Muscle tissue- part 2

When action potential reaches the interior of the muscle cell through T tubules, calcium will be released and that will lead to muscle cell contraction.

When stimulation occurs, nerve endings release certain neurotransmitters and they bind to certain receptors on the sarcolemma leading to depolarization and that depolarization will propagate and reach each myofibril within the cell and once it reaches the triad area it triggers the release of calcium ions from the sarcoplasmic reticulum.

Calcium (from the sarcoplasmic reticulum) will bind to troponin causing conformational changes that stimulate tropomyosin to leave the complex exposing the binding sites on actin and now the myosin head will interact with its binding site on actin.
We call the binding between actin and myosin: cross bridge.

In order for the myosin head to be released from actin it needs ATP (the cross bridge will be removed).

After death we have something called rigor mortis (rigor=stiffness, mortis=death) and that's because after death there is no oxygen and no ATP (mitochondrial activity stops after death). Myosin will not be able to detach from actin and the muscles are unable to relax. Rigor mortis means postmortem rigidity, and is one of the recognizable signs of death. It occurs in all muscles, all muscles become rigid and the body is hard to move. Rigor mortis usually starts after four hours and peaks at 12 hours, first in the face and generally smaller muscles. Decomposition of the myofilaments occurs 48 to 60 hours after the peak of rigor mortis by endogenous enzymes and bacteria

The junction between the motor neuron and the skeletal muscle cell is called the neuromuscular junction or the neuromuscular synapse or motor end plate

Motor unit:
The muscle cells that are supplied by a single neuron/axon, its size is variable according to the muscle action. EX: quadriceps muscle is a large muscle and its contraction is gross, a single axon supplies hundreds of muscle fibers. Another example is the hand muscles, they might have ten muscle cells supplied by a single axon (fine movement, small motor unit), muscles of the eye: one axon supplies one or two muscle fibers in order to produce a fine movement. The finer the movement, the fewer muscle fibers per motor unit (smaller motor unit)

Muscle spindle

- Acts as proprioceptors (proprioception: muscle sense)
- Acts as stretch detectors
- Provides the central nervous system (CNS) with data from musculoskeletal system
- A muscle spindle is encapsulated by modified perimysium
- Contains few thin modified muscle fibers filled with nuclei
- Called also intrafusal muscle fibers
- Sensory axons wrap around individual muscle fibers
- Detects any change in the length and tension of the muscle caused by body movement, and sends this information to CNS to detect the position of body parts
- Most of this proprioceptive information is processed at a subconscious level

Types of skeletal Muscle fibers:
We have 3 different types of skeletal muscle fibers in our body:
1. Slow fibers (Red Muscles)
2. Fast fibers (White Muscles)
3. Intermediate fibers.

The main difference between types is how they produce ATP. The color of the muscle is different (Grossly not histologically)

Slow Fibers (Red Muscles):

- ✓ They produce their ATPs by Oxidative phosphorylation in Mitochondria, which produces high amounts of ATP in a long time (slow) (Aerobic reactions inside the mitochondria = Oxygen is used)
- ✓ The fuel for the production of ATP is Fatty acids (mainly), fatty acids are produced by metabolism of fats, so in order to burn fat in your body, you need to work aerobically

(Aerobic exercises are called so because people are activating their red muscles to burn fats, so they are usually preceded with warm up exercises, to supply the muscles with adequate amount of oxygen)
(Thin people usually have higher amount of red muscle fibers than white muscle fibers).

- ✓ They look red because:

a. They have high amount of mitochondria
b. They are highly vascularized, because they need high amounts of O2 to produce contraction
c. They contain high amounts of Myoglobin (Hemoglobin like protein, has heme (iron), and is an oxygen binding protein)

All these features make fresh tissue rich in these fibers dark or red in color.

- ✓ The ATPase activity of their myosin heads is low, so the contraction is slow
- ✓ This slow contraction is prolonged (for a long time but slow). Remember here that we have significant amount of ATP to maintain contractions for long time
- ✓ They don't get Fatigue easily.

Examples: Spinal muscles, muscles of the back, hip flexors (postural muscles are mainly red fibers)

Fast Fibers (White Muscles)

- ✓ They are white in color, because they don't have high amounts of myoglobin and mitochondria.

- ✓ They don't need Oxygen to produce ATP (Anaerobic reactions in the cytoplasm instead of mitochondria).
- ✓ Glycolysis: production of ATP without the need of oxygen, it occurs in the cytoplasm directly and quickly.
- ✓ They are called Fast fibers because: They produce ATP quickly within the cytoplasm by glycolysis, they produce fast contractions
- ✓ The ATPase activity of their myosin heads is high
- ✓ They are larger than red fibers.
- ✓ They produce fast and strong contractions but for short time.
- ✓ Activated in weight lifting activities (resistance excersizes), for example if you are carrying a heavy object, you give maximum force but this contraction will not last for a long time

For Example: people who sprint (run at maximum speed for short distance) produce very strong contractions for a short period of time (have high amount of white fibers), while Marathon runners have higher amount of red fibers, they run long distance for a long period of time without getting fatigue (their speed is moderate).

- ✓ Why do they look white?

A. They have few mitochondria, less capillaries
B. They store high amount of glycogen

- ✓ They get fatigue easily because one of the byproducts of Glycolysis is Lactic acid (it causes burning sensation but it will be absorbed soon).
- ✓ The fuel for these muscles is mainly: Glucose.

Third: Intermediate Fibers:

1. They have characteristics between both the white and the red
2. They are more resistant to fatigue than the white fibers but less than the red.
3. They are faster than red muscle fibers.

MOTOR UNIT: number of muscle cells supplied by a single Axon
- Each motor unit is composed of certain type of muscle fibers, red or white. So *All muscle fibers of a motor unit are of the same type*

Skeletal Muscles contract when they are stimulated, if you cut the nerve supply, paralysis will occur

Muscle atrophy: loss of tone and mass from lack of stimulation. Muscle becomes smaller and weaker. This is could be a result of not using the muscle (disuse atrophy)

Muscle Hypertrophy:
Hypertrophy: is an increase in the size of the muscle.
By increasing the synthesis of their proteins (synthesis of more actin and myosin), so the myofibril itself gets thicker and so on, and the size of the muscle will increase.

Hyperplasia:
Hyperplasia: increase in the number of the cells
- Skeletal muscle cell can undergo hypertrophy (highly muscular people), and it can rarely undergo hyperplasia because the amount of the satellite cells is very minimal.

Note that satellite cells are undifferentiated stem cells (myoblasts) and they remain in the skeletal muscle tissue after differentiation
Satellite cells proliferate and produce new muscle fibers following muscle injury.

Remember, skeletal muscle cells cannot undergo mitosis (they are highly differentiated), however, the skeletal muscle tissue can still display limited regeneration. The source of regenerating cells is the satellite cells. After injury, satellite cells proliferate, differentiate and fuse to form new skeletal muscle fibers. So skeletal muscle cells have limited capacity for regeneration (because we have few satellite cells in skeletal muscle tissue).
Generally, skeletal muscle tissue is replaced by proliferating fibroblasts and growth of connective tissue, forming only connective tissue scars.

ALL OR NONE principle: each muscle fiber either contracts completely or not at all, why? due to the presence of T-tubules (invaginations from the sarcolemma and they reach each myofibril within the muscle cell) so when the action potential reaches the muscle cell, all the myofibrils within the muscle cell will contract/shorten leading to the all or none principle. This applies also to the motor unit, either there is contraction in all the muscle cells that belong to one motor unit or there is no contraction at all

Cardiac muscle

- ✓ Cardiac muscle cells are striated (composed of repeating units of sarcomeres inside the myofibril as in skeletal muscle cells)
- ✓ Self excitatory and electrically coupled: this means that these cardiac muscle cells are able to initiate contraction without nerve input (no motor end plate). This is called **Myogenic activity of the cardiac cells**
- ✓ **Myogenic activity:** they generate their own electrical impulses (pacemaker). Cardiac muscle fiber contraction is intrinsic and spontaneous, as evidenced by the continued contraction of the cells in tissue culture.
- ✓ Force of contraction is modulated by autonomic nervous system (sympathetic and parasympathetic)(only to control the force of contraction not to initiate it).
- ✓ Sympathetic: increases the force of contraction.
  Para sympathetic: decreases the force of contraction.

The main similarities between cardiac and skeletal muscle are:

1. Both are striated.
2. Both are composed of myofibrils, each myofibril is surrounded by a network of sarcoplasmic reticulum
3. Almost the same contraction mechanism.

The main differences between cardiac and skeletal muscle cells are:

1. The cardiac muscle cell is also called muscle fiber, but compared with the skeletal fibers, cardiac muscle cells are shorter and interconnected (branched, to provide waves of contraction).
2. Cardiac muscle cell is single-nucleated but sometimes it is bi-nucleated while skeletal muscle cell is multi-nucleated.
3. The single nucleus in the cardiac muscle cell is located in the center, while the multi-nuclei of skeletal muscle cell are found under the sarcolemma (at the periphery).
4. The striations of cardiac muscle cells are less distinct (obvious), while it‘s more obvious in skeletal muscle cells. ***Why***?

Because cardiac muscle cells have higher amount of mitochondria than skeletal muscle cells and larger in size, these mitochondria are located between the myofibrils. In addition, heart muscle cells store glycogen so the higher amount of mitochondria, glycogen, lipid inside the cytoplasm results in less obvious striations, while in the skeletal muscle, the sarcomeres are arranged above each other with little spaces in between the myofibrils, so it

appears uniformly striated, more obvious than the cardiac muscle. (But both skeletal and cardiac muscles are striated)

- ✓ The stored lipids and glycogen are used as a fuel for the cardiac muscle cells
- ✓ The heart muscle contracts all the time so it needs large amount of mitochondria (up to 40% of cell volume) in order to produce ATP for muscle contraction.

5. The sarcolemma of the cardiac muscle cell also has invaginations. T-tubules also surround each myofibril, but instead of having triads (as in case of skeletal muscle) we have diads. Diad (or dyad) is one T-tubule with one tubular end of SR. The sarcoplasmic reticulum of cardiac muscle cells is less extensive (smaller in size and less branched) than in skeletal muscle cells.

- ✓ In general T tubules in cardiac muscle are larger and occur near to the Z line of sarcomere.
- ✓ The cardiac muscle cells are branched, short and connected to each other by step-like lines called intercalated discs.

Intercalated discs:
Zigzag- like structure, Step-Like structure connecting two cardiac muscle cells together, it has two parts:
1. Horizontal Part
2. Vertical part

It contains 3 types of junctions:
A. **Gap junctions** (not exclusive to epithelial cells, we have them also between cardiac muscle cells). Gap junctions are located in the horizontal part of intercalated disc. Gap junctions allow movement of ions between cardiac muscle cells; this allows contraction of the whole muscle uniformly as one unit (although it's composed of many cells)

B. It also contains **desmosomes** and **fascia adherens** (Located in the vertical part of intercalated disc), to anchor cardiac cells together mechanically and prevent detachment and pulling apart of cells when the heart is contracting.

NOTE:

1. The fascia adherens has the same concept as Zonula adherens which is found between epithelial cells. In epithelium it is called zonula because it forms a belt like structure around epithelial cells. But between the heart muscle cells, it forms spot-like areas like the desmosomes)
2. The difference between desmosomes and fascia adherens: (desmosomes are associated with intermediate filaments while fascia adherens are associated with actin filaments).

- Cardiac muscle cells don't contain satellite cells therefore these cells are not able to regenerate in case of injury. They have very poor capacity for regeneration

- Hyperplasia doesn't happen in cardiac muscle, cardiac muscle cells don't regenerate, they have No satellite cells (skeletal muscles have limited ability to regenerate because they contain few satellite cells).

- They are trying to use stem cells inside the heart in order to regenerate cardiac cells to replace the damaged area of the heart, instead of heart implant (stem cell technology).
- The cardiac muscle cells can undergo hypertrophy (increase in the cell size).

Smooth muscle:

- ✓ Smooth muscle cells are called smooth because they don't have any striations, but this doesn't mean they don't have actin and myosin, they do have, but they are not arranged into sarcomeres. Therefore they don't appear striated (unstriated cells)

- ✓ Cardiac and skeletal muscle cells contain actin and myosin arranged into sarcomeres – striations
- ✓ FOUND INSIDE THE WALLS OF HOLLOW ORGANS AND TUBES IN THE BODY

6 major locations:
Inside the eye, wall of vessels, respiratory tubes, urinary organs, digestive tubes, reproductive organs.

Now, what is the importance of smooth muscles?
Note: the wall of bronchi is composed of smooth muscles.
The smooth muscles in the bronchi can control the diameter of these tubes. So when you are exercising you need more oxygen, so these muscles (of the bronchi) are going to relax in order to increase the diameter and to get more oxygen. At the same time the blood vessels that supply skeletal muscles (also have smooth muscles in their wall) will increase in diameter (vasodilation). They are going to relax, because you need more blood flow to supply your muscles.

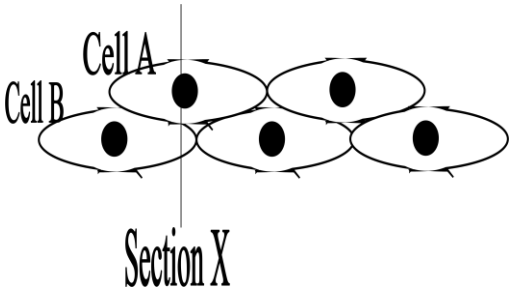
What about the blood vessels of the GI tract?
The smooth muscles in their walls are going to constrict because it is not important to supply the GI tract with blood during exercise.
(Contraction decreases the diameter while relaxation increases the diameter)

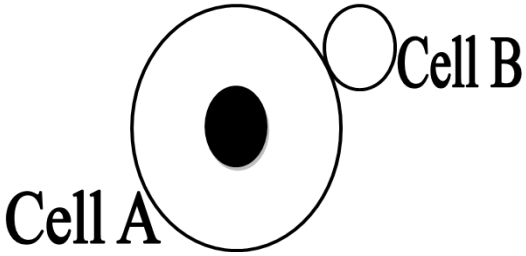
- ✓ Smooth muscles contraction is involuntary (not under our conscious control)
- ✓ They are spindle (fusiform) in shape, broad in the center and narrow at the periphery.
- ✓ Smooth muscle cells can be called also fibers (although they don't look like fibers, but in general all muscle cells are called muscle fibers).
- ✓ Smooth muscle cells are single-nucleated (one nucleus in the center of the cell)
- ✓ The smooth muscle cells are arranged into sheets (above each other), the narrow area of one smooth muscle cell is above the broad area of another smooth muscle cell (to have minimal spaces between the cells)
- ✓ They are tightly packed with small amount of loose connective tissue (endomysium)
- ✓ Usually, the sheets are perpendicular to each other (at right angles to each other).
- ✓ Smooth muscles don't get fatigue (the contractions are slow, sustained, and resistant to fatigue)

- ✓ If we look at a longitudinal section along the long axis of the smooth muscle cells, the previous features (spindle-shaped, tapering, single – nucleated,…) would be visible.

- ✓ If we take a cross section through smooth muscle cells, we'll see different rounded profiles with different diameters, some containing the nucleus and some do not (each cell contains a nucleus, but it depends on the plane

of the cut, if it's in the middle of the cell, the nucleus would be visible, if it's in the periphery, we wouldn't see the nucleus). In addition, if the section is in the middle of the cell, the circle would be big, but if it's on the periphery, the circle would be small.





- ✓ Smooth muscle cells produce peristalsis movement (الحركة المَعَوية) which is a continuous movement.
- ✓ Smooth muscle cells are connected by gap junctions, which allow small ions and molecules to pass from one cell to the next allowing the spread of depolarization, and acting as a single unit
- ✓ Smooth muscle cells in certain locations have high synthetic activity, like in the wall of blood vessels; they synthesize the components of ECM

<u>Do smooth muscle cells need nerve supply in order to contract?</u>

In general, we say that smooth muscles are controlled by neuro-endocrine impulses (neuro: receives nerve supply, endocrine: affected by local hormones that increase or decrease the contraction) and they are sensitive to stretch.

Examples:

1) They can be activated by stretch, When stretch happens in the urinary bladder for example (because of the accumulation of urine), the reflex of the muscles is to contract, Which means that smooth muscles don't always require a nervous signal (have Myogenic activity), they may be stimulated by stretching or hormones. Note that gap junctions also present between

smooth muscle cells and allow the multicellular tissue to contract as a single unit, providing better efficiency and force.
2) Smooth muscles in the walls of blood vessels for example receive nerve supply to contract and cause constriction

Refer to powerpoint slide:

- ✓ Notice: actin, myosin and intermediate filaments inside the smooth muscle cell.
- ✓ Dense bodies: are equivalent to Z-lines in the skeletal muscle cell
- ✓ Dense bodies are composed of α- actinin, the actin filaments are attached to dense bodies.
- ✓ Dense bodies have two types:
- o Dense bodies close to the plasma membrane (submembranous dense bodies)
- o Dense bodies within the cytoplasm, called "intra-cytoplasmic dense bodies".

- ✓ Instead of having Z-lines, we have dense bodies, actin filaments are attached to dense bodies and in between we find myosin filaments.
- ✓ When the cell contracts, the dense bodies get closer to each other, the overlap between actin and myosin increases
- ✓ Refer to PowerPoint slide: notice the difference in shape between the contracted muscle cell (scalloped) and the flattened (relaxed) muscle cell. When the cell contracts, it becomes rounded with scalloped surface.

Filaments inside the smooth muscle cell consist of 3 types:

- ✓ Actin
- ✓ Myosin
- ✓ Intermediate filaments (like desmin and vimentin) which connect dense bodies together.

- ✓ Intermediate filaments are the cytoskeleton of the smooth muscle cell; the intermediate filaments are connected to each other via dense bodies. The dense bodies (near the plasma membrane) are attached by desmosome junctions to other smooth muscle cells

- ✓ No troponin in thin filaments of smooth muscle (instead they have calmodulin-Calcium binding protein)
- ✓ Has scattered smooth endoplasmic reticulum (SR)

- ✓ On the plasma membrane of smooth muscle cells, we find certain structures called caveolae, short depressions of the sarcolemma (short and shallow invaginations of the plasma membrane) of the smooth muscle.
- ✓ The importance of these caveolae: They have high concentration of receptors (proteins and lipids) because these cells can be controlled by hormones, so we find this high concentration of receptors that have several functions in signal transduction and act as stretch sensors that can sense the stretching of the organ itself (these cells are easily activated).
- ✓ Smooth muscles can undergo Hypertrophy and Hyperplasia.

Example: the wall of the uterus, which is composed of smooth muscle cells, gets larger in size during pregnancy because these cells can undergo mitosis and increase in number (hyperplasia) in addition to increasing in size (hypertrophy).

- Smooth muscles are the only type that has high regeneration power. Why? The reason is because these cells are less differentiated and can undergo mitosis (cells have not lost the capacity to divide by mitosis)
- When the cells are less differentiated, they are able to divide. Skeletal muscle cells are highly differentiated (can't undergo division) and if regeneration of skeletal muscles occurs, it would be because of the satellite cells (myoblasts that remain inside the muscle tissue).

- Which type of muscles can undergo Hypertrophy? All types
- Which type of muscles can undergo Hyperplasia? Smooth muscles and rarely skeletal muscle

Note: in extreme cases like in highly-muscular bodies, Hyperplasia might happen in skeletal muscles. But normally it's hypertrophy that occurs.

So the three types of adult muscle have different potentials for regeneration after injury

1- Repair and regeneration can occur in skeletal muscle because of a population of reserve muscle satellite cells that can proliferate, fuse, and form new muscle fibers.
2- Cardiac muscle lacks satellite cells and has little capacity for regeneration.
3- Regeneration is rapid in smooth muscle because the cells/fibers are small and relatively less differentiated, which allow renewed mitotic activity after injury.

- ✓ All muscle cells in the 3 types are surrounded by loose type of connective tissue that contains high amount of reticular fibers (endomysium)
- ✓ Remember that reticular fibers support individual cells