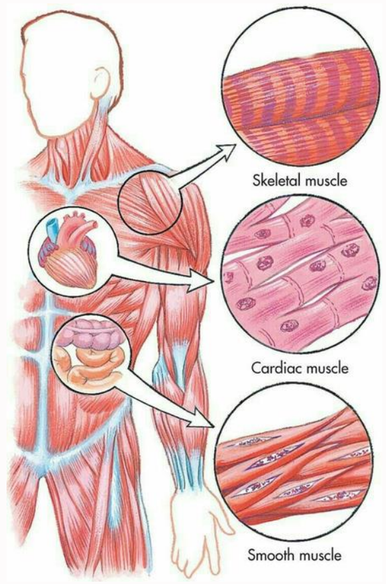
بسم الله الرحمن الرحيم

Histology | Final 10

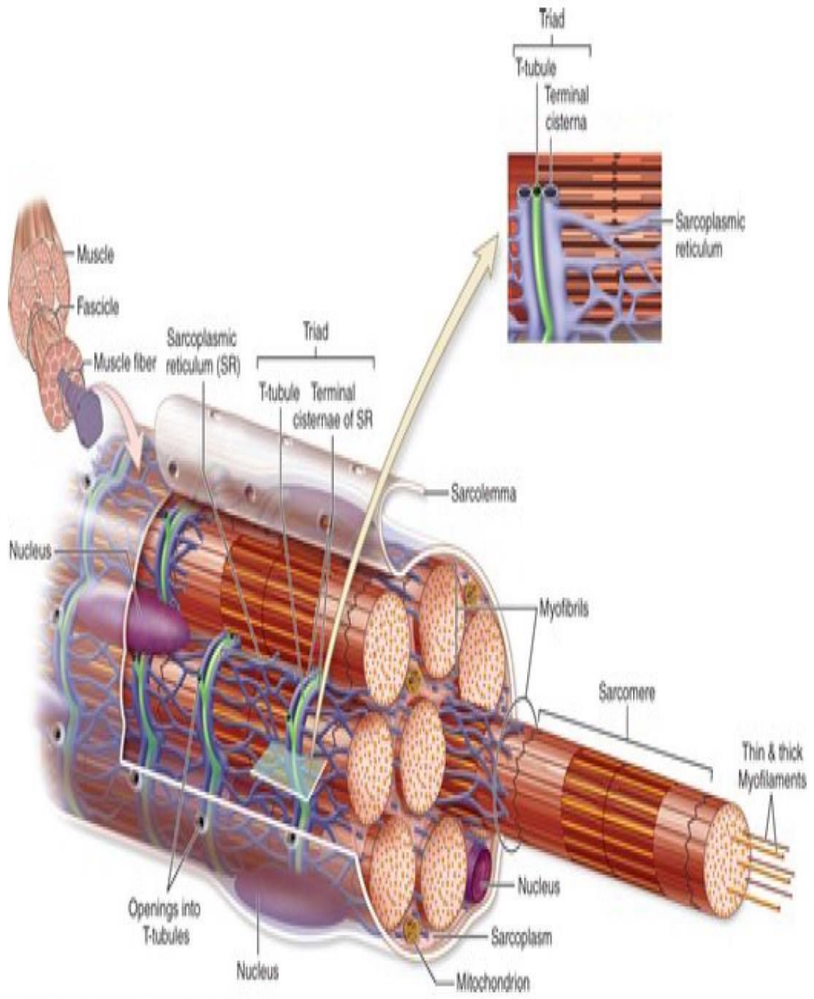
Muscle Tissue pt.2

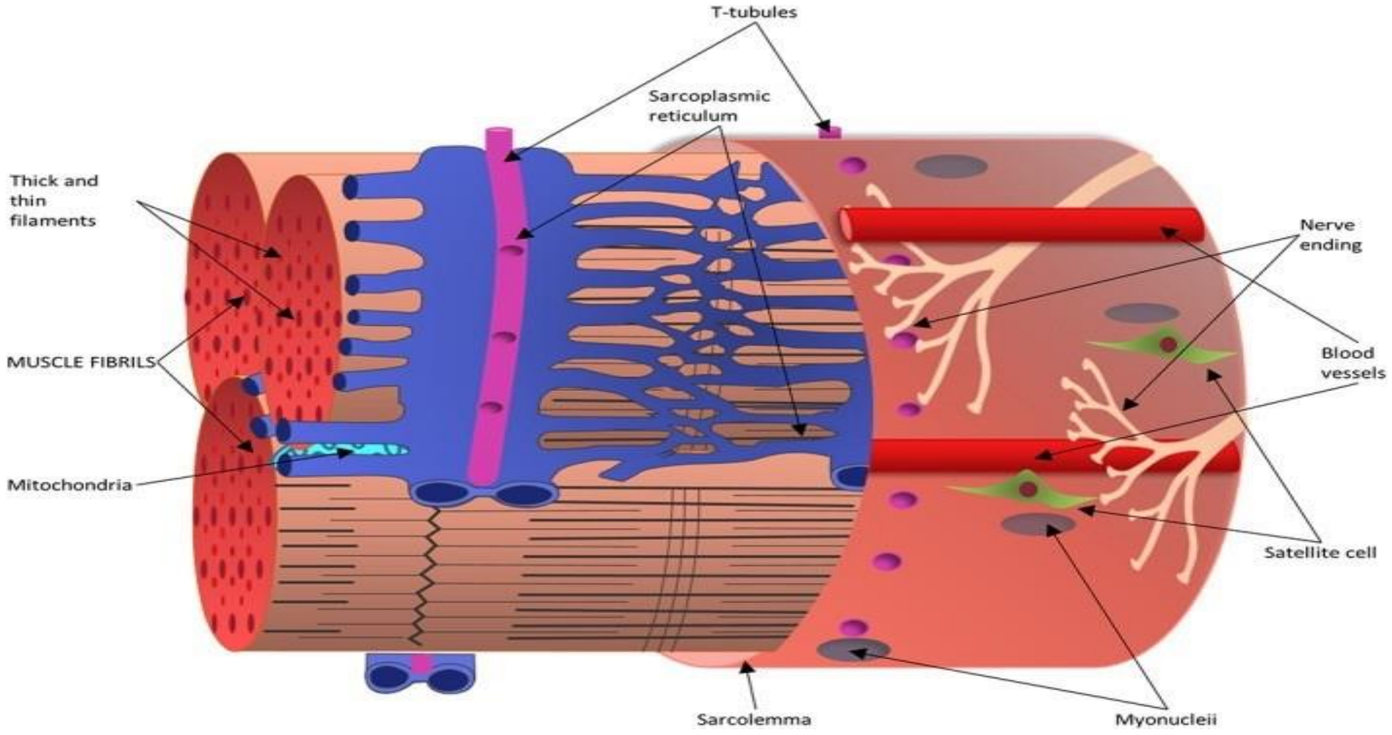


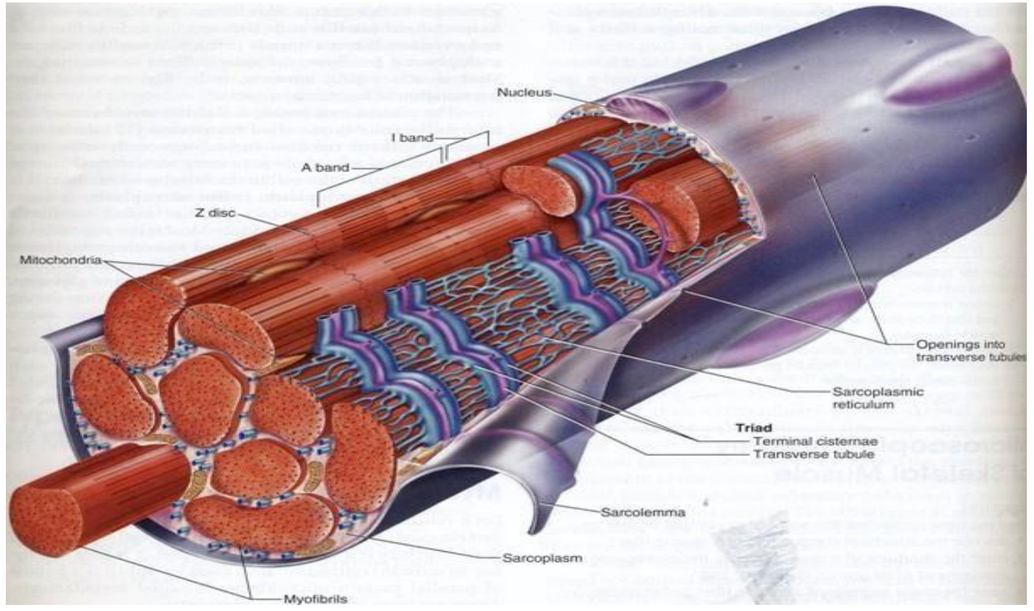
Written by : Jannat Nasri
Shorouq Matalkah
Maria Baroudi
Leen Al-Shannaq

Sarcoplasmic Reticulum & Transverse Tubule System

- The sarcoplasmic reticulum, contains pumps and other proteins for Ca^{2+} sequestration and surrounds the myofibrils.
- Calcium release from cisternae of the sarcoplasmic reticulum through voltage-gated Ca^{2+} channels is triggered by membrane depolarization produced by a motor nerve.
- The sarcolemma has deep invaginations called **T-tubules** that encircles each myofibril near I-A bands junction.
- Each of T-tubule becomes associated with two **terminal cisternae** of the sarcoplasmic reticulum…**TRIAD**



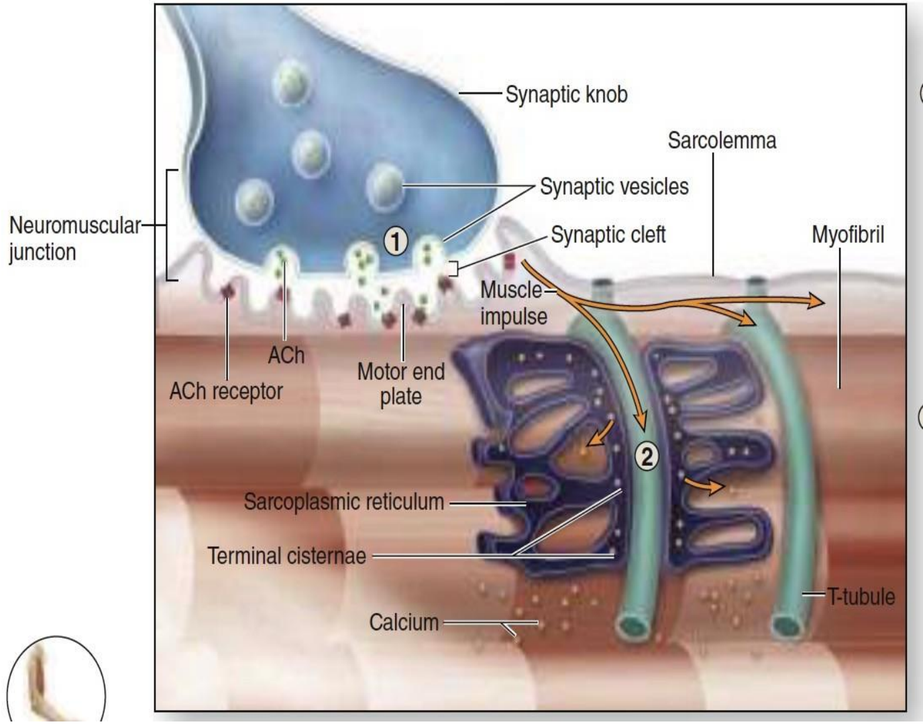

T-tubules
Sarcoplasmic reticulum
Thick and thin filaments
Nerve ending
MUSCLE FIBRILS
Blood vessels
Mitochondria
Satellite cell
Sarcolemma
Myonucleii


Nucleus
I band
A band
Z disc
Mitochondria
Openings into transverse tubules
Sarcoplasmic reticulum
Triad
Terminal cisternae
Transverse tubule
Sarcolemma
Sarcoplasm
Myofibrils

Innervation/contraction

- Myelinated motor nerves branch out within the perimysium, where each nerve gives rise to several unmyelinated terminal twigs that pass through endomysium and form synapses with individual muscle fibers.

- Schwann cells enclose the small axon branches.
- Each axonal branch forms a dilated termination---- neuromuscular junctions, or motor end plates (MEP).



The main purpose of the action potential in muscle fibers is to open calcium channels. The triad, especially the T-tubules, helps spread the action potential deep into the muscle fiber. This ensures a uniform release of calcium (Ca^{2+}), which is important for proper muscle contraction.

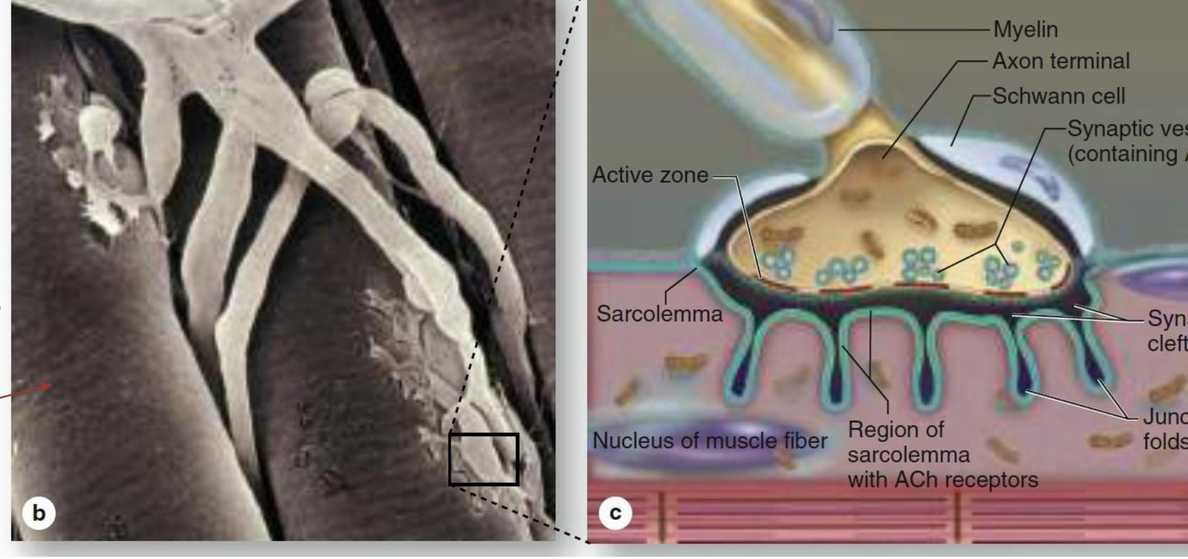
- The axon terminal contains mitochondria and numerous synaptic vesicles----neurotransmitter acetylcholine.

- Between the axon and the muscle is the synaptic cleft.
- Adjacent to the synaptic cleft---the sarcolemma---- deep junctional folds--- greater postsynaptic surface area and more acetylcholine receptors.

Innervation/contraction

b) This image was taken with SEM.

Muscle fiber



Sarcolemma creates the junctional folds which increase the number of receptors.

- Acetylcholine(the neurotransmitter) + receptor-----depolarizing the sarcolemma---muscle action potential.
- muscle action potential moves along the sarcolemma and along T-tubules.
- At triads the depolarization signal triggers the release of Ca^{2+} from terminal cisterns of the sarcoplasmic reticulum---contraction cycle.
- An axon can form MEPs with one or many muscle fibers.
- Innervation of single muscle fibers by single motor neurons--- precise control of muscle activity--- extraocular muscles (**eye movements**).
- Larger muscles---motor axons branch profusely---innervate 100 or more muscle fibers (**motor unit**).

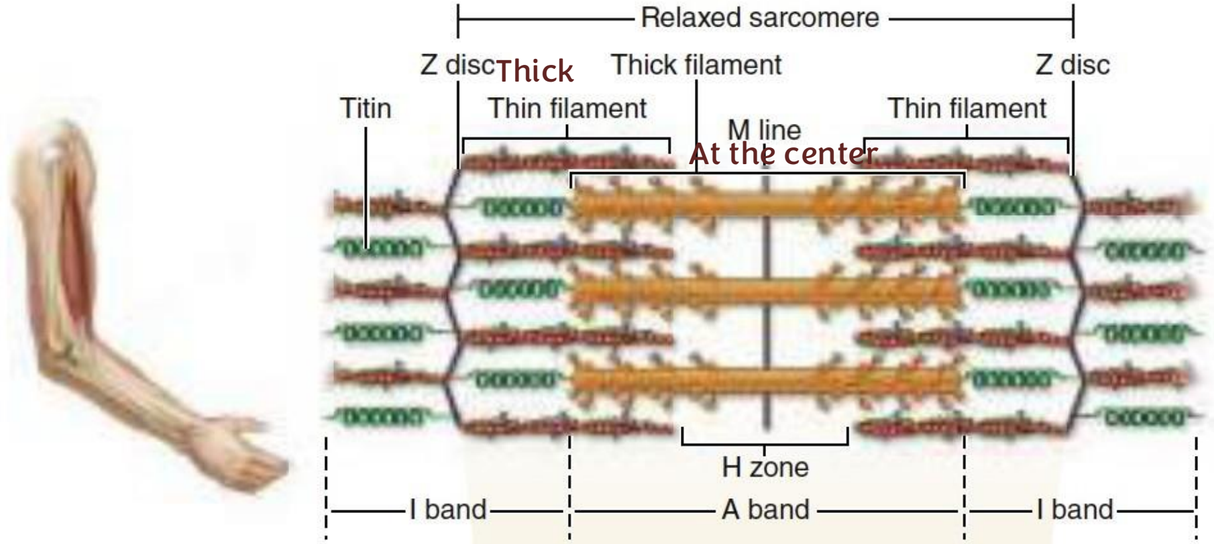
How many muscle fibers are innervated by a single axon.

The bigger motor unit, bigger muscle and the less precise its function.
The smaller motor unit, smaller muscle and the more precise its function.

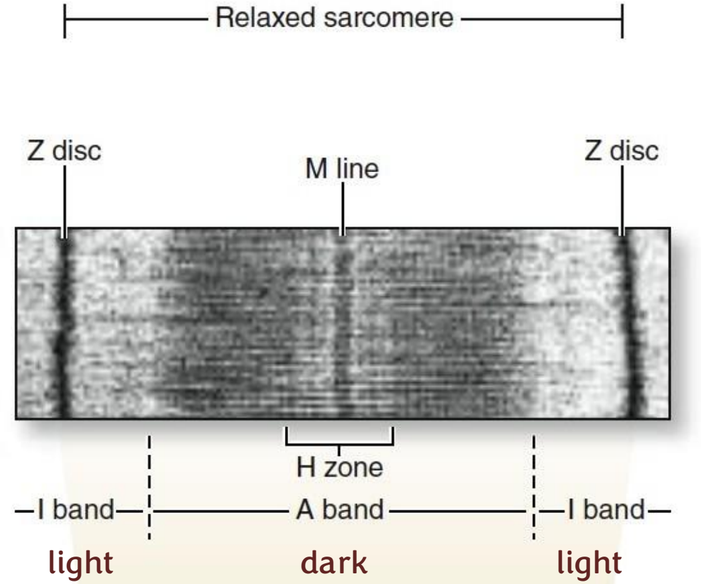
Innervation/contraction

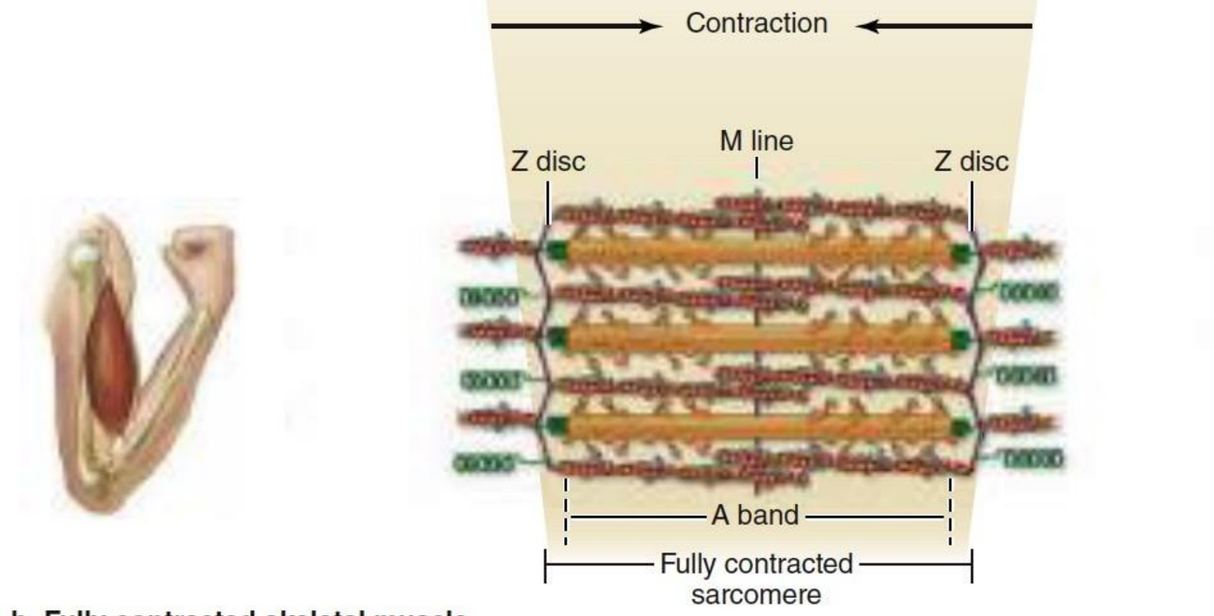
- Striated muscle fibers do not show graded contraction---**all or none**.
- To vary the force of contraction--- fibers within a muscle fascicle do not all contract at the same time.
- large muscles with many motor units---firing of a single motor axon ------tension proportional to the number of muscle fibers it innervates.

Relaxation versus contraction

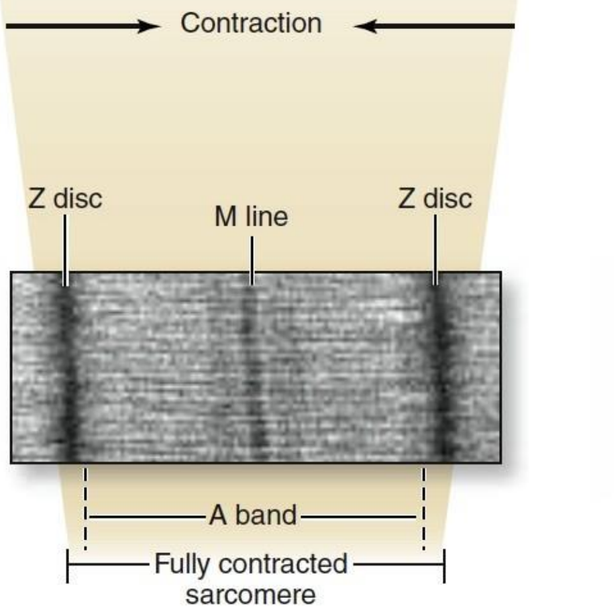


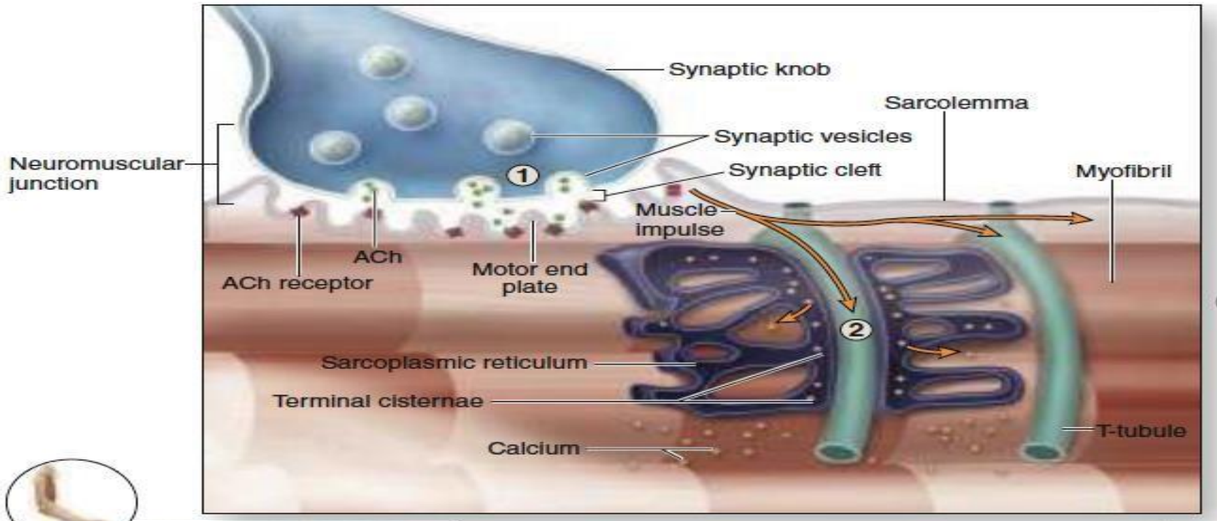
a Relaxed skeletal muscle





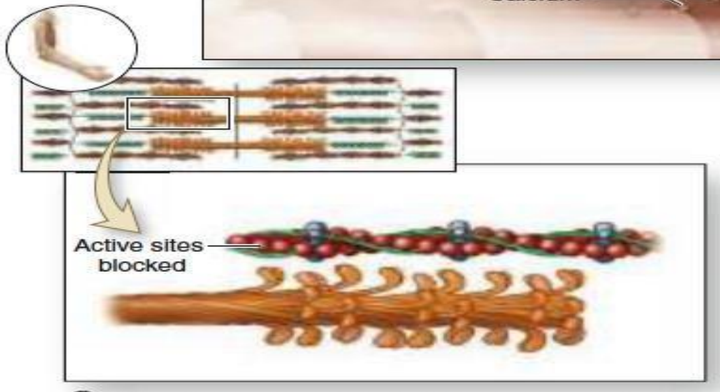
b Fully contracted skeletal muscle



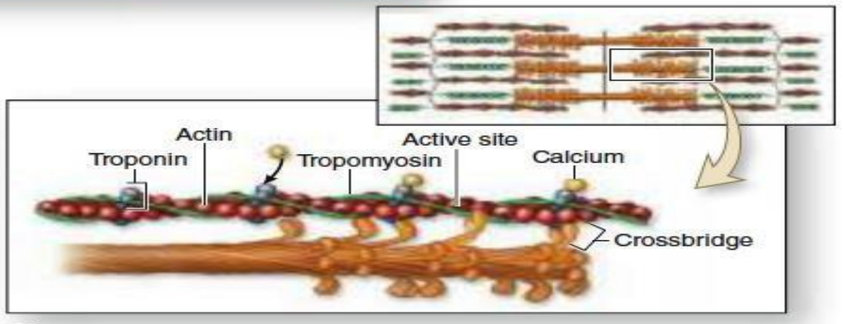


1 A nerve impulse triggers release of ACh from the synaptic knob into the synaptic cleft. ACh binds to ACh receptors in the motor end plate of the neuromuscular junction, initiating a muscle impulse in the sarcolemma of the muscle fiber.

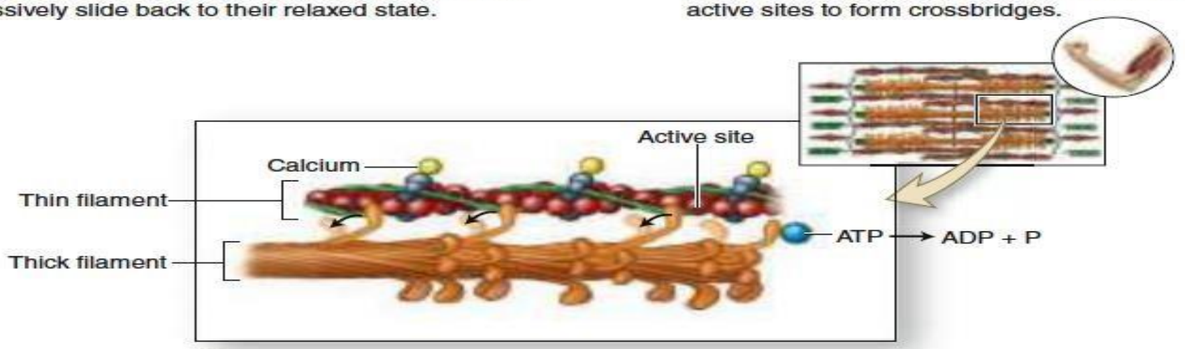
2 As the muscle impulse spreads quickly from the sarcolemma along T tubules, calcium ions are released from terminal cisternae into the sarcoplasm.



5 When the impulse stops, calcium ions are actively transported into the sarcoplasmic reticulum, tropomyosin re-covers active sites, and filaments passively slide back to their relaxed state.



3 Calcium ions bind to troponin. Troponin changes shape, moving tropomyosin on the actin to expose active sites on actin molecules of thin filaments. Myosin heads of thick filaments attach to exposed active sites to form crossbridges.

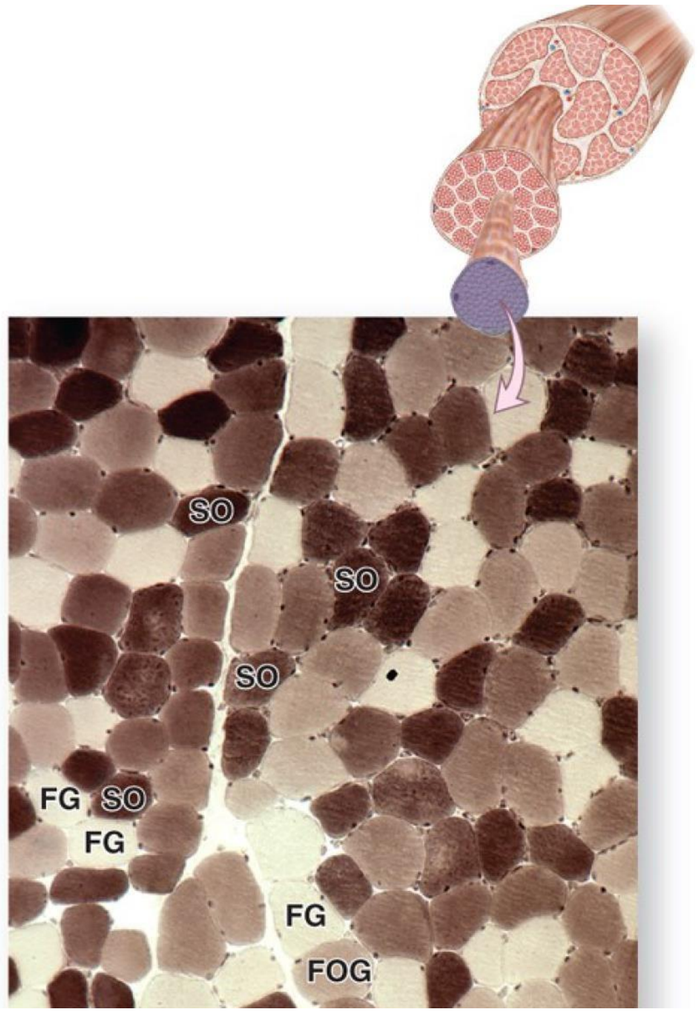


4 Myosin heads pivot, moving thin filaments toward the sarcomere center. ATP binds myosin heads and is broken down into ADP and P. Myosin heads detach from thin filaments and return to their prepivot position. The repeating cycle of *attach-pivot-detach-return* slides thick and thin filaments past one another. The sarcomere shortens and the muscle contracts. The cycle continues as long as calcium ions remain bound to troponin to keep active sites exposed.

Types of skeletal muscle fibers

Different types of fibers are based on:

1. Maximal rate of contraction (fast or slow fibers)---myosin isoforms.
2. Major pathway for ATP synthesis (oxidative phosphorylation or glycolysis).
3. Others: capillary density, # of mitochondria, content of glycogen and myoglobin (O_2 storage).



Slow oxidative

- Fibers are adapted for slow contractions over long periods without fatigue, many mitochondria, many surrounding capillaries, and much myoglobin, fresh tissue are dark or red in color.

Fast glycolytic:

- Fibers are specialized for rapid, short term contraction, few mitochondria or capillaries and depending largely on anaerobic metabolism of glucose derived from stored glycogen. Rapid contractions lead to rapid fatigue (lactic acid from glycolysis). appear white.

Fast oxidative-glycolytic

- Fibers have physiological and histological features intermediate between those of the other two types.

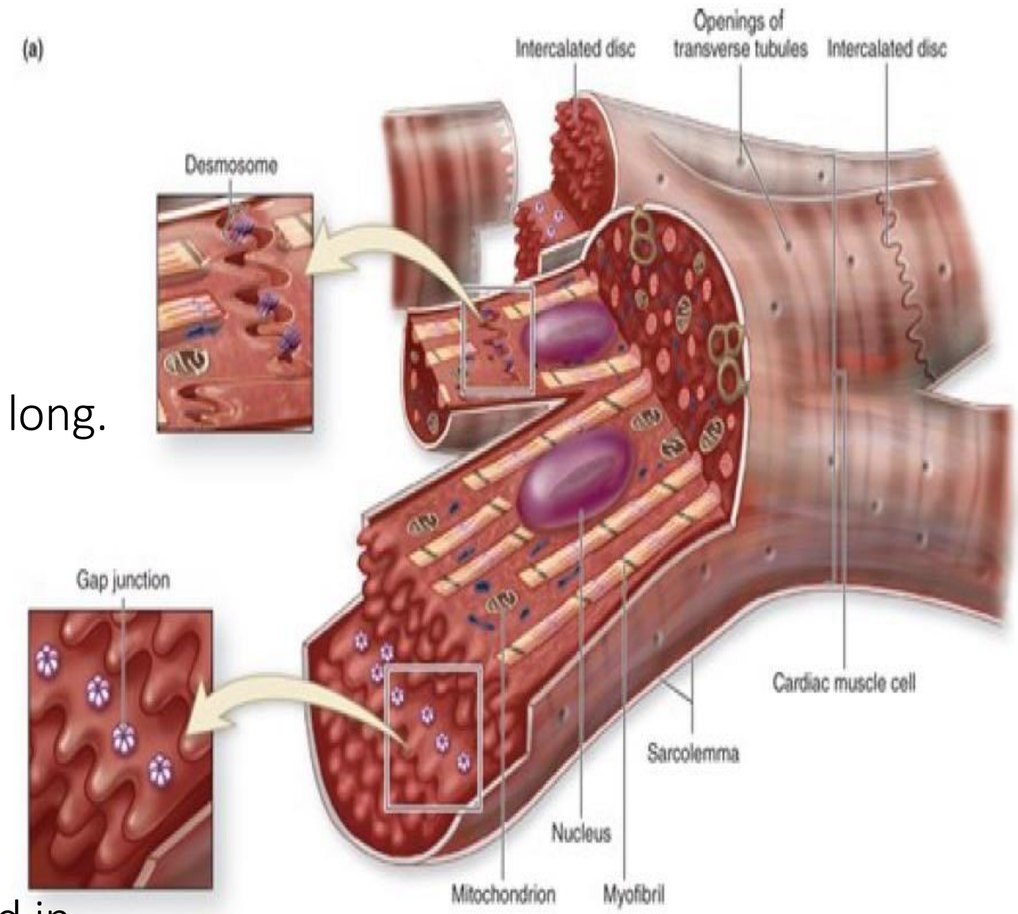
	Slow, Oxidative Fibers (Type I) Slow contraction	Fast, Oxidative-Glycolytic Fibers (Type IIa)	Fast, Glycolytic Fibers (Type IIb) Fast contraction
Mitochondria	Numerous	Numerous	Sparse
Capillaries	Numerous It needs high amount of oxygen	Numerous	Sparse
Fiber diameter	Small	Intermediate	Large
Size of motor unit	Small	Intermediate	Large
Myoglobin content	High (red fibers)	High (red fibers)	Low (white fibers)
Glycogen content	Low	Intermediate	High
Major source of ATP	Oxidative phosphorylation	Oxidative phosphorylation	Anaerobic glycolysis
Glycolytic enzyme activity	Low	Intermediate	High
Rate of fatigue	Slow	Intermediate	Fast Because of lactic acid
Myosin-ATPase activity	Low	High	High
Speed of contraction	Slow	Fast	Fast
Typical major locations	Postural muscles of back	Major muscles of legs	Extraocular muscles

Myoglobin: globular sarcoplasmic protein similar to hemoglobin which contains iron atoms and allows for O_2 storage

Cardiac Muscle

Unique characteristics : Branched cells , intercalated discs

- Cells align into chain-like arrays.
- Form complex junctions between interdigitating processes
- Cells within one fiber often branch..
- Mature cardiac muscle cells are 15-30 µm in diameter and 85-120 µm long.
- Striated
- One centrally nucleus located. **(Sometimes 2 but we'll stick with one)**
- Each muscle cells is a surrounded by endomysium with a rich capillary network.
- A thicker perimysium separates bundles and layers of muscle fibers and in specific areas (larger masses of fibrous connective tissue: cardiac skeleton) **(this is extremely important for the insulation of atria from the ventricles)**



- Gap junction are important

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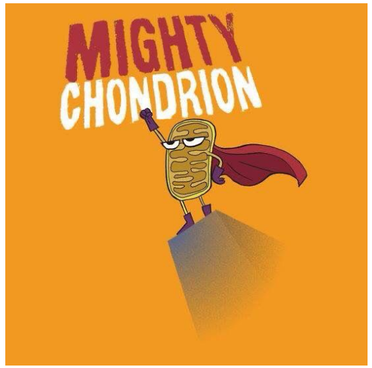
Cardiac Muscle

- Also we have some myoglobin in Cardiac muscles.
- Myofibril in cardiac muscles are way less than the skeletal muscles cuz I don't want to move a whole joint. I just need to shorten the muscle to push the blood out.
- How these muscle cells do not separate from each others ? Because of the intercalated discs (inside them we have junctional complexes)
- There is a delay allows the atria to complete their contraction.
- Contraction : down –> up

- **Mitochondria occupy up to 40%** cuz these cells got to do a lot of work, heart needs more energy to keep pumping.

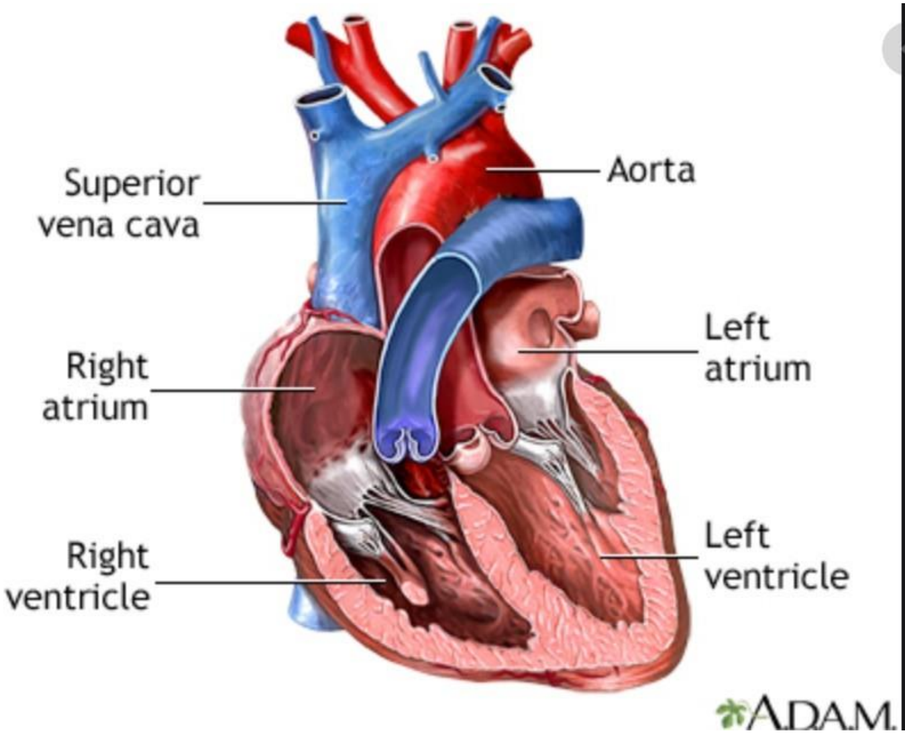


Cardiac Muscle

* If I need to control the heart rate, I should control the SA node

- Muscle of the heart ventricles is much thicker
- T-tubules in ventricular muscle fibers are well-developed.
- Sarcoplasmic reticulum is less well-organized.
- The junctions between its terminal cisterns and t-tubules involve only one structure of each type (**dyads**) (the same mechanism as triads but less developed resulting in its association with the T-tubule forming a single cisterna rather than encompassing it from all directions.)

*They are called dyads because they are two structures (1 T-tubule & 1 cisterna, and triads because they are 3 structures.)



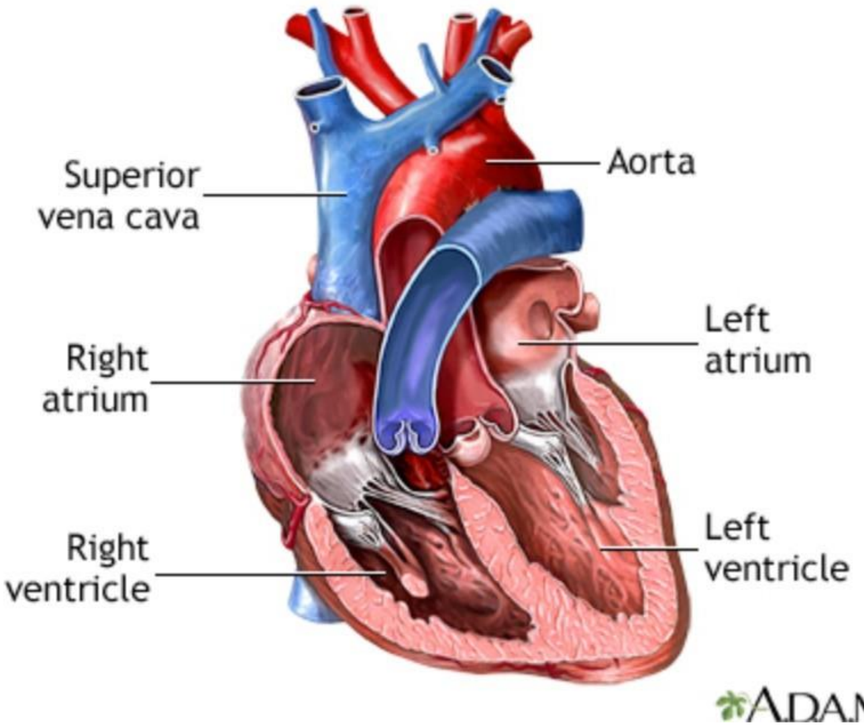
Cardiac Muscle

- Cardiac muscle fiber contraction is intrinsic and spontaneous

  *We don't need that huge force of contraction instead we need steady continuous ones.

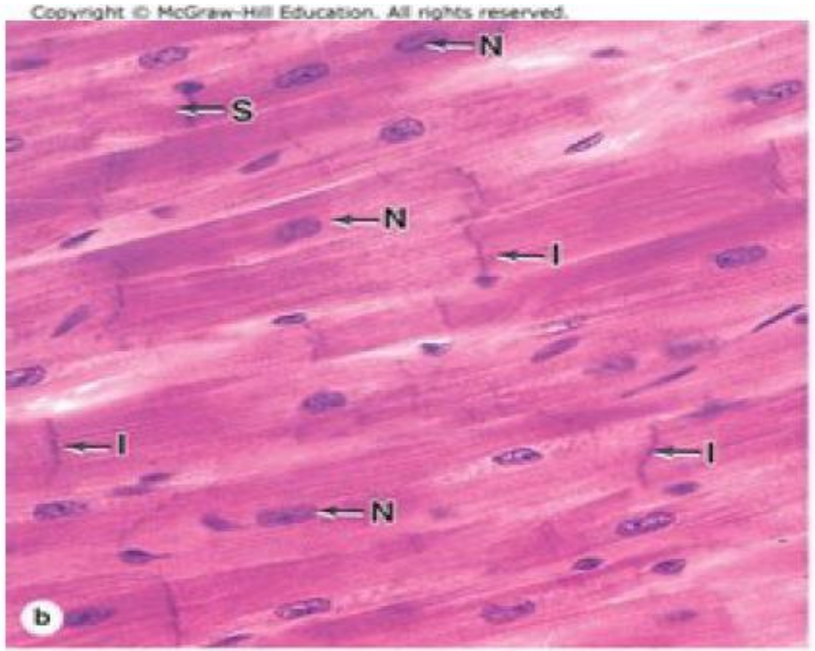
  *The idea in skeletal muscles -where we need stretch as long as we need- that I need it to contract now so we need a faster action potential (the pressure of the Calcium ions to be faster) and this is not what we need in the heart, we actually need continuity.

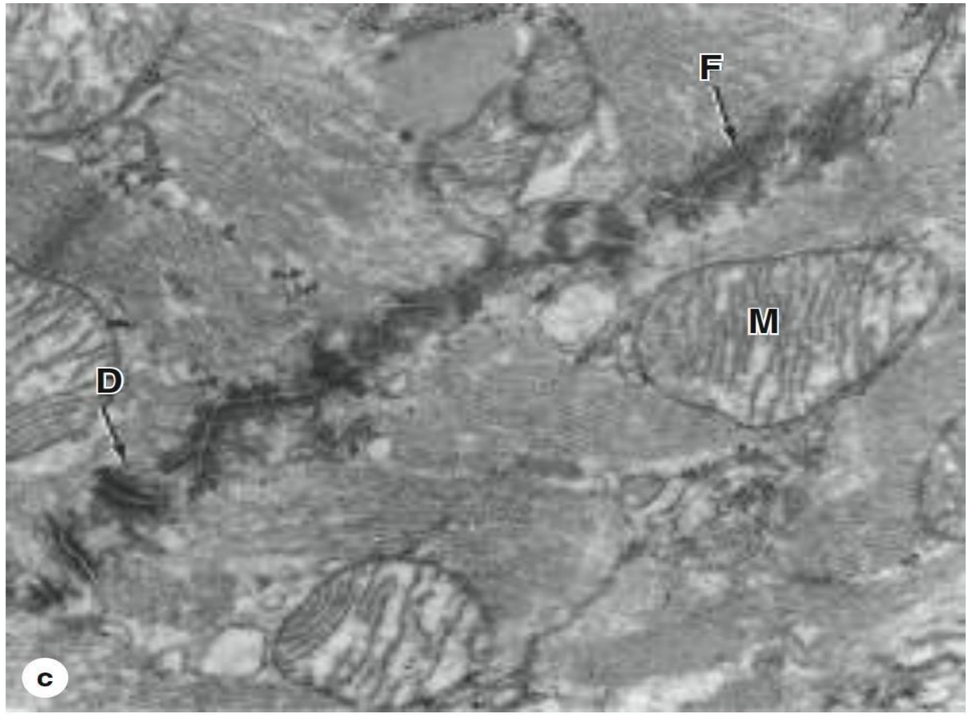
- Contraction initiated by nodes of unique myocardial fibers
- Contraction of individual myocardial fibers is all-or-none
- Rate of contraction is modified by autonomic innervation



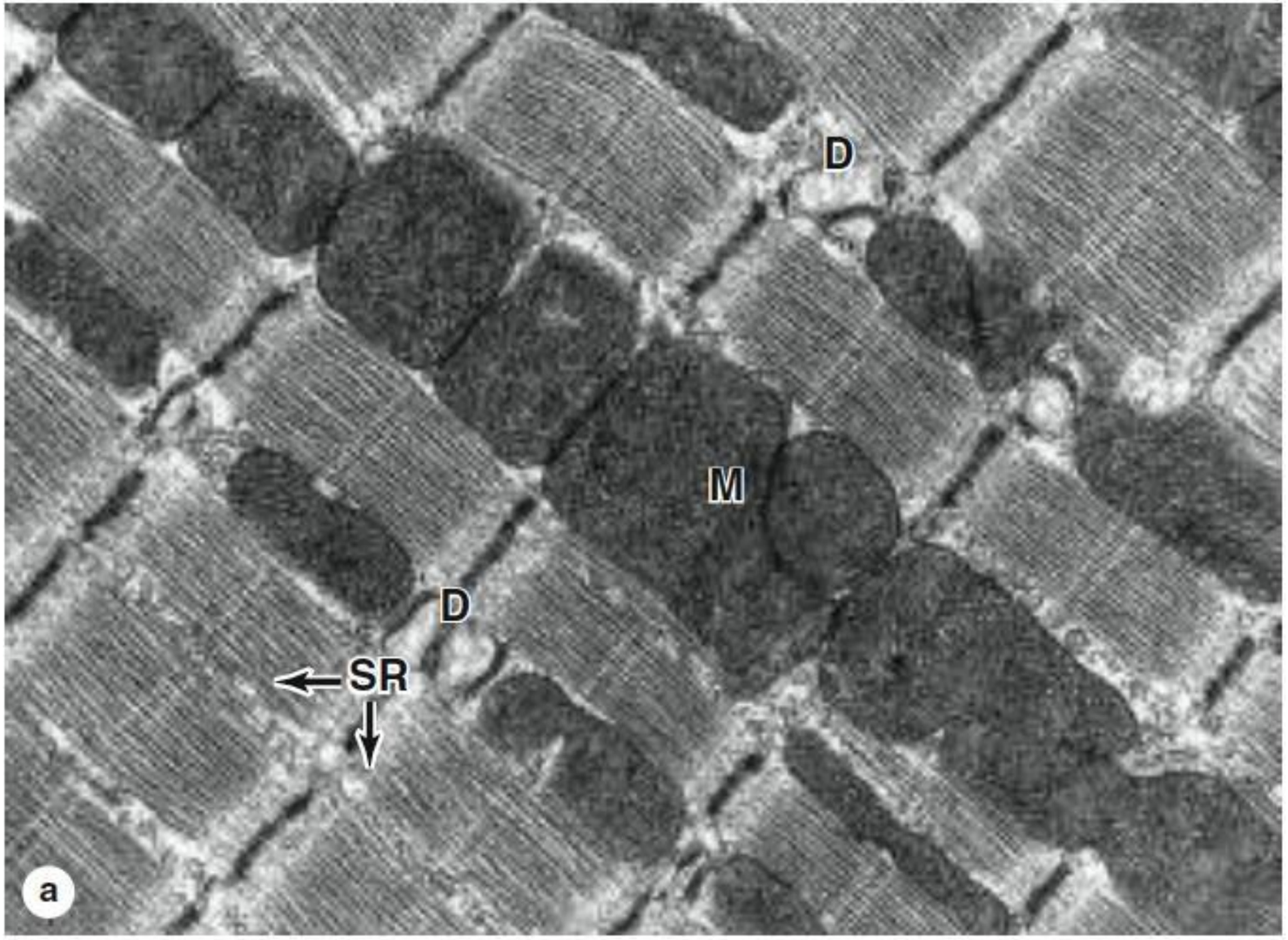
Cardiac muscle

- The fibers consist of separate cells joined at interdigitating regions called the intercalated discs.
- Intercalated discs: transverse lines that cross the fibers at irregular intervals where the myocardial cells join (junctional complexes).
- Transverse regions: many desmosomes and fascia adherens junctions--- strong intercellular adhesion.
- Longitudinally: run parallel to the myofibrils and are filled with gap junctions (ionic continuity between the cells).
- Central nuclei and myofibrils which are usually sparser and less well-organized





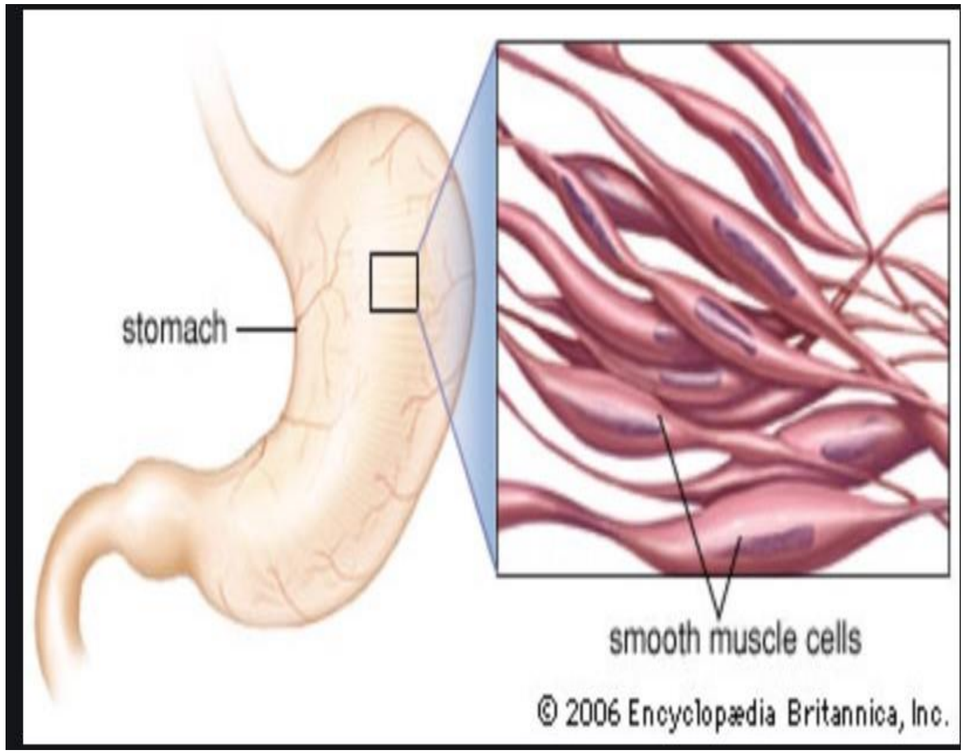
Where was this take from?



"NOT discused in the lecture"

Smooth Muscle

- Slow and steady contraction.
- Under the control of autonomic nerves and various hormones.
- Present in blood vessels, digestive, respiratory, urinary, and reproductive tracts.
- Fibers of smooth muscle are elongated, tapering, and unstriated cells.
- Enclosed by an endomysium (a network of type I and type III).
- Length is 20 µm - 500 µm.

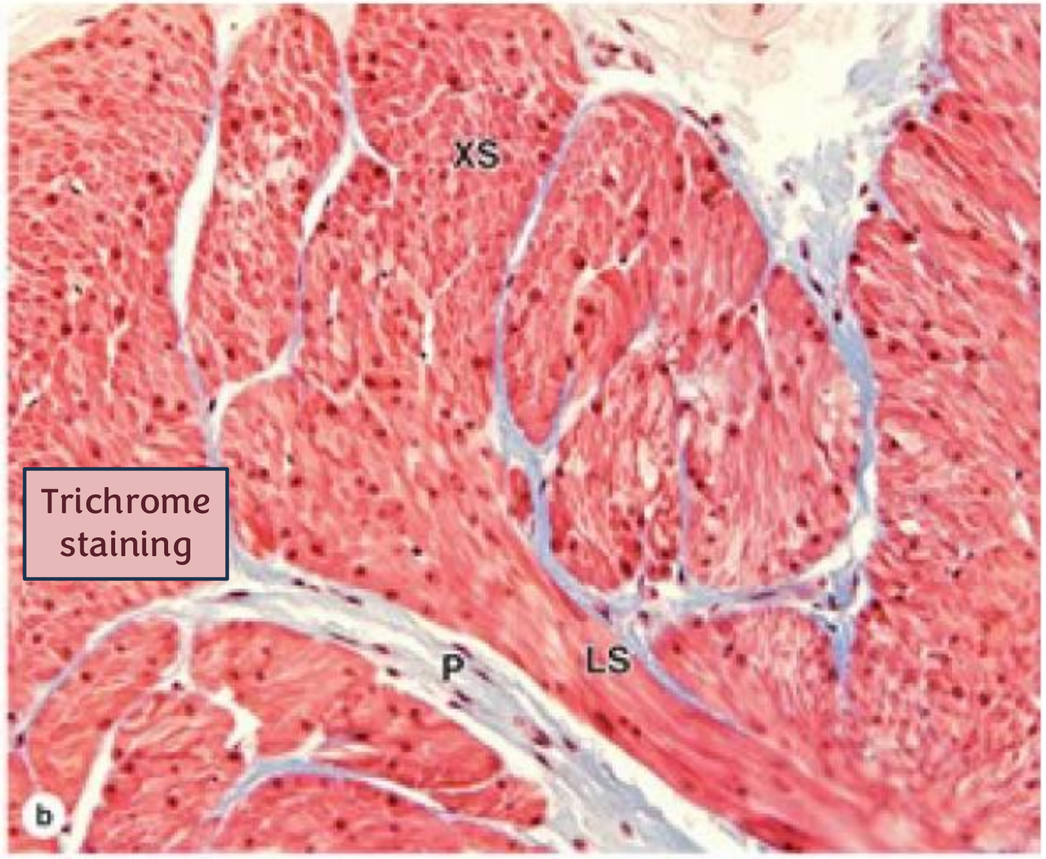


Smooth muscles are present everywhere even in your skin, for example, when you're cold, the hair on your body stand on end in what we call piloerection.

This is due to the attachment of the hair shaft to a smooth muscle that is called arrector pili, when this muscle contracts it pulls the skin downward so the hair erect (stand).

Smooth Muscles

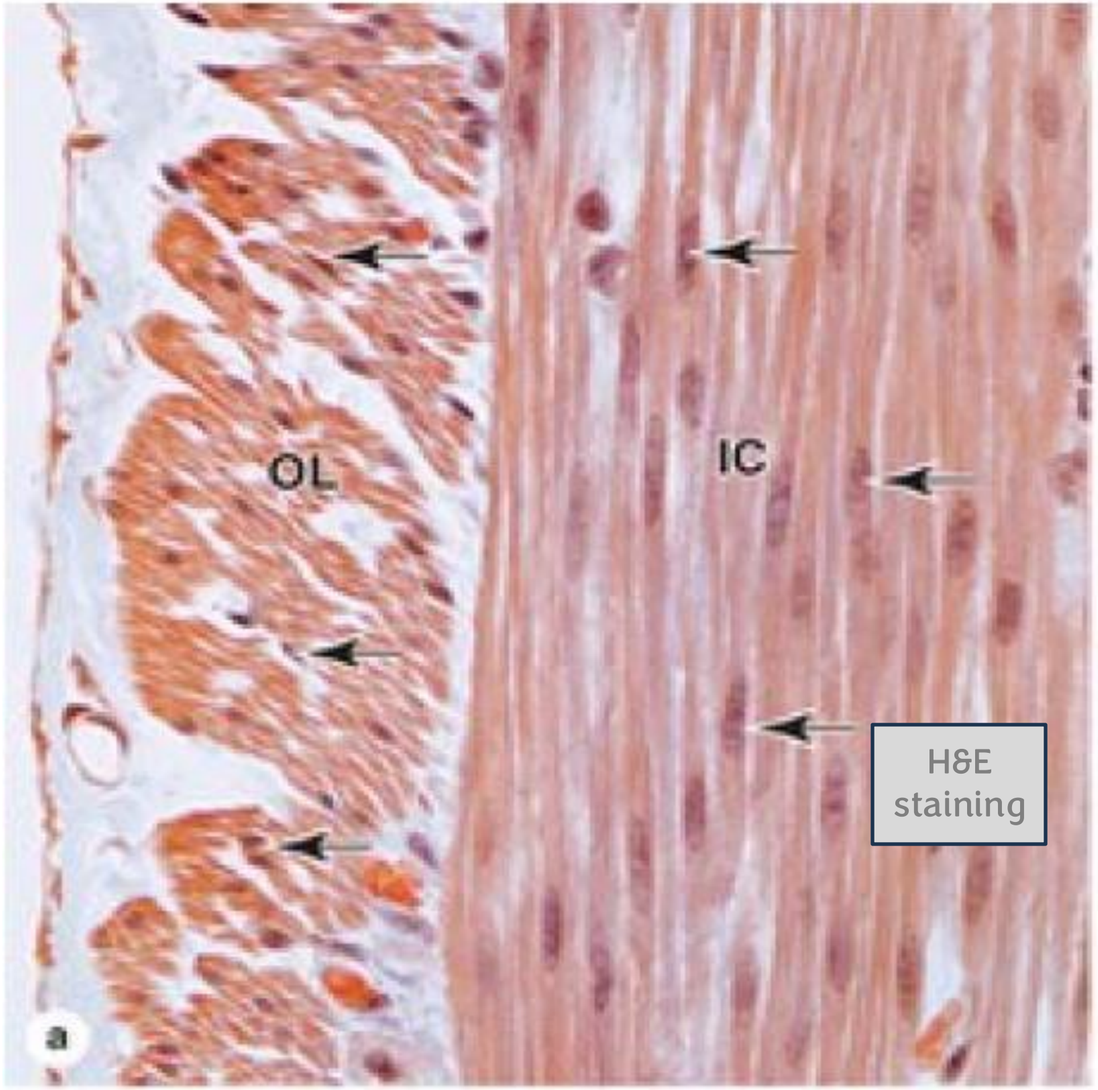
Relaxed smooth muscle



Trichrome staining

- The red colored part is the muscle
- The blue part is connective tissue with fibroblasts in between
- Spindle-shaped nuclei in response to spindle-shaped muscles

Contracted smooth muscle



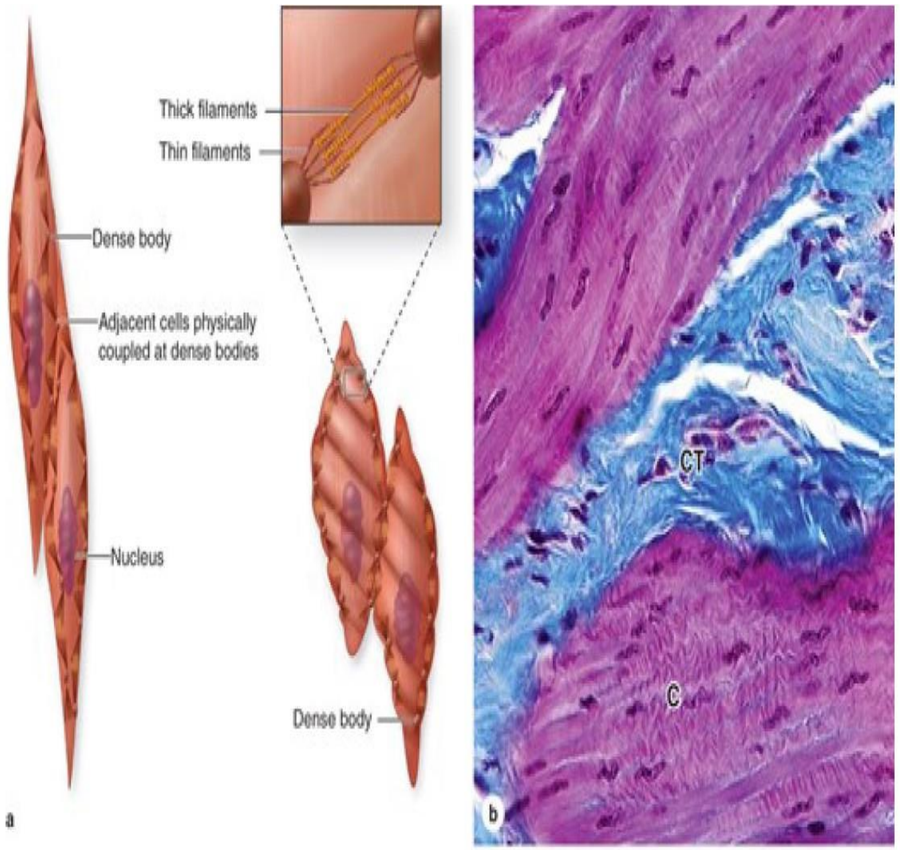
H&E staining

Characteristics and Contraction

- Dense bodies (similar to Z discs) is located in the cytoplasm and at the cell membrane (They are globular proteins that are scattered throughout the entire length of the muscle's membrane, dense bodies in smooth muscles are instead of z discs.)--> LACKING Z DISCS = NO STRIATION
- Both thin filaments and intermediate (for adhesive junctions between cells).

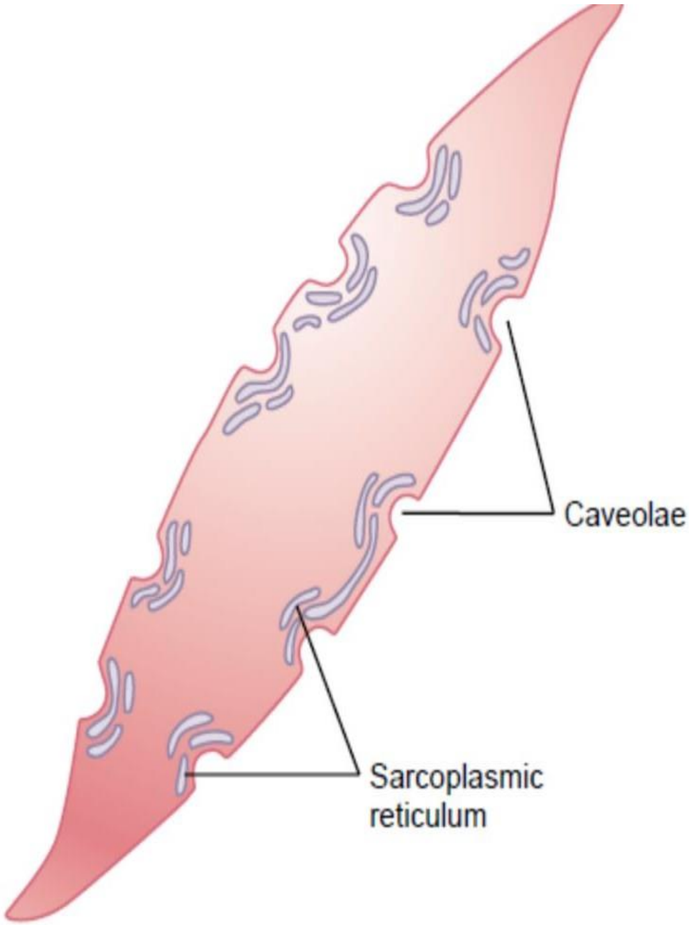
*Thin filaments are attached to the dense bodies, and thick filaments are in between (this arrangement is the most unique feature in smooth muscles)

- myosin filaments have a less regular arrangement and fewer crossbridges.
- Bundles of thin and thick myofilaments crisscross the sarcoplasm obliquely.
- Mitochondria, glycogen granules, and Golgi complexes located centrally



Characteristics and Contraction

- Rudimentary sarcoplasmic reticulum **and lack of T-tubules, so we describe smooth muscles as rudimental** (incompletely developped)
- Rich in gap junction.
- Caveolae are small plasmalemma invaginations which contain signaling components (ion channels). **Caveolae increase and accelerate the spread of the action potential (as the role of T-tubules in the cardiac & skeletal).**
- NO troponin **(TnC)** and tropomyosin instead there are calmodulin **(which binds to the calcium)** and Ca^{2+} -sensitive myosin light-chain kinase (MLCK)

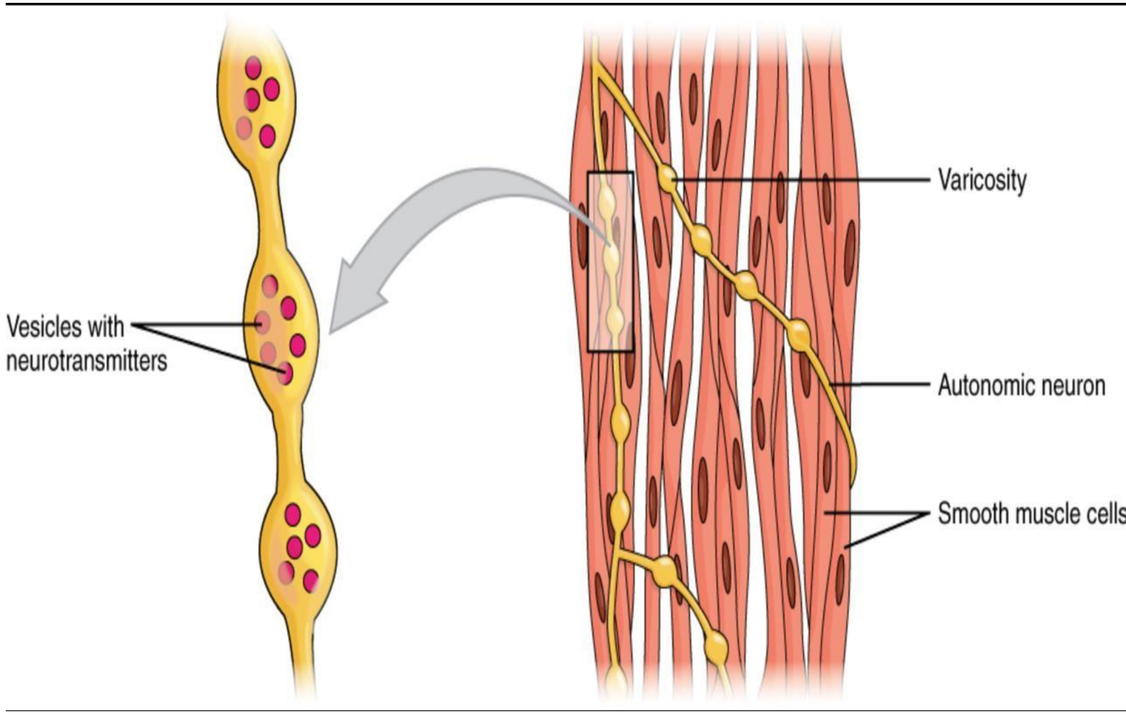


Characteristics and Contraction

- Smooth muscles fibers (or it's more accurate to say muscle cells) are fusiform in shape with a center-located nucleus and the cytoplasmic components are just like any other muscular cell.
- Contraction of smooth muscles is described slow and steady.
- It's somehow similar to the contraction of the heart.
- While contraction, the dese bodies will be closer to each other, the thin filaments will slide over the thick and undergo the same mechanism as other muscles (we need calcium, ATP, and all other things mentioned earlier in skeletal & cardiac.)
- While contraction, there is shortening but actually, shortening from one side a bit stretches in the other because it's a collective change in shape (it's not linear orientation as in skeletal muscles).

Smooth Muscle

- Lack well-defined neuromuscular junctions
- Axons of autonomic nerves have periodic swellings close to muscle fibers----synaptic vesicles----- acetylcholine or norepinephrine ---binds receptors in many muscle cells.
- Stimulation is propagated via gap junctions---- contract synchronously



Innervation of smooth muscles

- The nerve synapses with the smooth muscle but there is no motor end plate as in the skeletal.

- **HOW??**

In the end of the axon its terminals will sprinkle the neurotransmitter on the surface of the smooth muscles and the transmitter will bind to receptors and they will contract.

- When the neurotransmitter is sprinkled it doesn't reach all the muscle cells, so it's spread to the rest by gap junctions (smooth muscles are rich in gap junctions as heart muscles.)

- Since we are talking about smooth muscles, then the neurotransmitter is epinepherine.

Innervation

Cardiac:

In the heart there is no motor end plate, instead there is specialized cells that initiate the depolarization, which then spreads throughout via gap junctions.

Skeletal:

Every skeletal muscle fiber must have its own motor end plate (each one must recept a neurotransmitter then it contracts)

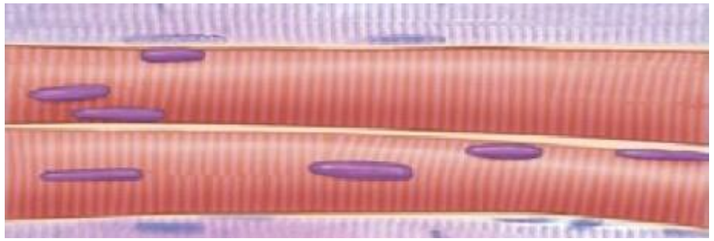
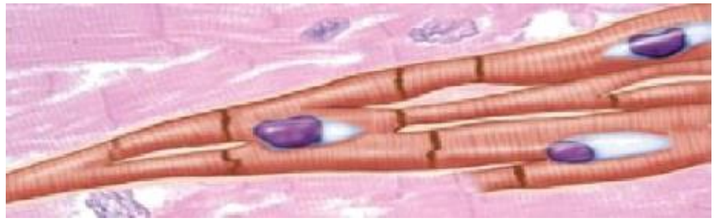
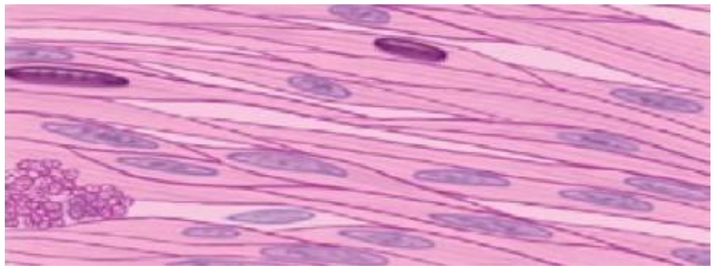
Smooth:

Some parts are similar to skeletal; they recept the neurotransmitter directly.
Others are like the mechanism in the cardiac; spreading of the transmitter via gap junctions.

contraction

- Cardiac & skeletal: all or none
  - Smooth muscles: graded contraction

For example:
In the GI tract the movement is steady and slow and continuous (one cell contracts then relaxes then the other contracts when the transmitter is transported to it via gap junctions, and so on until it spreads throughout the entire length of the GI tract.
The peristaltic movement starts from the second third of the esophagus (not from the first one because it's skeletal (the 1st third is purely skeletal/ the 2nd one is mixed skeletal & smooth/ the last one is purely smooth and after it we no longer see skeletal muscles except when we need control again in the external anal sphincter)

	Skeletal Muscle	Card 1ac Mu acte	Smooth Muscte
			
Fibers	Singlemultinucleated cells	Aligned cells in b*raxchin*g a*rran*gement	Single small, closely packed fusiform cells
Cen/fiber shape and size	Cylindrical, 10-100 µm diameter, many cm long	Cylincl*rica*l, 1o-zo \Jm clia re eve*r,* so-zoo yrno la n g	Fusiform, diameter 0.2-10 µm, length 50-200 µm
Strl at lo n s	Present	Present	Absent
Lac at i o n of	Periphe*ral* adjacent to sarcolemma	Centra l	Centra l, at wicJest pa rt of cell
T tubules	Center of trials at A-l jLenutions	In dyads at Z discs	Absent; caveslae may be fun ctionally sirriilar
reticulum (SR)	Well-cJeveloDecl, with two triads with T tobuie	, o cistern per sarcomere in dyad with T tubule	Irregular smooth ER without distinctive io
Special structural features	Very well-or ganized sarcomeres, SR, and transverse tu bule system	Intercalated discs joining cell, with many adherent and gap junctions	Gap jun ctions, caveola e, dense bodies
Co nt ro l eel contraction	Troponin. C Dinds Ca:z+, moving tropom yosin and exposing actin for myosin binding	Simi far to that.of skeleta l muscle	Actin-myosin Dinding occurs with myosin phosphorylation by MLCKtrig e*red*when calmodulin binds Ca2 ›

Connective tissue organization	Endomysium, perimysium, and epimysium	Endomysium; subendocardial and subpericardial CT layers	Endomysium and less-organized CT sheaths
Major locations	Skeletal muscles, tongue, diaphragm, eyes, and upper esophagus	Heart	Blood vessels, digestive and respiratory tracts, uterus, bladder, and other organs
Key function	Voluntary movements	Automatic (involuntary) pumping of blood	Involuntary movements
Efferent innervation	Motor	Autonomic	Autonomic
Contractions	All-or-none, triggered at motor end plates	All-or-none, intrinsic (beginning at nodes of conducting fibers)	Partial, slow, often spontaneous, wavelike and rhythmic
Cell response to increased load	Hypertrophy (increase in fiber size)	Hypertrophy	Hypertrophy and hyperplasia (increase in cell/fiber number)
Capacity for regeneration	Limited, involving satellite cells mainly	Very poor	Good, involving mitotic activity of muscle cells

Regeneration Of Muscle Tissue

Skeletal muscle,

- Although the multinucleated cells cannot undergo mitosis
- Mesenchymal satellite cells lying inside the external lamina can participate in limited regeneration.

Cardiac muscle **(the worst in regeneration)**

- lacks satellite cells **and there is a very small number of stem cells (so they are the worst in regeneration)**
- Very little regenerative capacity beyond early childhood.
- Defects or damage replaced by proliferating fibroblasts and CT formation leading to myocardial scars.

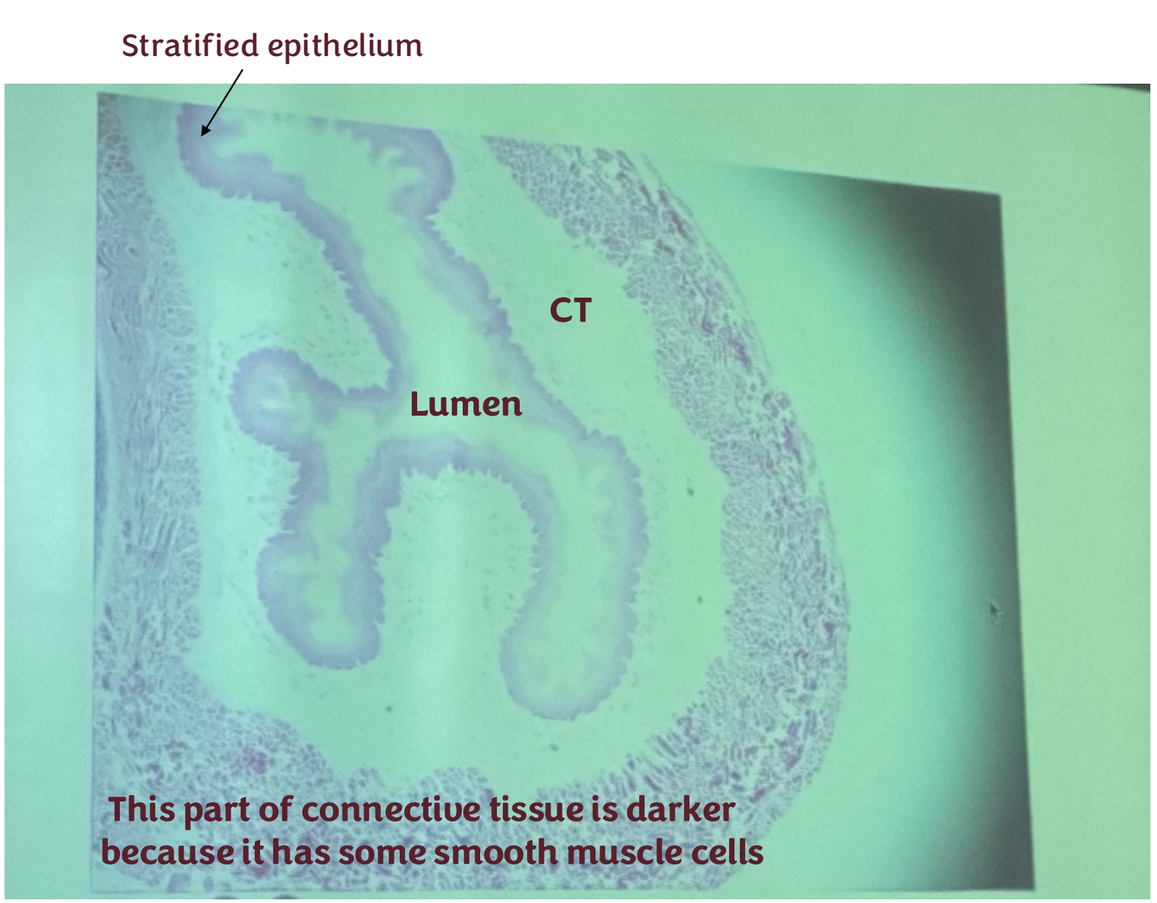
Smooth muscle **(the best in regeneration)**

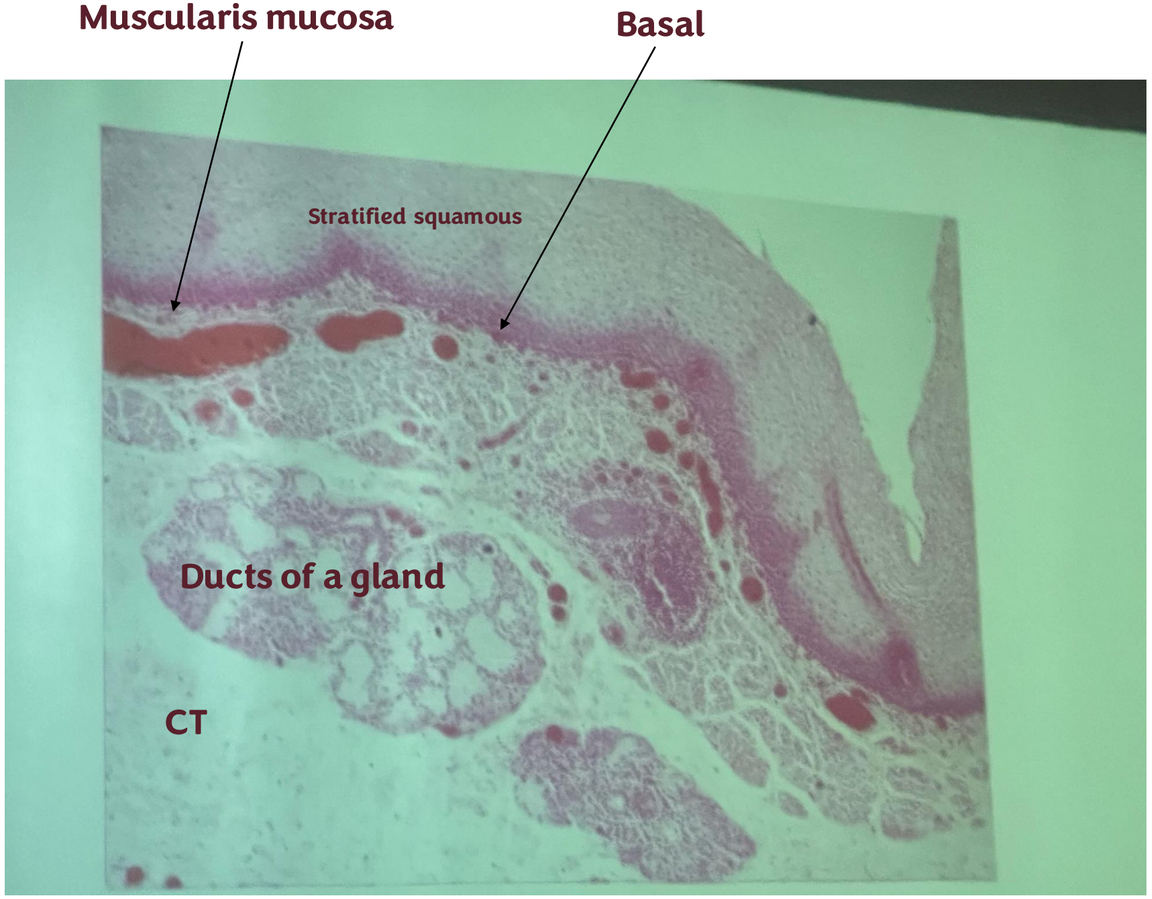
- **I**s capable of a more active regenerative response.
- Can undergo mitosis and replace the damaged tissue.
- it regenerates as if nothing has happened even if ¾ of it was damaged.

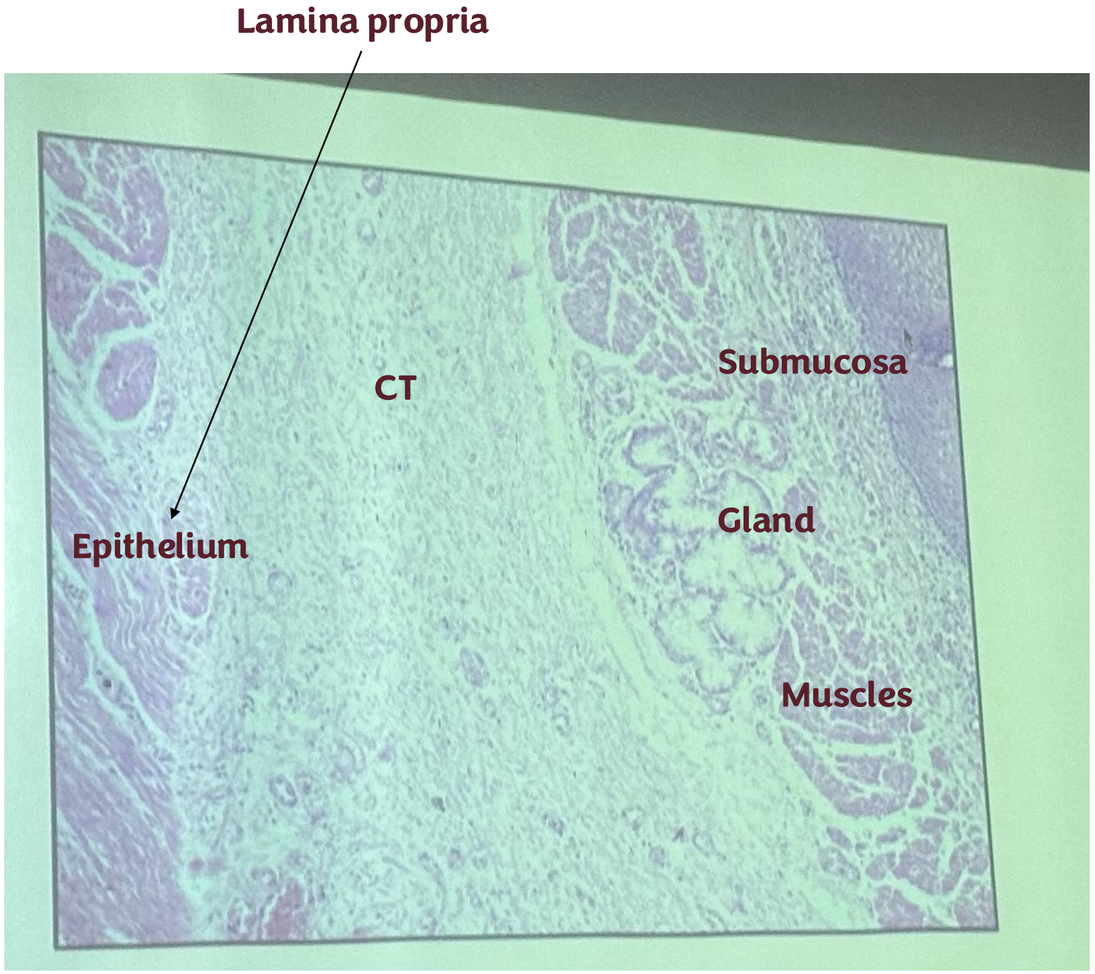
If there is a massive damage in the tissue, no way that the cells will compensate the muscle tissue, but if it's minor they might do).

›› MEDICAL APPLICATION

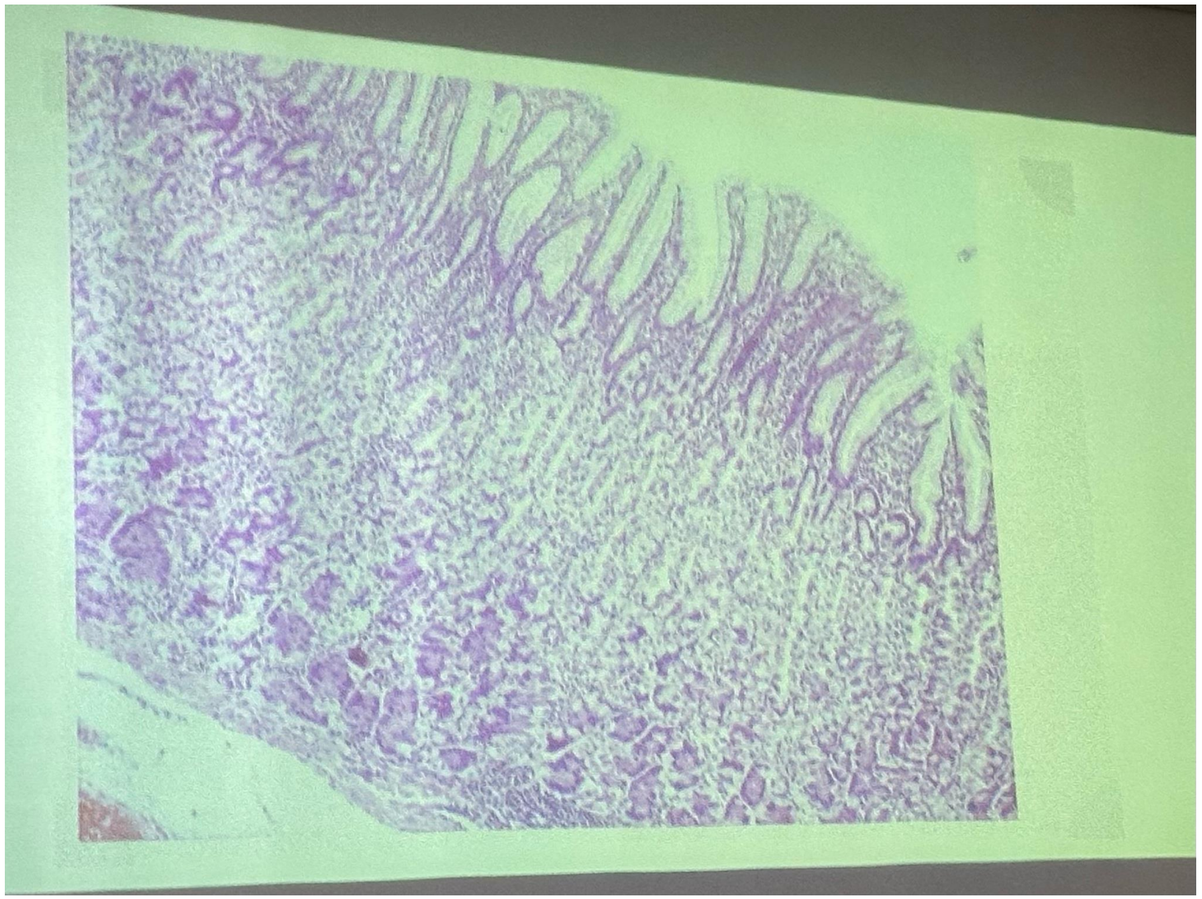
The most common injury sustained by cardiac muscle is that due to **ischemia**, or tissue damage due to lack of oxygen when coronary arteries are occluded by heart disease. Lacking muscle satellite cells, adult mammalian cardiac muscle has little potential to regenerate after injury. However, certain fish and amphibians, as well as newborn mice, do form new muscle when the heart is partially removed, despite the lack of satellite cells. Research on the possibility of mammalian **heart muscle regeneration** builds on work with the animal models, focusing primarily on the potential of mesenchymal stem cells to form new, site-specific muscle.


Stratified epithelium
CT
Lumen
This part of connective tissue is darker
because it has some smooth muscle cells

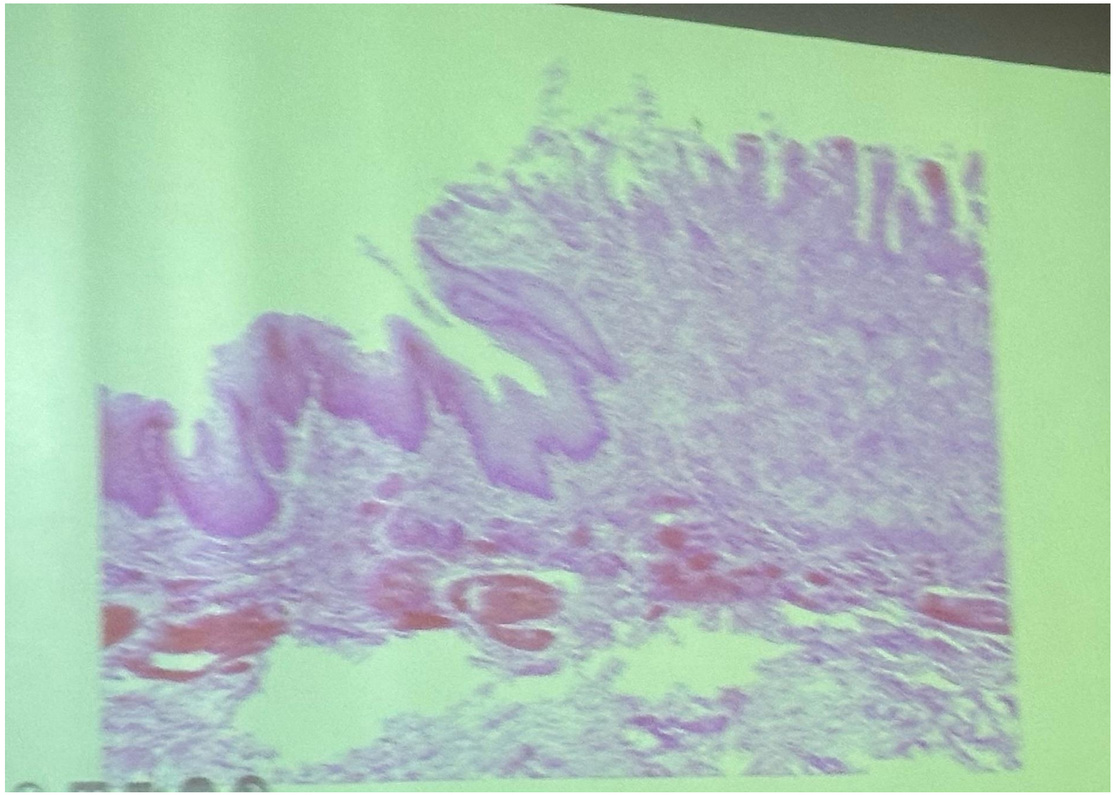

Muscularis mucosa
Basal
Stratified squamous
Ducts of a gland
CT



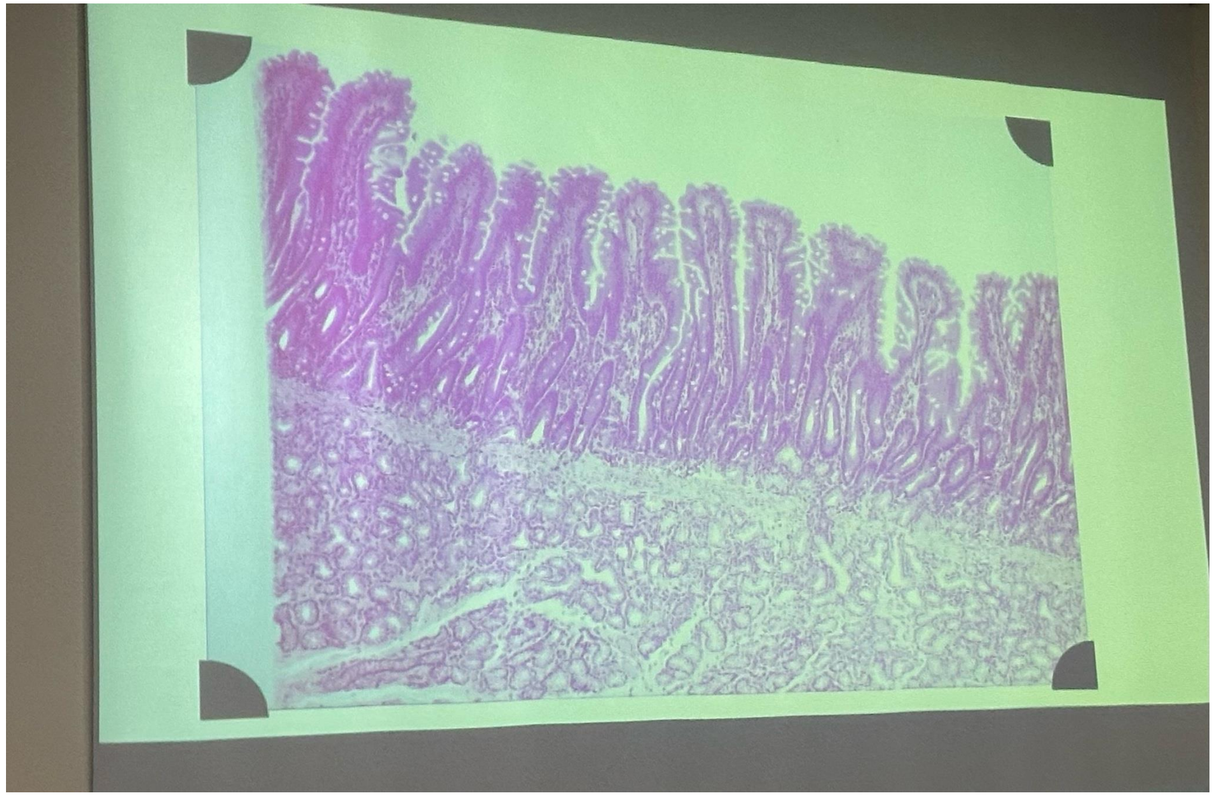
Taken from the stomach



Taken from the esophagus



From the stomach



رسالة من الفريق العلمي:

دخل صلى الله عليه وسلم على أم حرام بنت مِلحان وهي من محارمه، فأطعمته، ثم جلست تفلي رأسه، فنام رسول الله، ثم استيقظ وهو يضحك، فقالت: ما يضحكك يا رسول الله؟ قال: **(ناس من أمّتي، عُرضوا عليّ غُزاة في سبيل الله، يركبون ثبج -وسط- البحر، ملوكاً على الأسِرّة، أو مثل الملوكِ على الأسِرّة).**

اللهمّ ارزُقنا أن نكون جيشَ الفَتحِ المُنتظَر..

دفعتنا العزيزة، من منبرنا هذا نزفّ لكم خبر **انتهاءِ آخرِ (موديفايد) في هذا الفَصلِ**

فالحمد لله الذي قدّر لنا عيش لحظة كهذه، ضمّونا في دعواتكم ولكم بالمِثل

وعليكم السّلام والرحمة والبركة من الله، إلى لقاءٍ قريبٍ نبض

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1	16	Missing	Added
V1 → V2			