بسم الله العزيز الحكيم


The Physiology of the cardiac

Introduction:

We have three types of muscles in our body:

1. Skeletal muscle.
2. Smooth muscle.
3. Cardiac muscle.

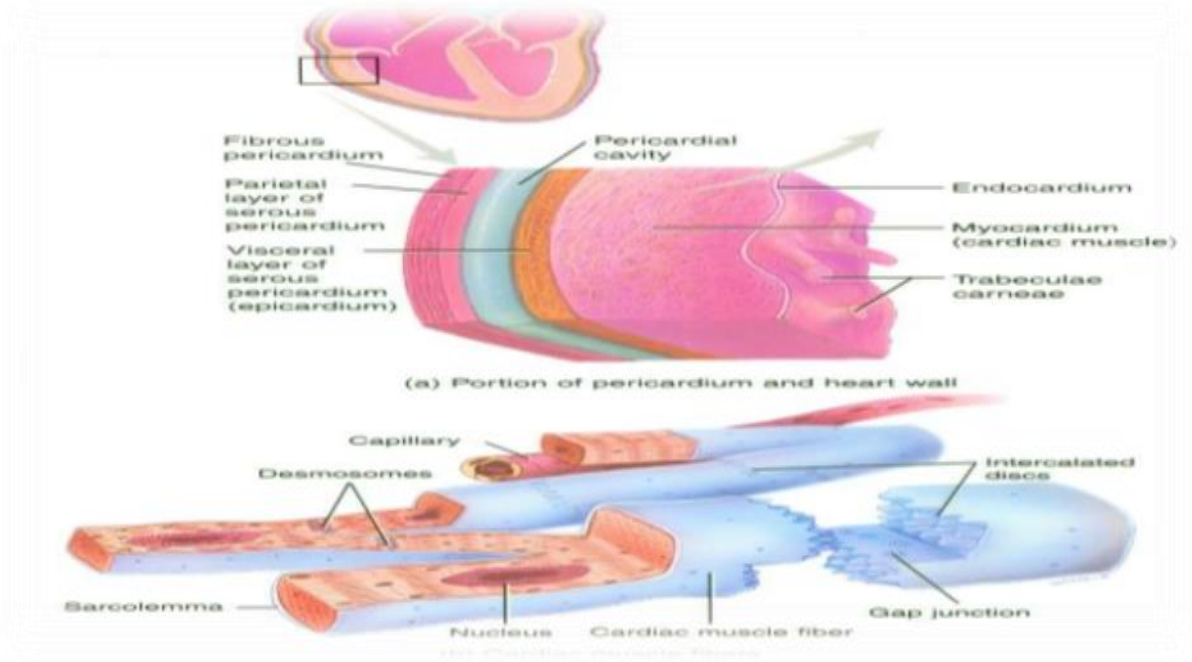
The cardiovascular system consists of: heart (pump) and cardiac vessels.

The Heart:

The heart is the center and the pump of the cardiovascular system by the action of its muscle layer, it pumps blood to the circulations. We have two circulations: The greater circulation that distributes the blood to all over the body and is also called systemic because it distributes the blood to all systems except the lungs, they receive blood through the lesser (or pulmonary) circulation.

Done by Osama Abu Shawar

The wall of heart has three layers: (from inside to outside)
1. Endocardium (innermost layer, epithelium)
2. Myocardium (major layer, Muscle)
3. Pericardium (outermost layer, two layers: Visceral (close to the heart), and Parietal with the pericardial space in between which contains a fluid for protection).



A comparison between Skeletal and Cardiac Muscles:

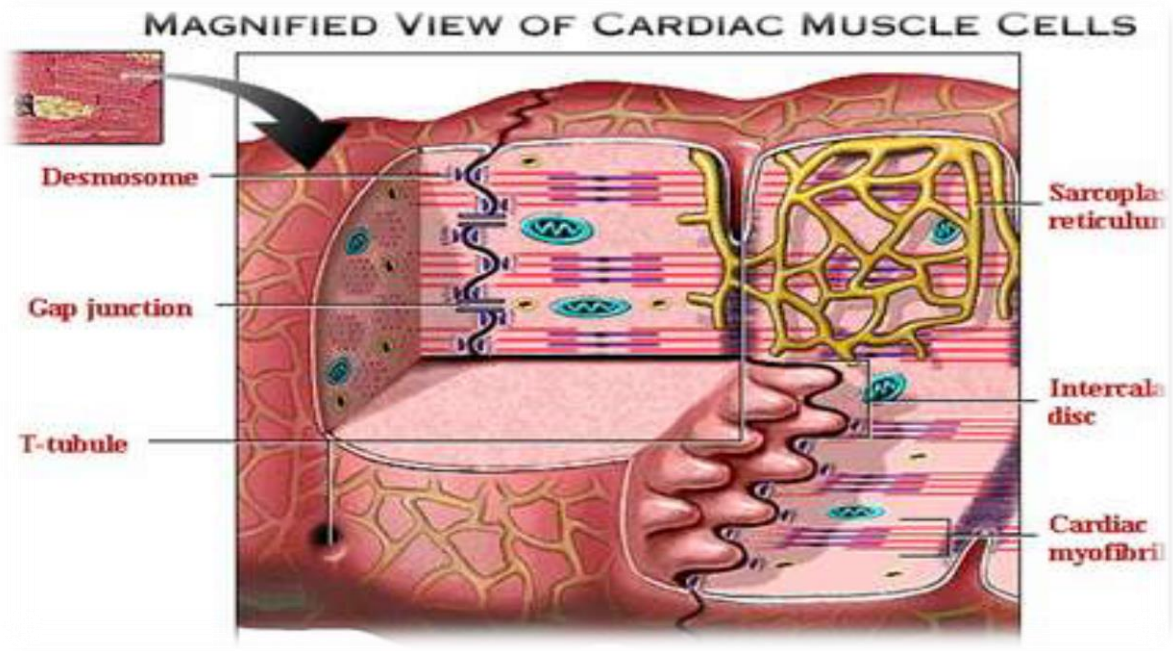
- Skeletal muscles are spindle in shape and start form the origin to the insertion so they are long, while the cardiac muscle cells are rectangular in shape and smaller.
- Both are striated due to the presence of sarcomeres that contain contractile muscle fibers (proteins). There are four types of contractile proteins: Myosin forming the thick filaments, and the thin filaments are three types: Tropomyosin forming the doubly helical line to witch actin "beads" are connected. And Troponin.
- Skeletal muscle cells are not connected to each other, and motor nerves supply a number of fibers to cause their contraction (a motor unit). While cardiac muscle cells are connected with each other by intercalated disks with gab junctions between them. The gab junctions conduct electricity from one cell to another; so they form low resistance areas, and they open or close as

response to a change in voltage (voltage-gated channels). When they open the ions move from one cell to another fast, and thus cardiac muscles are electrically coupled. Any change (action potential) in one cell spreads into all cells at the same time through gap junction. This electrical change (action potential) is followed by a mechanical change (the contraction), and since the cells receive the action potential at the same time they contract at the same time as one unit and the heart will work as a pump.
Pathologically, if each cardiac muscle cell contracts by itself (Atrial or Ventricular fibrillation) the heart will not function and ventricular fibrillation will cause death.
Gab junctions are hexagonal proteins with an open and a close conformation.

- Skeletal muscles are voluntary, it cannot contract unless it is innervated. While cardiac muscles are involuntary, although it is supplied by the autonomic nervous system (sympathetic and parasympathetic). This innervation of the cardiac muscle is not important for the initiation of cardiac muscle contraction (during cardiac transplants the autonomic supply is cut but the heart is still running). The contraction of cardiac muscle follows (None or All law).
  - In the muscle we call:
    The plasma membrane ⟶ sarcolemma SL.
    The endoplasmic reticulum ⟶ sarcoplasmic reticulum SR.
    The cytoplasm ⟶ sarcoplasm.
- The sarcolemma of cardiac and skeletal muscles have deep invaginations called the T-tubules or transverse tubules. The T-tubules of skeletal muscles is slender and longer and occur in the I band so each sarcomere has two T-tubules, while in the cardiac muscle they are wider and shorter and occur at the Z line (disk) so each sarcomere has one T-tubule.
  The sarcomere is the distance between two Z lines.
- The sarcoplasmic reticulum (which stores Ca^{++}) in the skeletal muscle is well-developed, while it is less developed in the cardiac muscle so the cell doesn't store enough Ca^{++} for its contraction and needs an extra source of Ca^{+} from outside (extracellular fluid around cells – interstitial fluid). That's why during heart transplant, the heart is put into a solution with Calcium.
- Cardiac muscle is contracted all the time which requires more energy, that's why it has lots of mitochondria to supply ATP compared to skeletal muscles that, on the other hand, have much more nuclei.

*Ca^{+} ions bind to troponin to initiate contraction while relaxation occurs when Ca^{+} unbinds from troponin.

*after contraction Ca+ gets back to the SR or leaves the cell through Na\Ca exchanger and Ca pump.

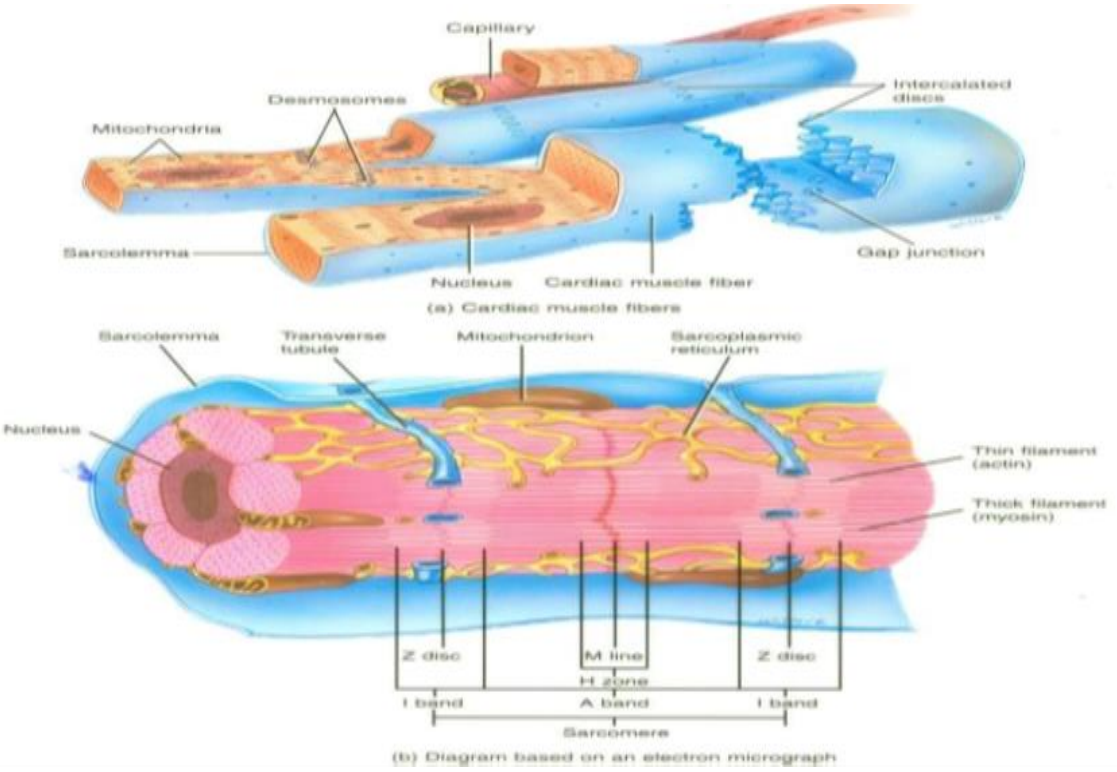


(الفقرتان أدناه فقط لتوضيح المعلومه)

In both cardiac and skeletal muscles, muscular force production is controlled primarily by changes in the intracellular Ca+ concentration. In general, when calcium raises, the muscles contract and, when calcium falls, the muscles relax.

Troponin is a component of thin filaments (along with actin and tropomyosin), and is the protein complex to which calcium binds to trigger the production of muscular force.

	T tubule	sarcomere	mitochondria	shape	nuclei
Skeletal muscle	Longer and cylinder	two	poor (less)	spindle	more
Cardiac muscle	Shorter and wider	one	rich (more)	rectangular	less



Action potential of skeletal muscle

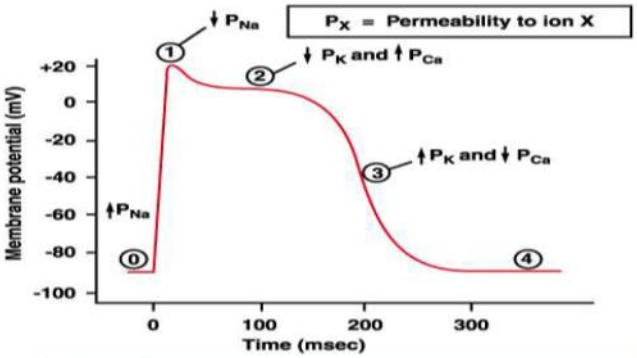
- Resting stage due to K+ diffusion starts at -70.
- Slow depolarization till it reaches the threshold.
- Fast depolarization (firing stage) due to the fast open Na+ voltage gated channels.
  (Trying to reach the equilibrium potential for Na+ {+61} but it doesn't get there because other ions are involved).
- Repolarization (falling stage) due to opening K+ channels.
- Very short (between .1 msec to 10 msec maximum)

Action potential of cardiac muscle

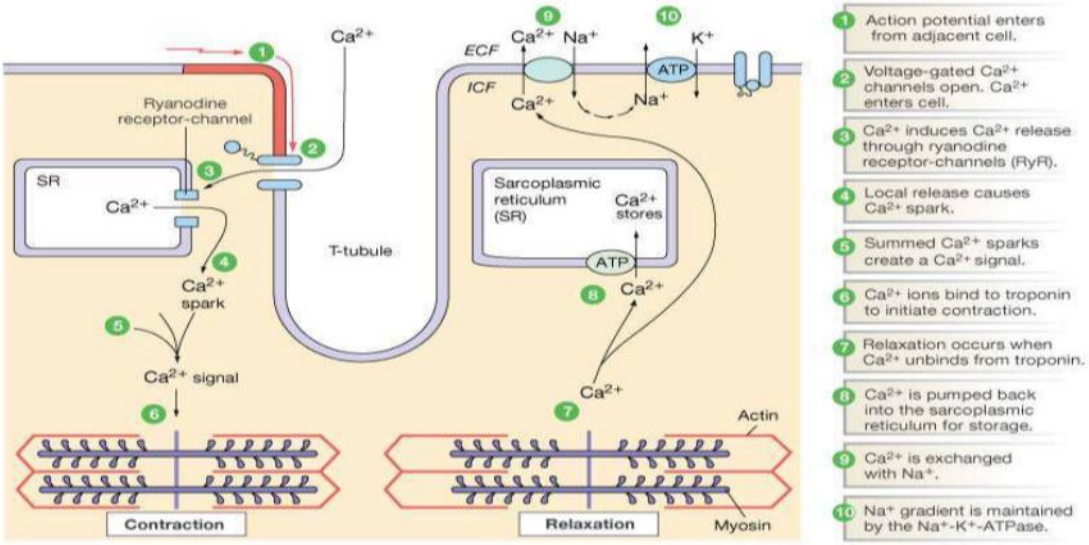
- The resting membrane potential is -90mV (more negative). Phase 4.
- Fast depolarization is due to the opening of Na+ voltage gated channels. Phase 0.

(There's an increment in the permeability of Na+ and decrease in the permeability of K+).

- Partial repolarization is due to the opening of transient K+ and Cl- specialized channels. Phase 1.
- Plateau (maintaining depolarization) is due to slow opening of Ca+ channels. Phase 2.
  (This induces releasing Ca+ from SR and this process plays the main role in contraction).
- Repolarization is due to the opening of K+ voltage gated channels. Phase 3.
- Return to resting stage by the Na-K pump for the rearrangement of ions. Phase 4.
- Longer, occurs in about 200 – 400 (normally 300 msec) thanks to the long refractory period (an absolute refractory period from the beginning to half of the repolarization stage where the muscle cannot contract, and a relative refractory after it where the muscle may contract to a stronger stimulus)



Phase	Membrane channels
0	Na^+ channels open
1	Na^+ channels close
2	Ca^{2+} channels open; fast K^+ channels close
3	Ca^{2+} channels close; slow K^+ channels open
4	Resting potential



The Contraction and Tetanization:

In the skeletal action potential:

Because of the short action potential, if there's another stimuli, new action potential and another contraction will start in the relative refractory period of first action potential and this is called tetanus or spasm (summation of contraction⟶ no relaxation).

(Relative refractory period: the last half of the repolarization phase till the action potential has ended).

In the cardiac action potential:

The muscle contracts and relaxes before a new action potential starts (no tetanus). Why?.

Due to the very long action potential (long absolute refractory period) in the heart (plateau).

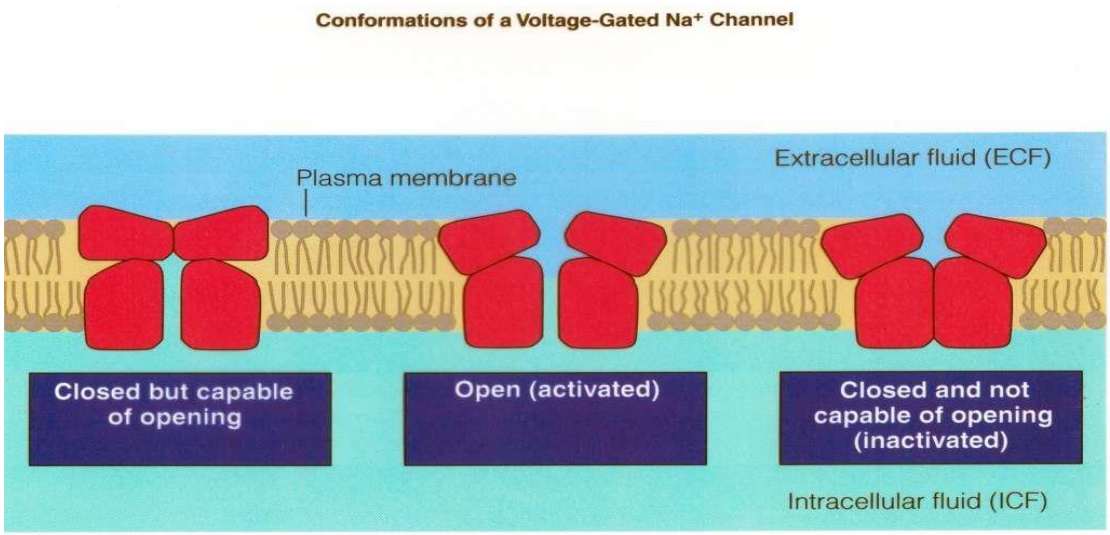
(ما تبقى من الصفحه هو مقدمة للمحاضرة القادمه)

** Na+ channels have M gate (activated) and H gate (inactivated).

	M gate	H gate
Location	Extracellular	intracellular
During resting stage	Closed	opened
During depolarization (less negative)	Opened	closed
Time constant (that's need to open)	Fast	slow

During depolarization:

1. M gate opens.
2. Na enters.
3. H gate closes (due to the threshold is reached).



<u>Summary:</u>

	Resting membrane potential	Number of phases	Partial repolarization	plateau	Ca+ channel	tetanus	time

Skeletal action potential	-70	two	___	___	___	present	10 msec
Cardiac action potential	-90	five	present	present	present	___	300 msec

Phase 0	Phase 1	Phase 2	Phase 3	Phase 4
Depolarization (Na+ influx)	Partial repolarization (K+ efflux and Cl- influx).	Plateau (slow Ca+ influx)	Fast repolarization (K+ efflux)	Resting membrane potential

*cardiac muscle cells connected with each other through gap junction.
*the skeletal muscle cell has to be stimulated by impulses to contract, but cardiac muscle is able to contract involuntarily.
*the cardiac muscles are syncytium structure that's why they receive the action potential as a one unit.
*the electrical change is followed by mechanical change in cardiac muscle.
*the decrease in the permeability of K+ at phase 0 & 1 contributes to the maintenance of depolarization in phase 2 (plateau).

ستة أعوام.....

حتما سنواجه فيهن.....

مادة صعبه!.....
دكتور ما بشرح!.....
امتحانات كالنار!.....
مادة لا تنتهي!.....
تعب وسهر!.....
هموم وأرق!....

والحل؟؟!!!

قال تعالى: **{وإذا سألك عبادي عني فإني قريب أجيب دعوة الداع إذا دعان فليستجيبوا لي وليؤمنوا بي لعلهم يرشدون}**.....

Quiz

1. In which phase the number of positive charge entering is more than the number of positive charge leaving:
   A. phase 2.
   B. phase 0.
   C. phase 4.
   D. phase 1.
   E. phase 3.

2. The low resistance pathway between myocardial cells that allow for the spread of action potentials are:
   A. mitochondria.
   B. intercalated discs.
   C. t tubules.
   D.gap junction.
   E. sacroplasmic reticulum.

3. Which phase coincides with diastole (relax):
   A. phase 2.
   B. phase 0.
   C. phase 4.
   D. phase 1.
   E. phase 3.

4. During which phase is the conductance to Ca^{+} is the highest:
   A. phase 2.
   B. phase 0.
   C. phase 4.
   D. phase 1.
   E. phase 3.

5. During which phase is the membrane potential is closest to the K^+ equilibrium potential:
   A. phase 2.
   B. phase 0.
   C. phase 4.
   D. phase 1.
   E. phase 3.

إعداد: أسامة أبو شاور...

All of these questions are (past paper).

1	2	3	4	5
B	D	E	A	C