHIL (PHYSIOLOGY)
MHPE (SCHOLAR)

Learning objectives:

1. Describe the contractile mechanisms in smooth muscles

2. Describe excitation and contraction of smooth muscle.

3. Identify the types of smooth muscles.

4. Describe the chemical and physical basis for smooth muscle contraction.

5. Compare smooth and skeletal muscle contraction.

6. Chemical basis of smooth muscle contraction, Physical basis of smooth muscle contraction.

7. Explain how the calcium ions regulate the contraction.

8. Regulation of smooth muscle contraction by the calcium ions

9. Enlist the excitatory and inhibitory transmitter substances secreted at the smooth muscle neuromuscular junction

Learning objectives:

1. Describe following

a. Muscle hypertrophy

b. Muscle atrophy

c. Muscle hyperplasia

d. Rigor mortis

e. Muscle dystrophy

f. Recovery of muscle contraction in poliomyelitis

Types of Smooth Muscle

Smooth muscle can generally be divided into two major types

1. Multi-Unit Smooth Muscle
2. Unitary Smooth Muscle

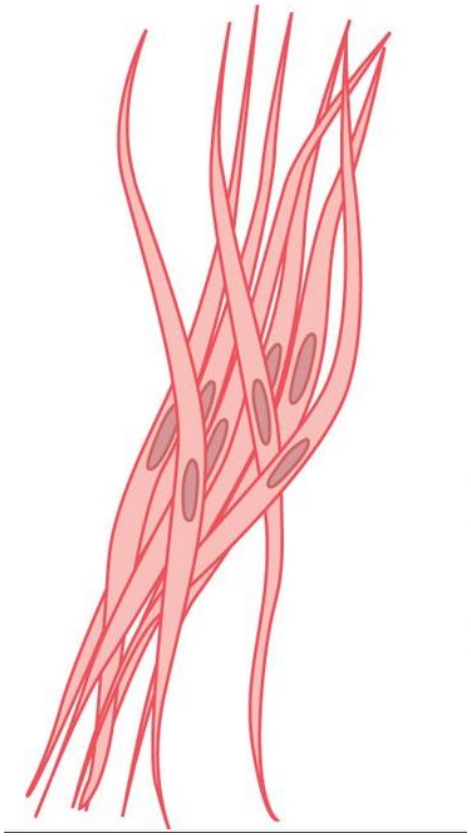
Multi-Unit Smooth Muscle

This type of smooth muscle is composed of discrete, separate smooth muscle fibers. Each fiber operates independently of the others and often is innervated by a single nerve ending

The most important characteristic of multi-unit smooth muscle fibers is that each fiber can contract independently of the others

E.g. ciliary & the iris muscle of the eye

Multi-Unit Smooth Muscle



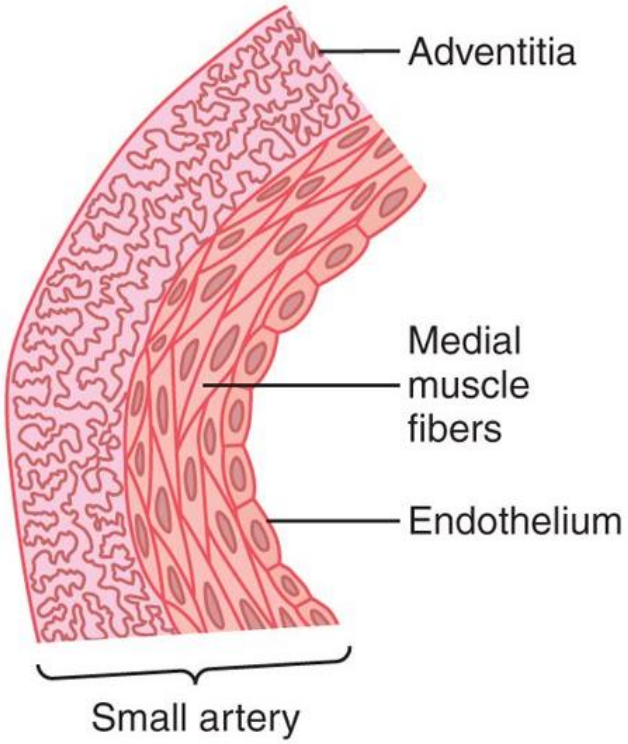
Unitary Smooth Muscle

Also known as “*syncytial smooth muscle* or *visceral smooth muscle*”

The term "unitary" is confusing because it does not mean single muscle fibers. Instead, it means a mass of hundreds to thousands of smooth muscle fibers that contract together as a single unit.

The fibers usually are arranged in sheets or bundles, and their cell membranes are adherent to one another at multiple points so that force generated in one muscle fiber can be transmitted to the next

Unitary Smooth Muscle



Contractile Mechanism in Smooth Muscle

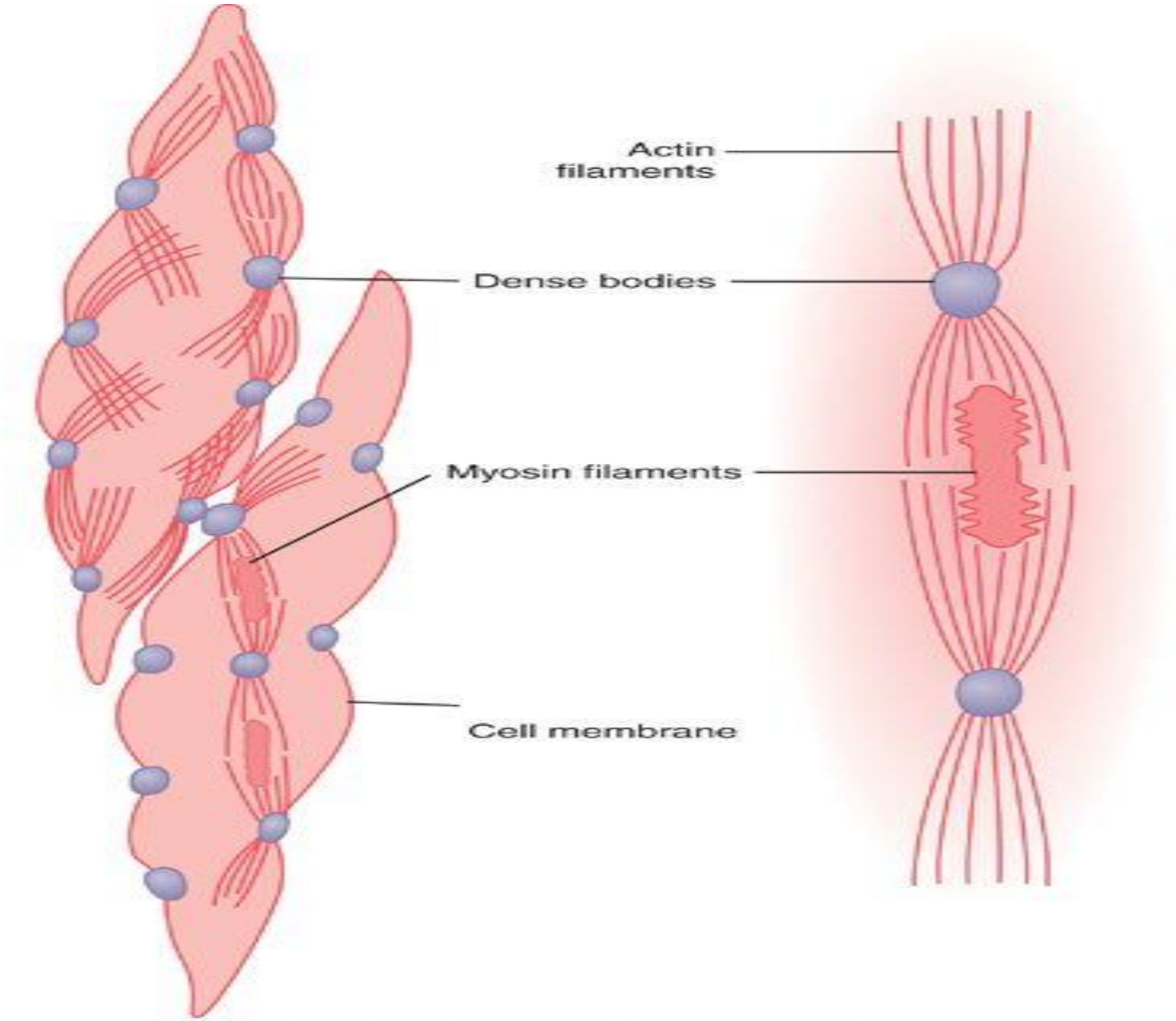
Smooth muscle contains both *actin* and *myosin filaments,* having chemical characteristics like those of the actin and myosin filaments in skeletal muscle. **It does not contain the normal troponin complex**

Also, some differences in excitation-contraction coupling, control of the contractile process by calcium ions, duration of contraction, and amount of energy required for contraction.

Cont….

Smooth muscle does not have the same striated arrangement of actin and myosin filaments as is found in skeletal muscle.

Large numbers of actin filaments attached to so-called *dense bodies*


Actin filaments
Dense bodies
Myosin filaments
Cell membrane

Regulation of Contraction by Calcium Ions

Smooth muscle does not contain troponin

Calcium Ions Combine with Calmodulin to Cause Activation of Myosin Kinase and Phosphorylation of the Myosin Head

1. The calcium ions bind with calmodulin.
2. The calmodulin-calcium complex then joins with and activates *myosin light chain kinase,* a phosphorylating enzyme.

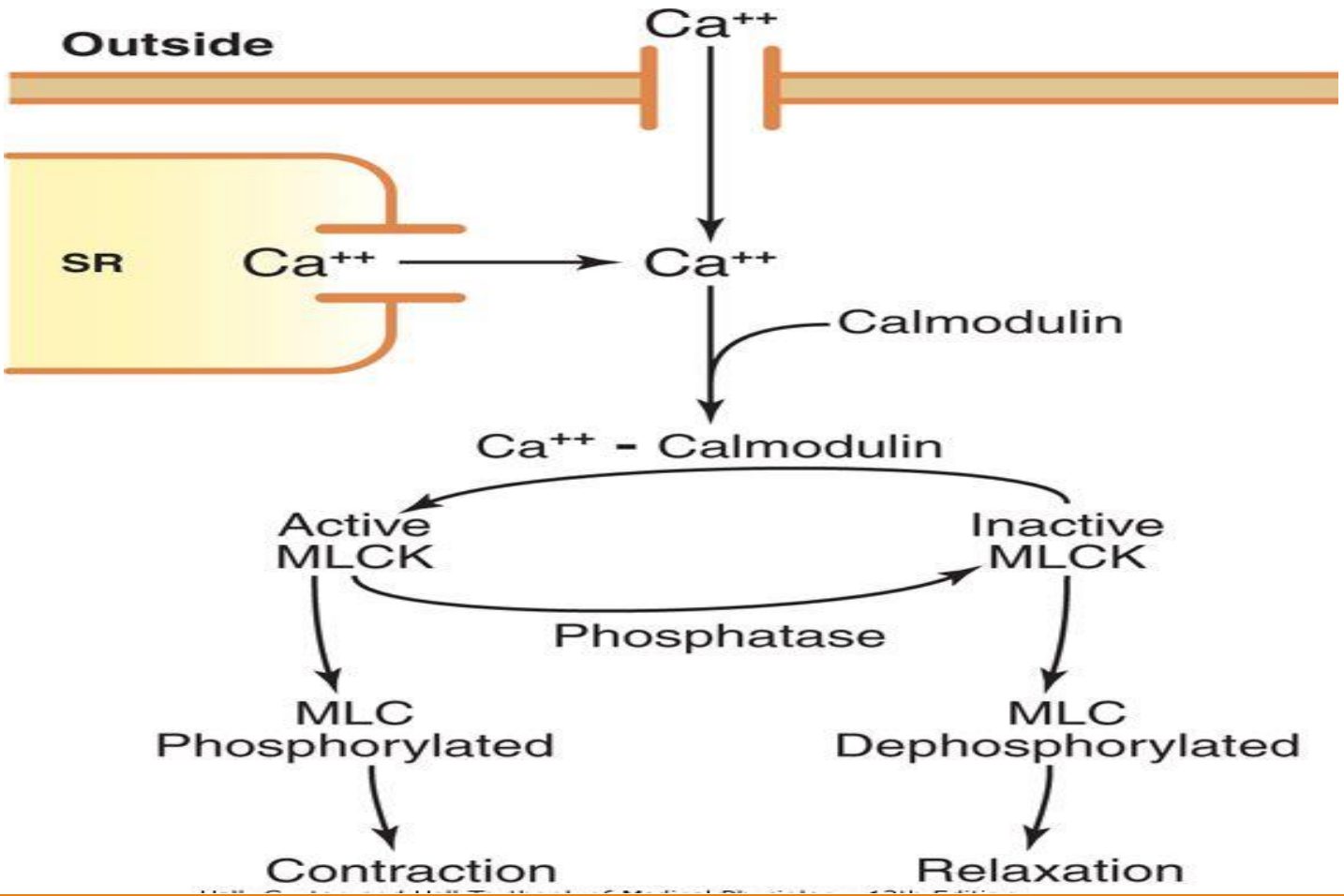
Regulation of Contraction by Calcium Ions

3. One of the light chains of each myosin head, called the *regulatory chain,* becomes phosphorylated in response to this myosin kinase.

   The head has the capability of binding repetitively with the actin filament and proceeding through the entire cycling process of intermittent "pulls," the same as occurs for skeletal muscle, thus causing muscle contraction.

   Myosin Phosphatase Is Important in Cessation of Contraction

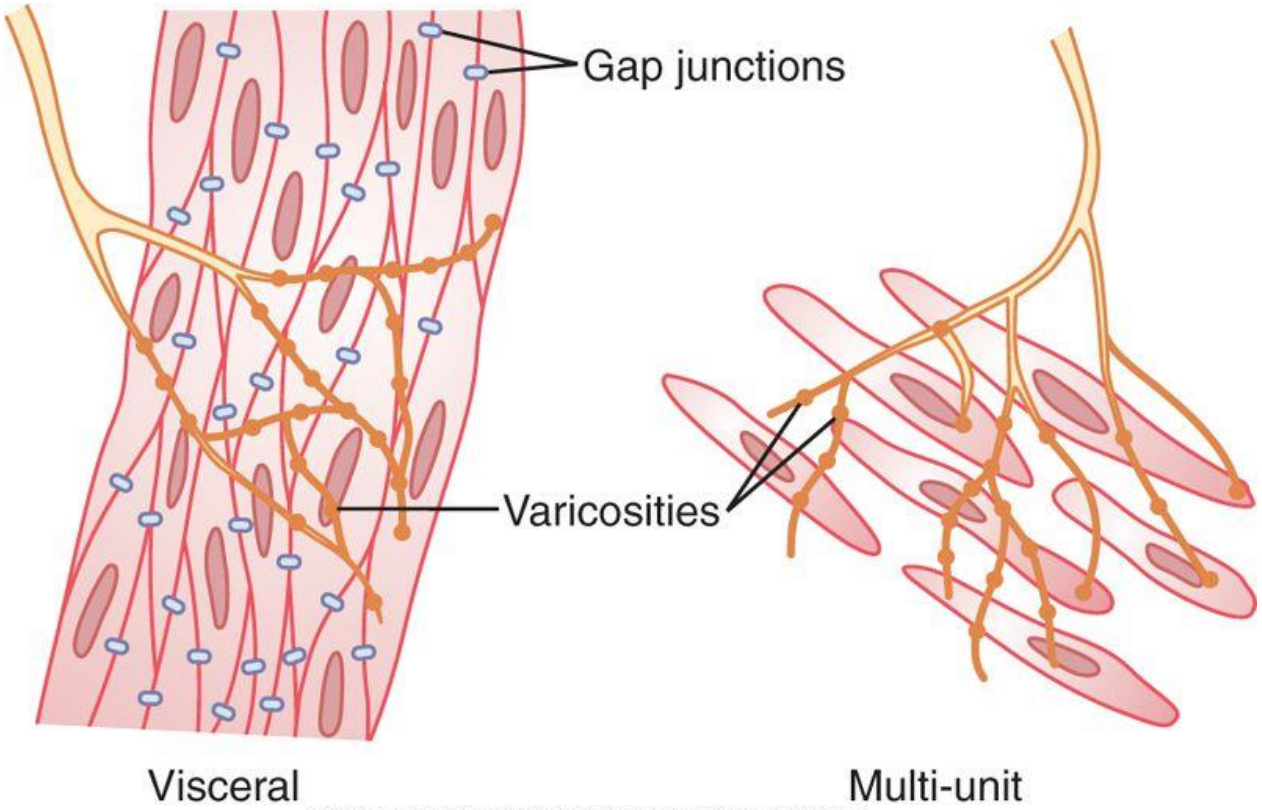
Regulation of Contraction by Calcium Ions



Neuromuscular Junctions of Smooth Muscle

- Do not have proper NMJ
- *Autonomic nerve fibers* that innervate smooth muscle generally branch diffusely on top of a sheet of muscle fibers
- They are *Diffuse junctions* that secrete their transmitter substance into the matrix coating of the smooth muscle
- The transmitter substance then diffuses to the cells

Neuromuscular Junctions of Smooth Muscle



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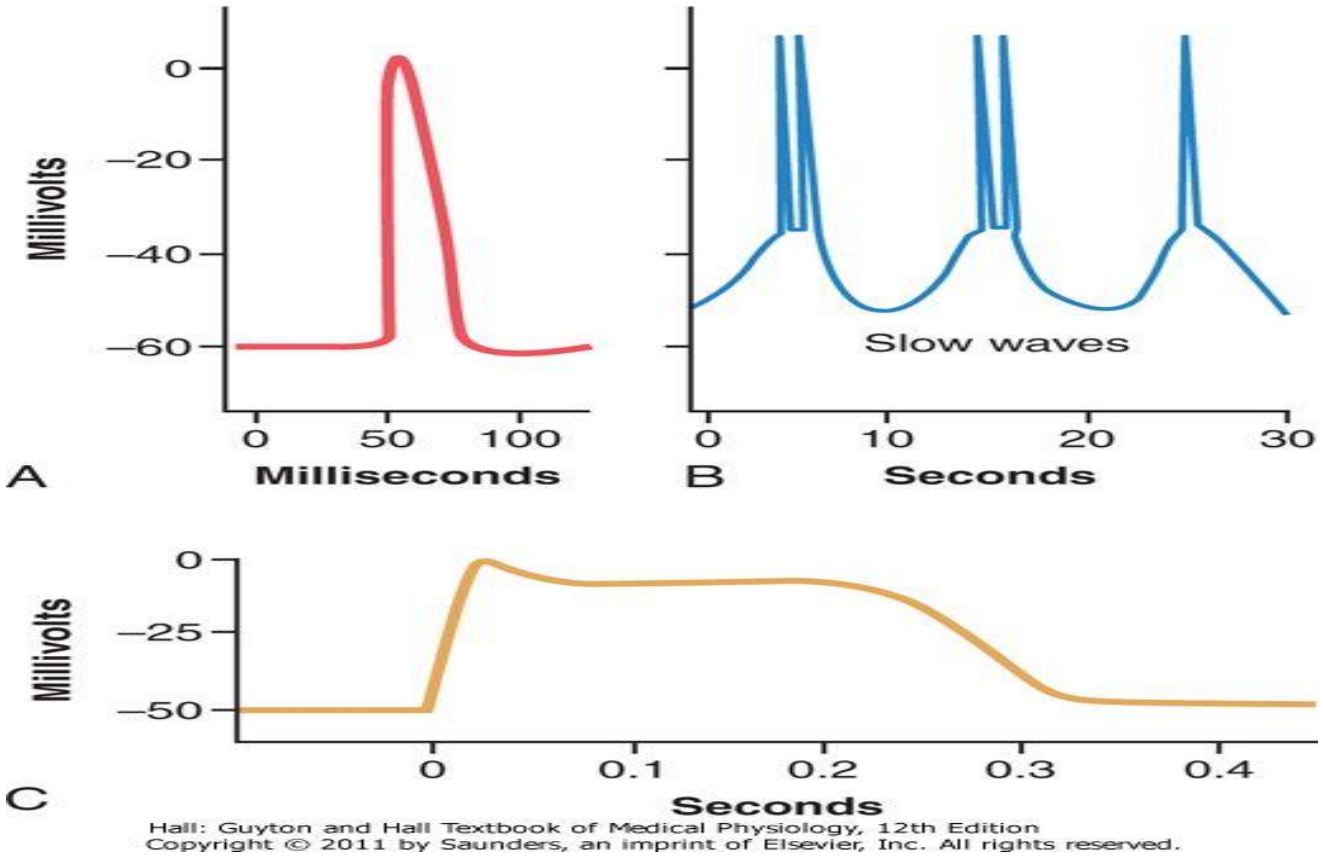
Membrane Potentials and Action Potentials in Smooth Muscle

-50 to -60 mill volts

Action potential can occur in one of two forms in smooth muscles

1. Spike
2. Plateau



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Effect of Local Tissue Factors and Hormones to Cause Smooth Muscle Contraction Without Action Potentials

Two types of non-nervous and non action potential stimulating factors often involved are

1. Local tissue chemical factors
2. Various hormones

Comparison of Smooth Muscle Contraction and Skeletal Muscle Contraction

1. Slow Cycling of the Myosin Cross-Bridges
2. Low Energy Requirement to Sustain Smooth Muscle Contraction
3. Slowness of Onset of Contraction and Relaxation of the Total Smooth Muscle Tissue
4. Maximum Force of Contraction Is Often Greater in Smooth Muscle Than in Skeletal Muscle
5. "Latch" Mechanism Facilitates Prolonged Holding of Contractions of Smooth Muscle
6. Stress-Relaxation of Smooth Muscle
7. Smooth Muscle Contraction Is Dependent on Extracellular Calcium Ion Concentration

Slow Cycling of the Myosin Cross-Bridges

Cycling of the myosin cross bridges in smooth muscle is much slower than in skeletal muscle, as little as 1/10 to 1/300 that in skeletal muscle.

fraction of time is greatly increased in smooth muscle, which basically determines the force of contraction.

Cause of slow cycling , reduced ATPase activity.

Low energy requirement to sustain smooth muscle contraction

Only 1/10 to 1/300 as much energy is required to sustain the same tension of contraction in smooth muscle as in skeletal muscle.

Low energy utilization by smooth muscle is important to overall energy economy of the body.

Slowness of onset of contraction and relaxation of the total smooth muscle tissue

Smooth muscle tissue begin to contract 5200 milliseconds after it is excited and reaches maximum contraction about .5 seconds later and then declines in contractile force in another one to two seconds giving total contraction time of 123 seconds

This is about 30 times as long as a single contraction of an average skeletal muscle fiber

The maximum force of contraction is often greater in smooth muscle there in skeletal muscle

Despite few myosin filaments in smooth muscle and even slow cycling time of cross bridges maximum force of contraction of smooth muscle is greater than that of skeletal muscle, as great as 4-6 kg/cm2 cross- sectional area for smooth muscle in comparison with 3-4 kg for skeletal muscle.

The “Latch” mechanism facilitates prolong holding of contractions of smooth muscle

Once smooth muscle has developed full contraction, amount of continuing excitation can usually be reduced to far less then the initial level even though the muscle maintains its full force of contraction.

Further energy consumed to maintain contraction is often reduced to as little as 1/300 of the energy required for comparable sustained skeletal muscle contraction this mechanism is called as “latch” mechanism

Significance of latch mechanism:

It can maintain prolonged tonic contraction in smooth muscle for hours with little use of energy.

Stress relaxation of smooth muscle

An important characteristic of smooth muscle, especially the visceral unitary type of smooth muscle of many hollow organs is its ability to return to nearly its original force of contraction seconds or minutes after it has been elongated or shortened.

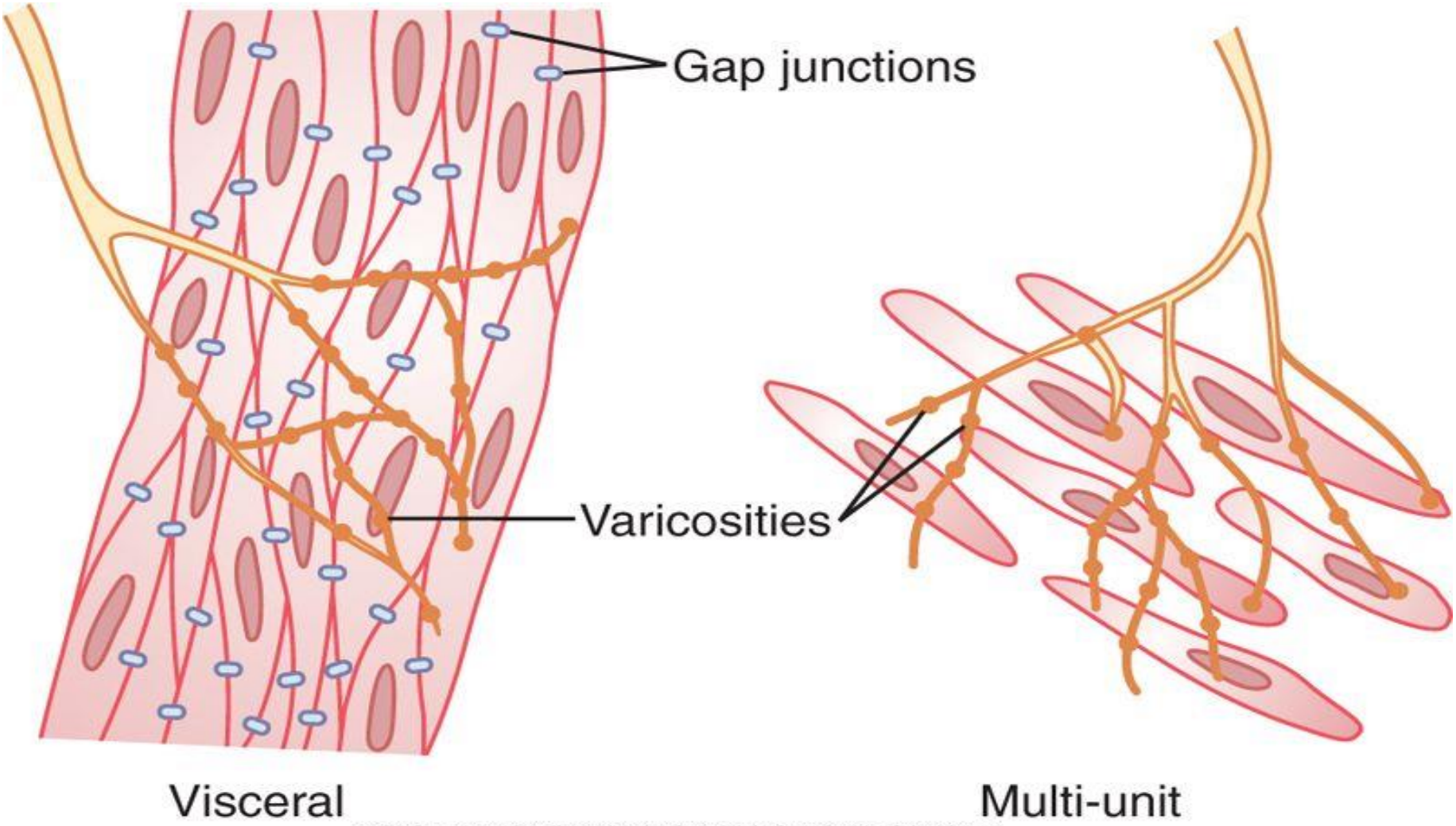
Nervous and hormonal control of smooth muscle contraction

- Smooth muscle are stimulated by multiple types of signals

  nervous signals
  - hormonal stimulation,
  - stretch of the muscle,
  - and in several other ways.

- Smooth muscle membrane contains many types of receptor proteins which can initiate the contractile process or inhibit it.

Neuromuscular Junctions of Smooth Muscle



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Diffuse junctions

- ***Autonomic nerve fibers*** that innervate smooth muscle generally **branch** diffusely on top of a sheet of muscle fibers
- There is **no direct contact** of nerve fibers with the smooth muscle fiber cell membranes but form ***diffuse junctions***
- These junctions **secrete their transmitter** substance into the matrix coating of the smooth muscle often a few nanometers to a few micrometers away from the muscle cells;
- Transmitter substance then **diffuses to the cells**.

Varicosities

- Terminal axons have multiple *varicosities* distributed along their length.
- At these points, the *Schwann cells* that envelop the axons are interrupted so that transmitter substance can be secreted through the walls of the varicosities.
- Vesicles of the autonomic nerve fiber endings contain *acetylcholine* in some fibers and *norepinephrine* in others-and other substances as well.

Contact junctions

- Varicosities are separated from the muscle cell membrane by as little as 20 to 30 nanometers. These are called *contact junctions*
- Function is the same as synaptic cleft of the skeletal muscle neuromuscular junction
- Contraction of these smooth muscle fibers is faster than that of fibers stimulated by the diffuse junctions.

Receptors

- Acetylcholine and norepinephrine excite or inhibit smooth muscle by first binding with a *receptor protein* on the surface of the muscle cell membrane.
- Some of the receptor proteins are *excitatory receptors,* others are *inhibitory receptors.*
- **The type of receptor determines whether the smooth muscle is inhibited or excited** and determines which of the two transmitters, acetylcholine or norepinephrine, is effective in causing the excitation or inhibition.

Smooth Muscle Contraction in Response to Local Tissue Chemical Factors

- Control of contraction of

  the arterioles,

  meta-arterioles,

  precapillary sphincters.

- The smallest of these vessels have little or no nervous supply.
- Yet the smooth muscle is highly contractile, responding rapidly to changes in local chemical conditions in the surrounding interstitial fluid

In the normal resting state, many of these small blood vessels remain contracted.
But when extra blood flow to the tissue is necessary, multiple factors can relax the vessel wall, thus allowing for increased flow.
In this way, a powerful local feedback control system controls the blood flow to the local tissue area.
Some of the specific control factors are as follows:
1. Lack of oxygen in the local tissues causes smooth muscle relaxation and vasodilatation.
2. Excess carbon dioxide causes vasodilatation.
3. Increased hydrogen ion concentration causes vasodilatation

Local vasodilators

All cause **local vasodilatation**

- Adenosine,
- Lactic acid,
- Increased potassium ions,
- Diminished calcium ion concentration.
- Increased body temperature

Effects of Hormones on Smooth Muscle Contraction

Norepinephrine, epinephrine, acetylcholine, angiotensin, endothelin, vasopressin, oxytocin, serotonin, and *histamine.*

A hormone causes contraction of a smooth muscle when the muscle cell membrane contains ***hormone-gated excitatory receptors*** for the respective hormone.

A hormone causes inhibition if the membrane contains ***inhibitory receptors*** for the hormone

- Inhibition, occurs when the hormone *closes the sodium and calcium channels* to prevent entry of these positive ions
- Inhibition also occurs if the normally closed *potassium channels are opened,* allowing positive potassium ions to diffuse out of the cell.
- Both actions increase the degree of negativity inside the muscle cell, a state called ***hyperpolarization,*** which strongly inhibits muscle contraction

Other mechanism is through ***second messengers*** .

The cAMP or cGMP has many effects, one of which is to change the degree of phosphorylation of several enzymes that **indirectly inhibit contraction**.

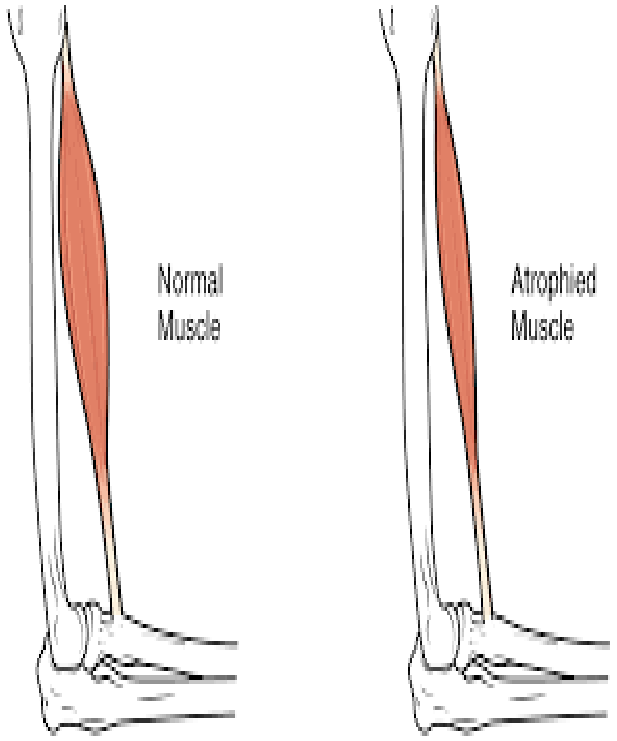
Calcium ion pump moves Ca+ from the sarcoplasm into the SR is activated, and cell membrane pump that moves calcium ions out of the cell itself; these effects reduce the calcium ion concentration in the sarcoplasm, inhibiting contraction.

Muscle Atrophy

Weakening and shrinking of a muscle

May be caused

- Immobilization
- Loss of neural stimulation



Muscular Atrophy

When the total mass of a muscle decreases, it is called Muscle Atrophy. If a muscle is not used, its actin and myosin content decreases, its filaments become smaller and the muscle decreases in mass and becomes weaker.

Physiologic Basis:

1. When the muscle is prevented from doing work even though the nerve supply is intact. e.g. in bed-ridden patients, in a limb in a plaster of Paris cast. This type is thus called **Disuse Atrophy**.
2. Atrophy also seen nerve supply to the muscle is lost. This can be due to an accident or when motor neurons supplying a muscle are destroyed .e.g. Poliomyelitis.

- Muscle fiber becomes thin & low in proteins, glycogen and ATP.
- When muscle continuously shortened then **sarcomeres** at the end of the muscle fiber actually disappear

Muscle Hypertrophy

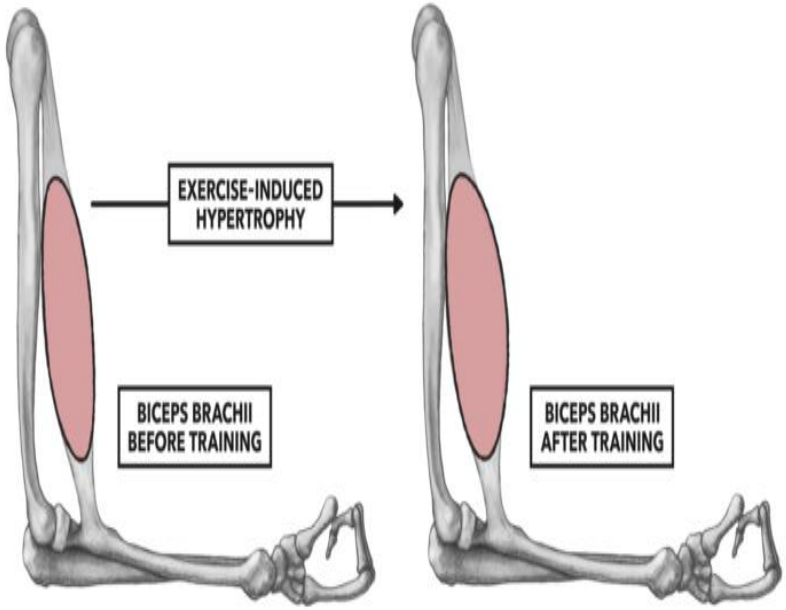
Enlargement of a muscle, increase in the size of cells.

More capillaries

More mitochondria

Caused by

- Strenuous exercise
- Steroid hormones



Muscle Hypertrophy

When the total mass of a muscle increases, this is called **Muscle Hypertrophy**. The resulting muscle enlargement comes from an increase in diameter of the muscle fibers. It is in response to a regular & intensive use of that particular muscle. e.g. body building.

Physiologic Basis:

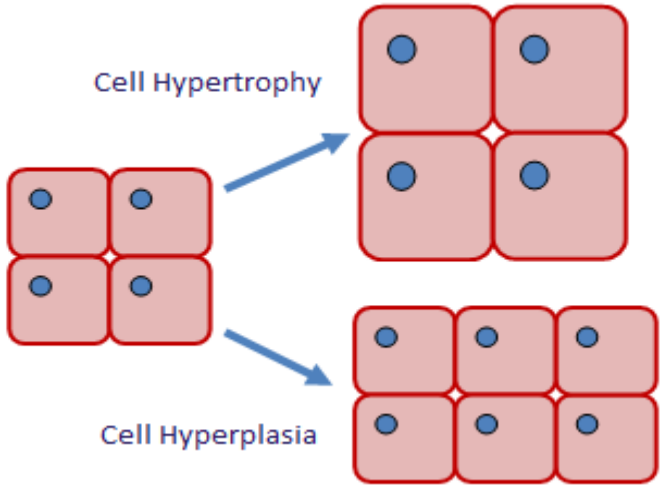
↑in the number of actin & myosin filaments causing increase in thickness of individual muscle fibers---called **fiber hypertrophy**

Rate of synthesis of actin & myosin far greater

Signaling proteins triggered that turn on genes that direct the synthesis of more of these contractile proteins.

Muscle Hyperplasia

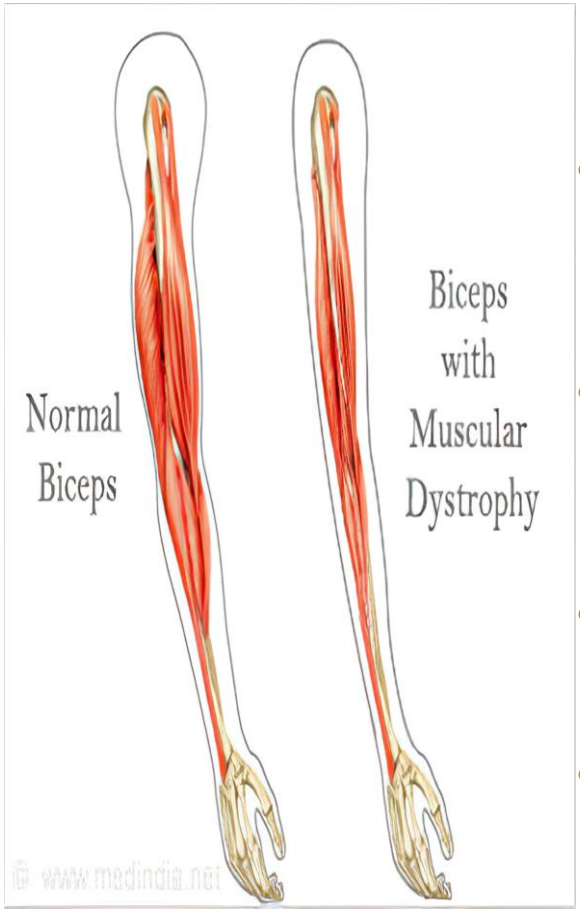
Increase in the number of muscle cell fiber is called as muscle Hyperplasia.



Muscle Hyperplasia

Under rare conditions of extreme muscle force generation, the actual number of muscle fibers increase, in addition to the fiber hypertrophy ----This increase in fiber number is called **Muscle Hyperplasia**.

Mechanism: Linear splitting of previously enlarged fibers



Muscular Dystrophy

- **Muscular dystrophy** is a group of diseases that cause progressive weakness and loss of **muscle** fibers.
- In **muscular dystrophy**, abnormal genes (mutations) interfere with the production of proteins needed to form healthy **muscle**.
- They are usually inherited, and dystrophy occurs over the passage of time.
- One of the most common forms is *Duchenne muscular dystrophy.*

Rigor Mortis

Several hours after death, all the muscles of the body go into a state of *contracture* called "rigor mortis“

The muscles contract and become rigid, even without action potentials.

Rigor Mortis

- This “Stiffness of death” is a generalized locking in place of the skeletal muscle that begins 3 to 4 hours after death and completes in about 12 hours.
- This rigidity occurs as a result of loss of all ATP which is needed to cause separation of the cross bridges from actin filaments during relaxation process.

Basically, there are 2 reasons for this contracted state

1. Following death cytosolic concentration of calcium begins to rise because the inactive muscle membrane cannot keep out extracellular calcium so the Ca+ begins to leak out of lateral sacs. This Ca+ moves aside the regulatory proteins and let the actin bind with myosin cross bridges which were already charged with ATP before death.

2. Dead cells cannot produce ATP so actin and myosin once bound cannot detach as they lack fresh ATP.

As Ca+ ATPase pump does not work in dead cells therefore Ca+ cannot be actively pumped back in SR leading to no relaxation phase i.e. contracted state

The muscles remain in rigor until the muscle proteins deteriorate about 15 to 25 hours later, which presumably results from autolysis caused by enzymes released from lysosomes. All these events occur more rapidly at higher temperatures.

Recovery of Muscle contraction in Poliomyelitis

- Immediately following paralytic polio, surviving motor nerve cells in the brain stem and spinal cord extend new branches to re-connect the nerve cell to the muscle. These are called *sprouts*.
- The new sprouts are now capable of triggering contraction in the muscles and muscle function can be partially or fully regained.
- These new sprouts are not indefinitely stable.
- After many years, these motor neurons begin to break down, causing new muscle weakness.

Cont……

- Thus, many motor nerve cells end up supplying several times the number of muscle fibers they would normally supply.
- Recovery is usually complete in 6 to 8 months.
- A single motor neuron that once controlled 200 muscle cells might control 800 to 1000 cells.

Thank you

References

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