Subject | physiology

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There is a group of drugs increase the output force of the heart (the contractility of the cardiac muscles) by inhibiting sodium-potassium ATPase pump, they are used to treat atrial fibrillation and heart failure,

their mechanism of action is to inhibit Na+- K+ pump, causing Na+ to accumulate inside the cell. In order to get rid of excess sodium, Na+-Ca+2 exchangers will work in the opposite direction pumping Ca+2 in and Na+ out, this will accumulate Ca+2 intracellularly and cause cardiac

contraction.

***The figure below is to show you the effects of slow Ca+2 channel blockers:**

Here we have two doses of the drug Diltiazem which works as a Ca+2

channel blocker, it affects the action potential and the force of contraction in cardiac muscles.

The drug will block the slow voltage-gated Ca+2 channels, which are

important in the maintenance of the plateau.

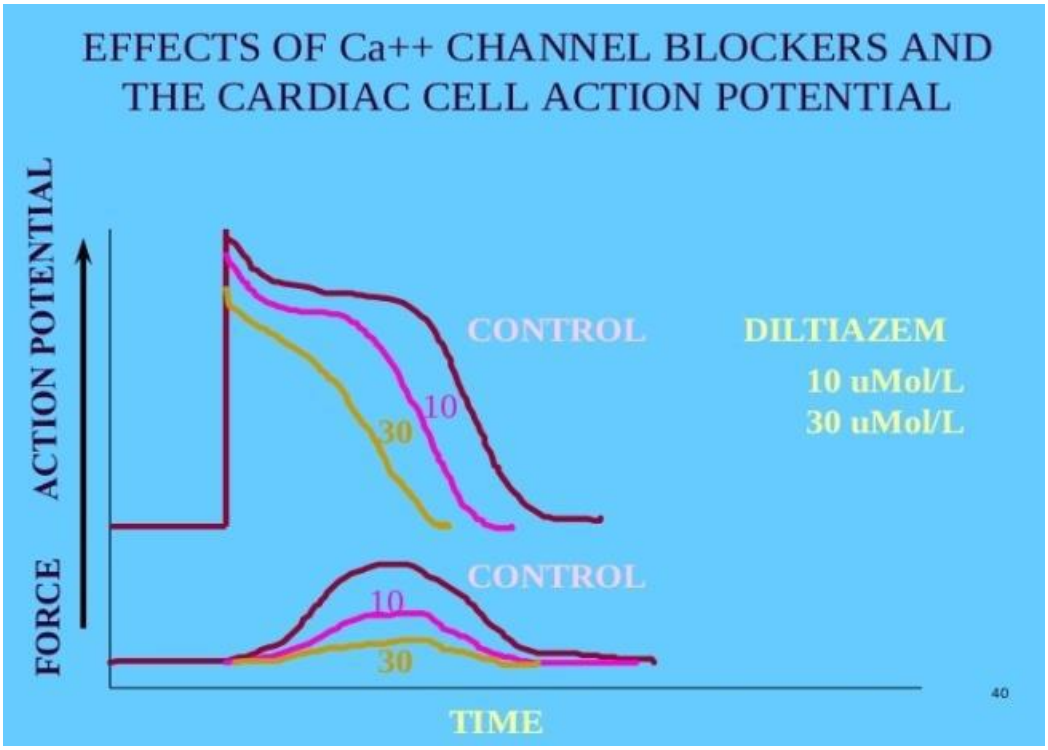
When these channels are blocked, nothing will stop the K+ influx from causing the repolarization phase (phase 3), so this will result in shortening the duration of action potential.

Theoretically, using high doses of this drug will convert the action potential of the cardiac muscle into something like the action potential

of skeletal muscle due to the complete block of Ca+2 channels and the

complete absence of the plateau.

Increase the dose will shorten the plateau and decrease the force of contraction.



*Cardiac Muscle action potential Vs. Skeletal Muscle:

Note:

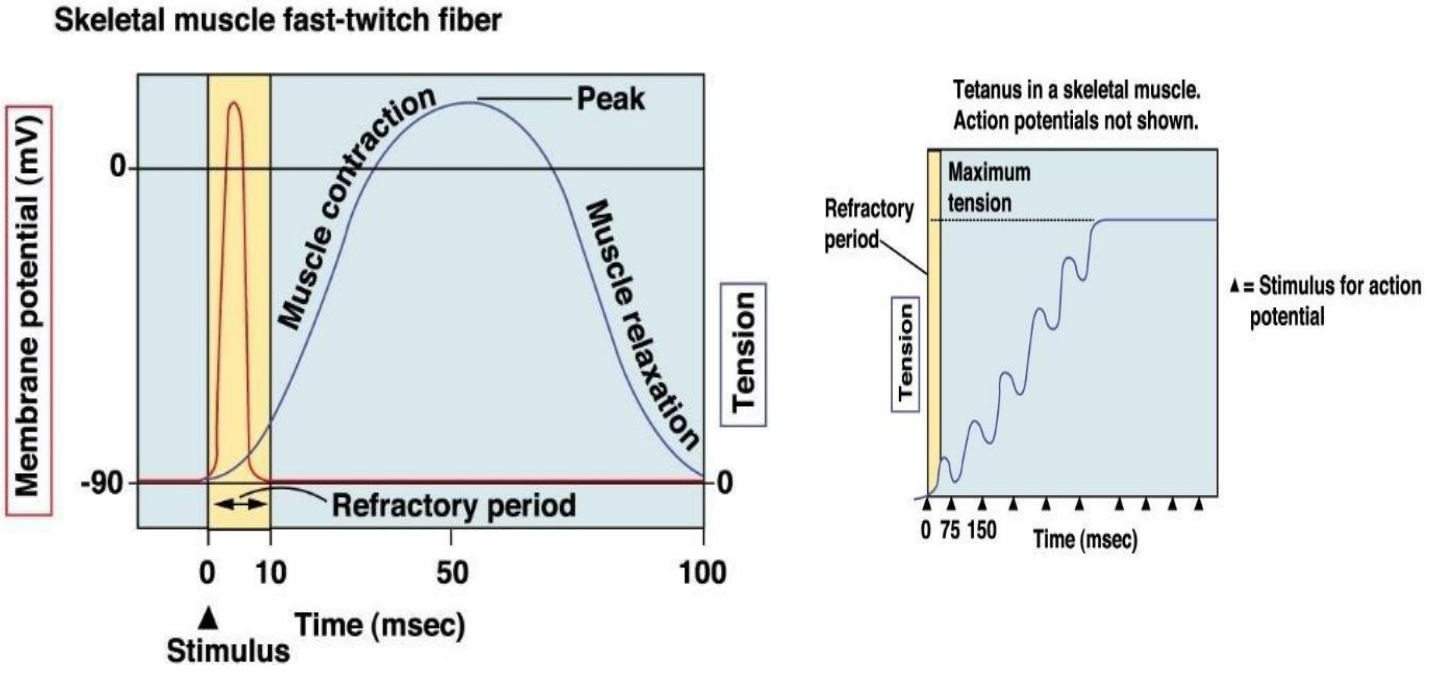
In skeletal muscle -→ action potential is short

in skeletal muscle –>no calcium channel

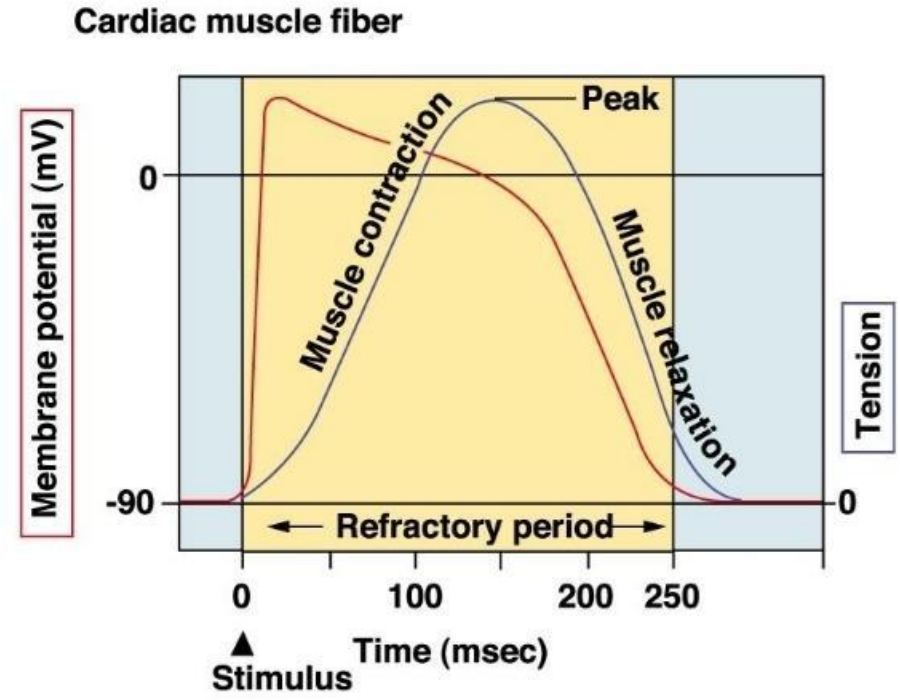
Phase number	Name	Cardiac muscle & Skeletal muscle	Ions involved
0	depolarization	same	Na+ influx
1	Partial repolarization	For cardiac	K+ efflux CL- influx
2	plateau	For cardiac	Ca+2 influx
3	repolarization	same	K+ efflux
4	Resting phase	same	

***The action potential of the skeletal muscle occurs at the latent period before muscle contracts. So, if another action potential is induced before the absolute refractory period, the muscle will contract at a higher force.**

When another and another....) are induced, it will cause summation of the contractions without giving the muscle a chance to relax, finally leading to what is called Tetanus.



*While in the cardiac muscle, the plateau causes elongation in the absolute refractory period, so the muscle has enough time to relax, thus if we induce another action potential while it's still contracted, it won't respond as it's still in the absolute refractory period--→ So, tetanisation doesn't occur in the cardiac muscle.



Cardiac muscle contraction

Note: cardiac muscle contraction has the same pathway of skeletal musle contraction except cardiac muscle doesn't have neuromuscular junction

These two pictures show:

*Things written in blue weren't mentioned by the doc., just for your understanding.

- Sarcomere: the area between the two Z discs.

- Thin filaments: three contractile proteins; actin, tropomyosin, and troponin.

Actin is organized in a double helix structure and tropomyosin is wrapped around them covering the binding site of myosin head, when Ca+2 binds troponin it will cause conformational changes and move tropomyosin thus exposing myosin binding sites, myosin will bind, and the contraction will occur.

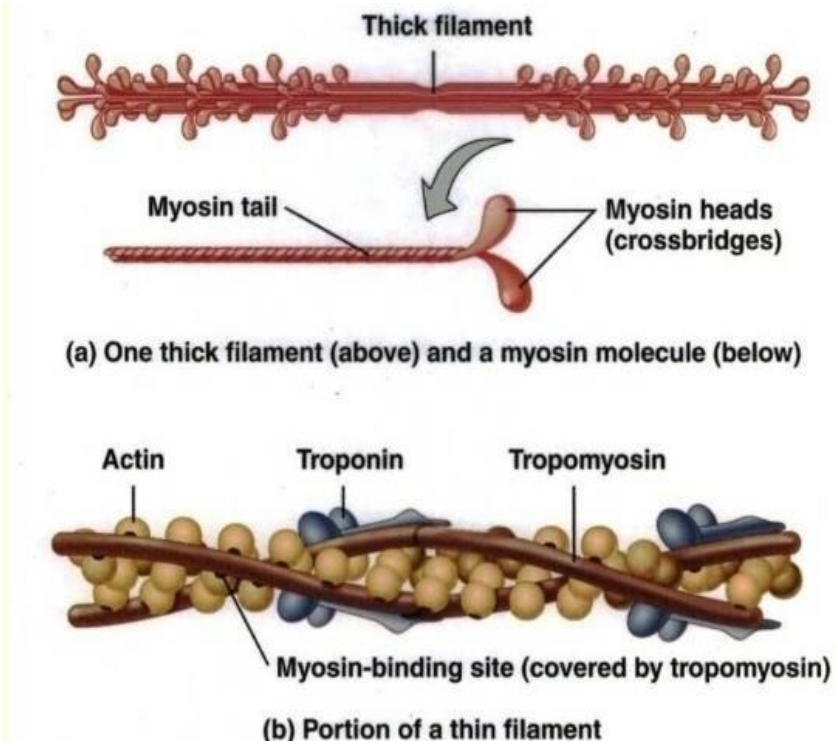
- Thick filaments: myosin with two heads and one tail.

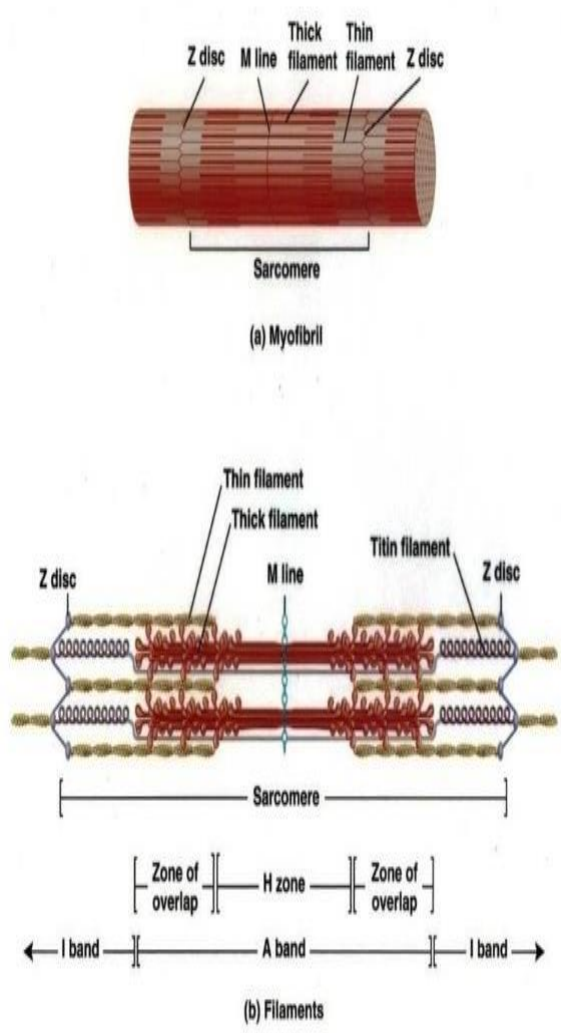
- A-band: composed of the overlapping area between thick and thin filaments.

- I-band: composed of thin filaments.

- Titin filaments: spring-like structures (Elastic elements), they're not contractile fibres and have an elastic recoil activity.

They're found highly in skeletal muscles; the fibres in cardiac muscles are interconnected thus there isn't much elastin.





The cardiac and skeletal muscles have the same components. The only difference is the elastic elements.

IMPORTANT NOTES:

- The sliding filaments in the two muscles are the same.

- As we said before, there is no tetanus in the cardiac muscle.

- Fatty acids are the main source of energy in cardiac muscle,(takes place in the mitochondria) unlike skeletal muscle which do Anaerobic and Aerobic respiration

- highly activation of the mucsle during exercise---high production of lactic acid----leading to muscle crumps).

Attachment and detachment cycle and ATP dependence is the same.

- ADP must be bound to myosin head in order to be able to bind actin and form cross bridging.

No ADP---→ No binding

- Also, Ca++ must be found in the active site of actin in order to be able to bind myosin.

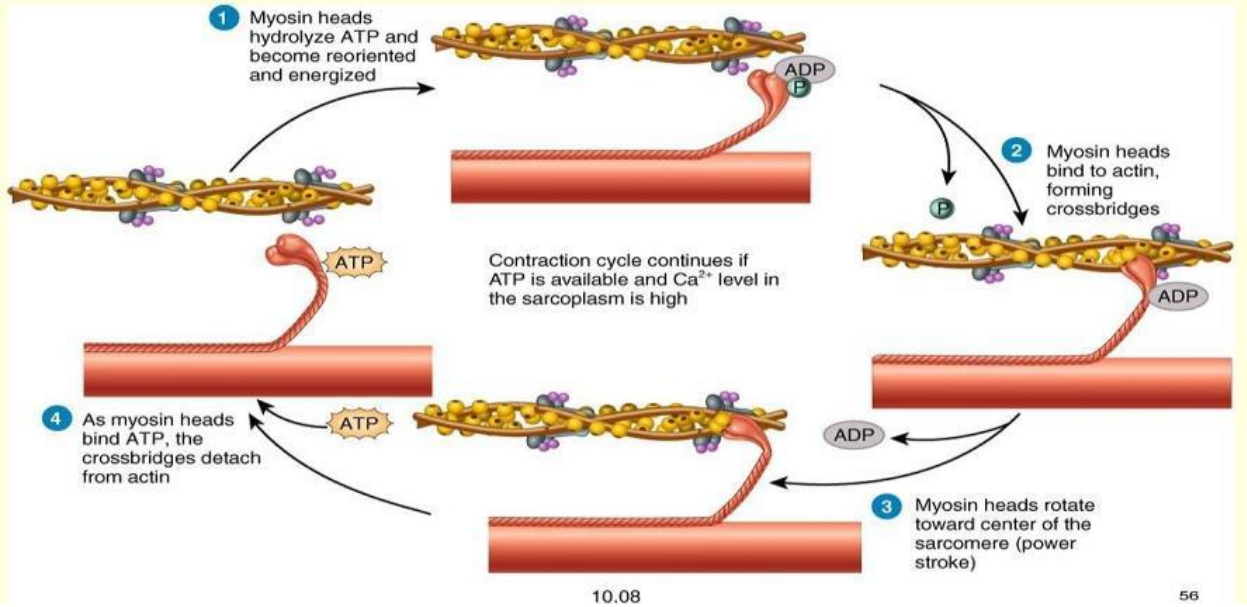
- Once myosin binds to actin, they will form actomyosin, which releases ADP+ P. At the same time, myosin heads will slide over actin filaments towards the center of the sarcomere (toward the inside) and shortening it. This is called the power stroke.

- Myosin heads will remain attached to actin until another ATP molecule binds to myosin and detach it from actin.

- Myosin hydrolyses this ATP into ADP + Pi, to be in its energized state and able to bind actin to start the cycle again.

- Both, attachment and relaxation need ATP (this ATP molecule is the same that used in the attachment and relaxation)

See the picture in the next page



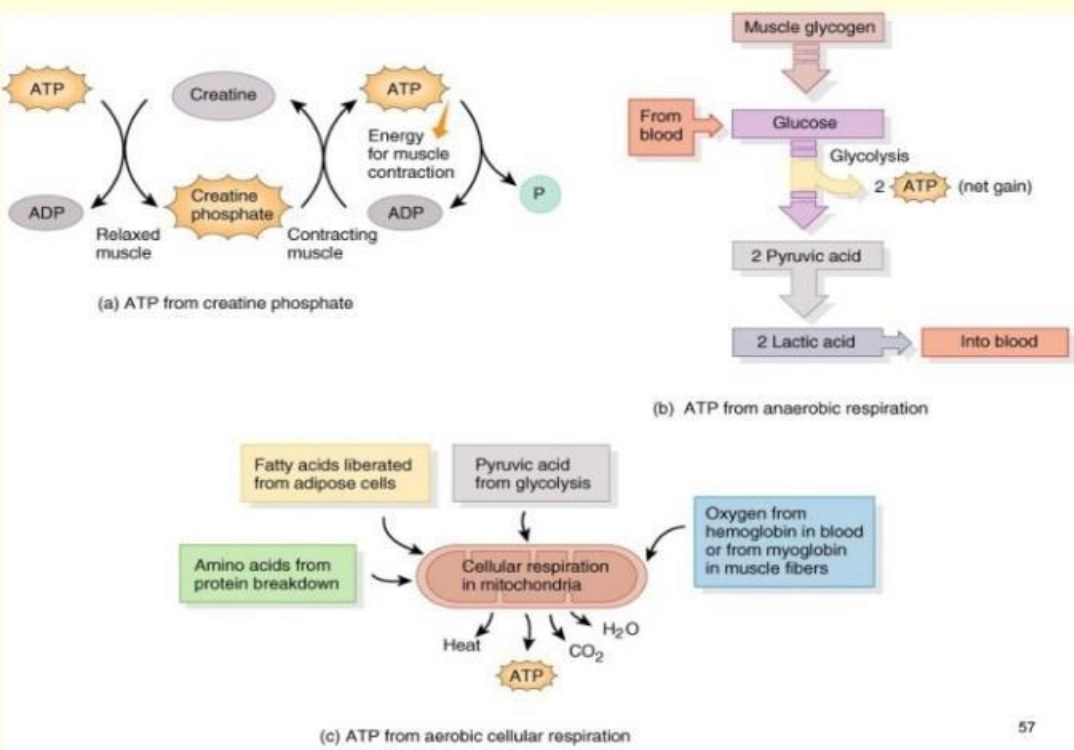
Remember: in skeletal muscles a medical condition called Rigor mortis, which is a sustained contraction of muscles after death, due to the absence of ATP which is needed for relaxation (detachment of myosin heads).

Energy sources:

1. The first immediate source of energy is ATP which comes from creatine phosphate **(used only with 10 seconds "100 meter")**, so when there is MI, there is a lack of ATP, so CPK (creatine phosphate kinase will be activated to transform creatine phosphate to creatine and produce ATP). So, CPK is the first enzyme we analyse when the patient have MI.
2. Anaerobic glycolysis which results in the formation of 2 ATP molecules. (in skeletal muscle)

3. Oxidative phosphorylation in the mitochondria, which results in the formation of sufficient amount of ATP, remember that there is a large number of mitochondria in the cardiac muscle cells.

So, as we said before fatty acids are the main source of energy in the heart.



**Length-Tension Relation for Skeletal Muscle:

- There is a law called (Frank-Starling law) which states:

-starling first scientist who discover hormones which release from endocrine glad

*When there is an increase in the resting tension (or the length of the muscle) within physiological range, it will cause an increase in the active tension (the force of contraction).

* Imagine you have a rubber band, on its own it will be in its optimal length, any increase in that length will cause a tension called the passive tension (tension due to its elastic properties), in case of heart this tension will be achieved by increasing the volume.

* Muscles can contract because they contain thin and thick filaments, not only elastic elements. Their contraction causes what we call active tension (tension due to the contractile fibres).

*Force of contraction keeps increasing as the length of the muscle (resting tension) keeps increasing within the physiological range, until it reaches its maximum force of contraction (the physiological limit), once we exceed the physiological limits, any increase in the resting tension will result in decrease in the force of contraction.

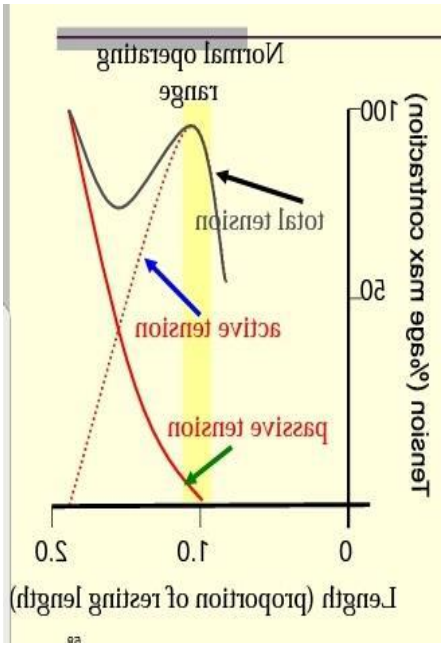
*See the figure which shows the relationship between the length of the skeletal muscle and the tension developed in it:

- X axis represents the length while the y axis represents the isometric tension.

- The passive tension develops when the muscle's length is at its optimal length and increases when the length increases.

- The active tension decreases, when increasing the length more than the muscle's optimal length.

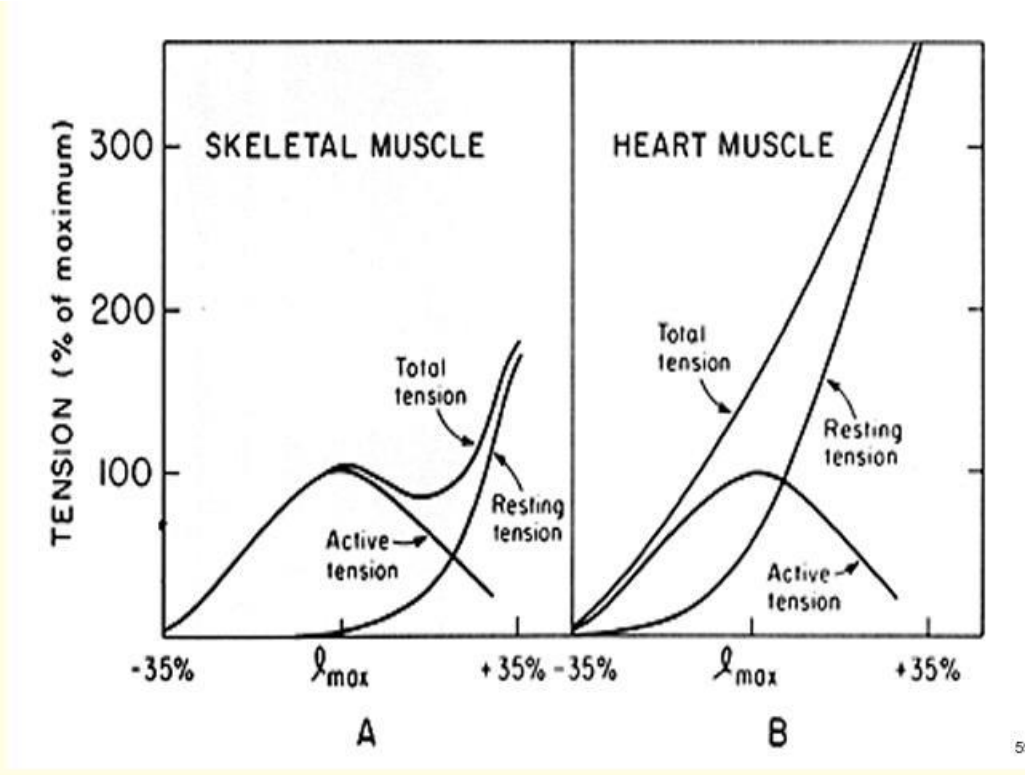
- There are two peaks for skeletal muscles, because they have elastic elements while in the cardiac muscle it has only one peak, as elastic elements will be relaxed after strong tension thus giving the second peak كلما تشدها بتصير ترخي اكثر .



The following figure is for cardiac muscles:

- The passive tension develops before the muscle reaches its optimal length (the muscle works at much less length than its optimal length) and increases when the length increases.

- The active tension decreases when increasing the length more than its optimal length.



When active tension reaches zero, the total tension will be equal to passive tension.

- We can calculate the total and passive tensions directly, but active tension is calculated by the equation:

**In case of the rubber band, in order to contract it needs to overcome the force which tense it outside then it will contract, so the active tension will equal the difference between the total tension and the passive tension

Active tension (AT)= Total tension (TT) – Passive tension (PT)

- Skeletal muscle usually works at its optimal length, so when we increase the length it won't increase the tension.

- While the passive tension of the cardiac muscle develops before the muscle reaches its optimal length (the muscle works at much less length than its optimal length) and increases when the length increases.

*Look at the picture below:

- When the muscle is contracted: actin filaments are bound to myosin from the other side creating a force in the opposite direction reducing the active tension. (1.8um)

- When the muscle is in the optimal length: There is maximum overlapping between thin and thick filaments, creating maximum active tension (2.2 um).

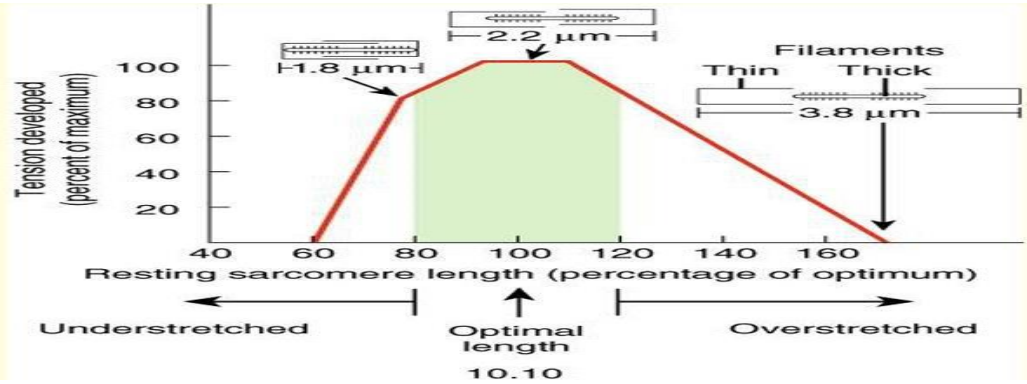
- When the muscle is overstretched: This will reduce the overlapping between thin and thick filaments thus reducing active tension.

Note :

cardiac muscle works below its optimal length but in the skeletal muscle works within the optimal length

Isometric contractions: the length stays the same but the tension increases.

Isotonic contractions: the tension stays the same but the length changes. (Shortening of the muscle)



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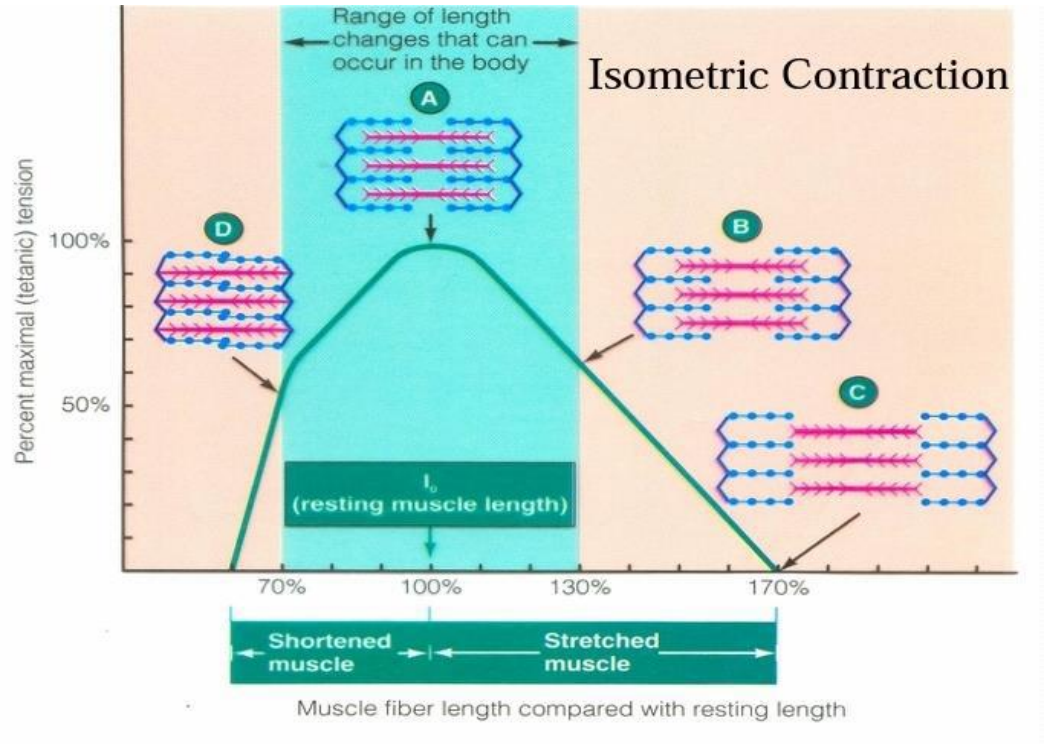

Conduction System of the Heart

- The heart can contract even without stimulation, so if you remove the heart from the body in heat transplant, the heart will keep pumping if we put it in a solution contains calcium.

- This means that the source of the action potential comes from an **intrinsic source** of impulses within the heart itself that is called the conduction system of the heart. To produce action potential intrinsically without any stimulation

*Parts of the conduction system:

1. **SA (sinoatrial) node** (Pacemaker)(located in the right atrium on the posterior wall just below the opening of superior vena cava)→ when it produced action potential will spread into the artrium muscle which is located around SA

2. **AV (atrioventricular) node**.(between the right atrium and right ventrical)

* but between the muscles in the atrium and ventrical are no connection so we need something called A-V bundle

3. **A-V (atrioventricular) bundle**.

4. Bundle branches (right and left bundle branches).--→form about 2/3 of the heart

5. **Purkinje fibers**.

- Note all the 5 parts can produce action potential.

GOOD LUCK