PHYSIOLOGY

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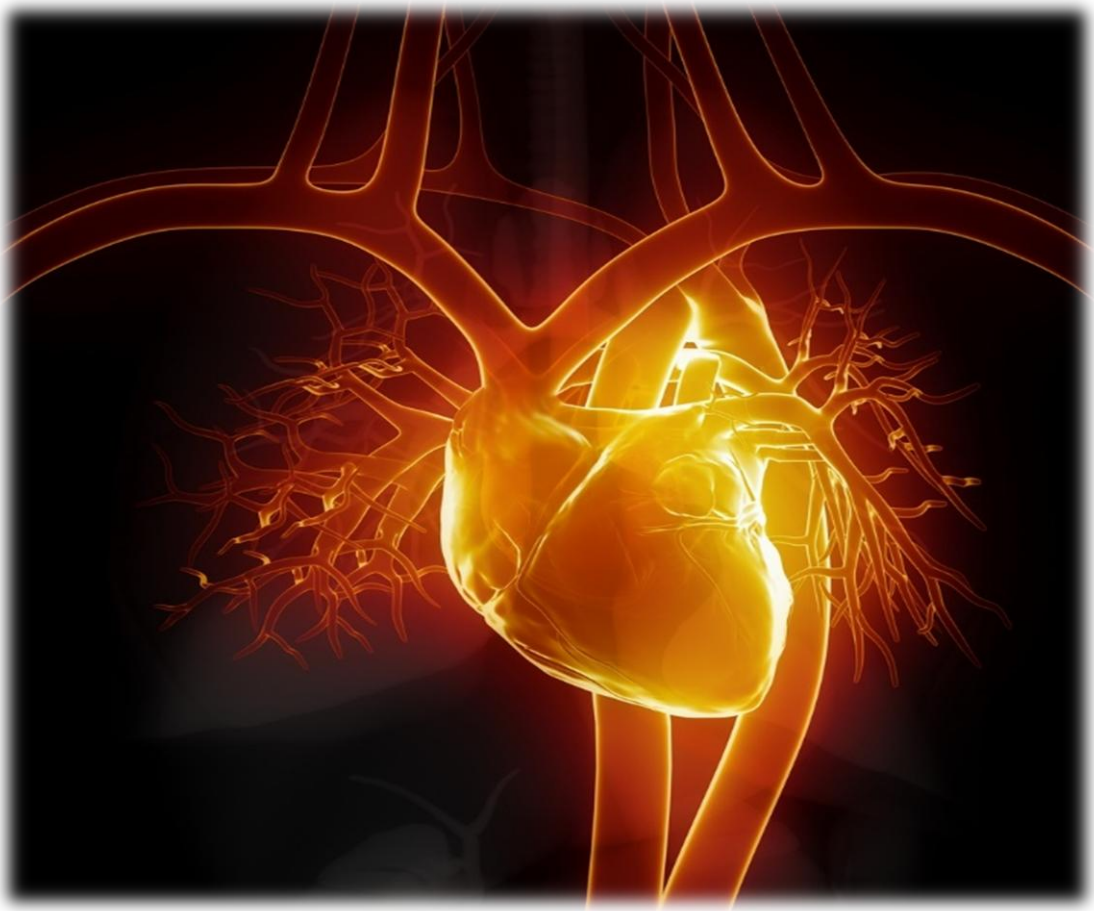
" Introduction to Cardiovascular physiology "



Lectures : 18 +19

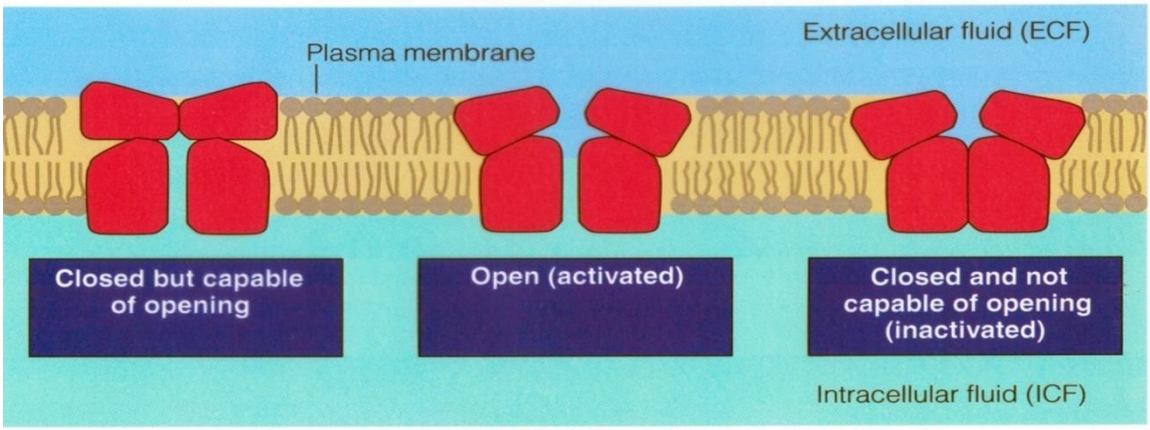
" Heart Conduction system season 1 "

- lecture 18 -

Episode 1 : Two important introductions :

1) Sodium channels :
   They have two gates, they're voltage gated.
   (1) An outer gate in the extracellular matrix is called activation gate or M gate.
   (2) The innermost gate is called inactivation gate or H gate.
   So sodium channels have 2 gates; activation gate and inactivation gate. During rest, the membrane is polarized (resting membrane potential in the heart -90, or in the skeletal muscle -70) during this stage the activation gate is closed (the outside gate) and the inactivation(inside) gate is opened. It's like a fence with two gates; an outer one and an inner one, if only one of these gates is closed nothing will pass through that fence, The activation gate opens when the membrane potential becomes less negative(depolarization), and the inactivation gate closes when the membrane potential is becoming less negative. One opens the other closes. But what makes the difference is the **timing**. The activation gate responds very fast, the inactivation gate responds slowly. So when the membrane potential is getting less negative the activation gate opens before the inactivation gate closes and that will cause influx of sodium ion inside the cell and depolarization because the inactivation gate responds slowly. After a while time the inactivation gate closes and that will prevent the sodium from entering even though the activation gate is opened .

Conformations of a Voltage-Gated Na^+ Channel



2) extracellular calcium :

We said that we need extracellular calcium. During phase 2 calcium enters the cell through slow voltage gated Ca channel, the calcium that enters through the slow calcium channels it goes to the SR (sarcoplasmic reticulum) and induces or triggers release of calcium from the SR. The calcium that enters through the slow calcium channel plus the calcium that's released from the SR they initiate the process of contraction in the sarcomere. So the calcium that enters through the slow calcium channels is important because as we noticed it helps to trigger the increase in calcium ion in the sarcomere by inducing it's release from the SR.

Now when relaxation happens, we have to decrease calcium, because calcium is the ion that causes contraction if it increases, if it decreases it will cause relaxation. How can we decrease it? , the first thing calcium will be re-uptaken to the SR actively through the calcium pump (calcium ATPase), but a lot of calcium entered not only from the SR also from the extracellular fluid. Calcium is going to go outside the cell by a transporter, called sodium – calcium counter transporter ,calcium goes out in exchange with sodium that goes in , three sodium per one calcium (electrogenic process)This is secondary . active transport. The third method is the calcium pump in the SL(SarcoLemma) it pumps calcium outside. So how many methods do we have for calcium to come back to the normal? Three.

1- Calcium pump in the SR(primary active transport)

2- calcium-sodium exchanger in the SL(Secondary active transport)

3- Calcium pump in the SL(primary active transport)
All of that happens normally, but now if there was too much calcium abnormally, there's another process which is the fourth process that happens abnormally . In pathological stage, the mitochondria will takes the extra calcium .

- lecture 19 -

Episode 2 : Definition of Conduction system and it's parts

The heart is different from skeletal muscle If we take the heart out and put It in a solution that contains calcium a lot of contracting will occur , but this contraction will not occur unless there is an electrical change , that means there must be an action potential . also there are no nerves , so there must be a source of action potential inside the heart not out . so there is an intrinsic system of producing action potential inside the heart , and we call it conduction system of the heart , that conduction system consist of modified (in term of structure and in term of function) cardiac muscle cells not nerves

hassa bg3od 10 mins w hweh yhki 3n el story of discovery of the relation btw el Ca solution w el heart ... estno 5lena nstna y5ls .. Hmmmmm sho a5barko ma 7ketole kefko ?

yla nrja3 khls ☺

so, In term of structure they don't have myosin and actin .

in term of function :

our aim here is to list the parts that comprise the conduction system . The mechanism of the pacemaker potential (how the potential happened and spread) .

The first part is called SA nodes (Sinoatrial node), it exists in the posterior aspect of the right atrium just below the superior vena cava . The second part is AV node , it is in the right atrium , at the junction between the atrium and ventricle that we call it atrioventricular node . from this node a bundle continues called (AV bundle) or sometimes we call it his bundle , Then this AV bundle divide into right bundle branch and left bundle branch, right

bundle branch supply the right ventricle and left bundle branch supply the left ventricle . they end by a lot of fibers called purkinje fibers . So , this system consist of :

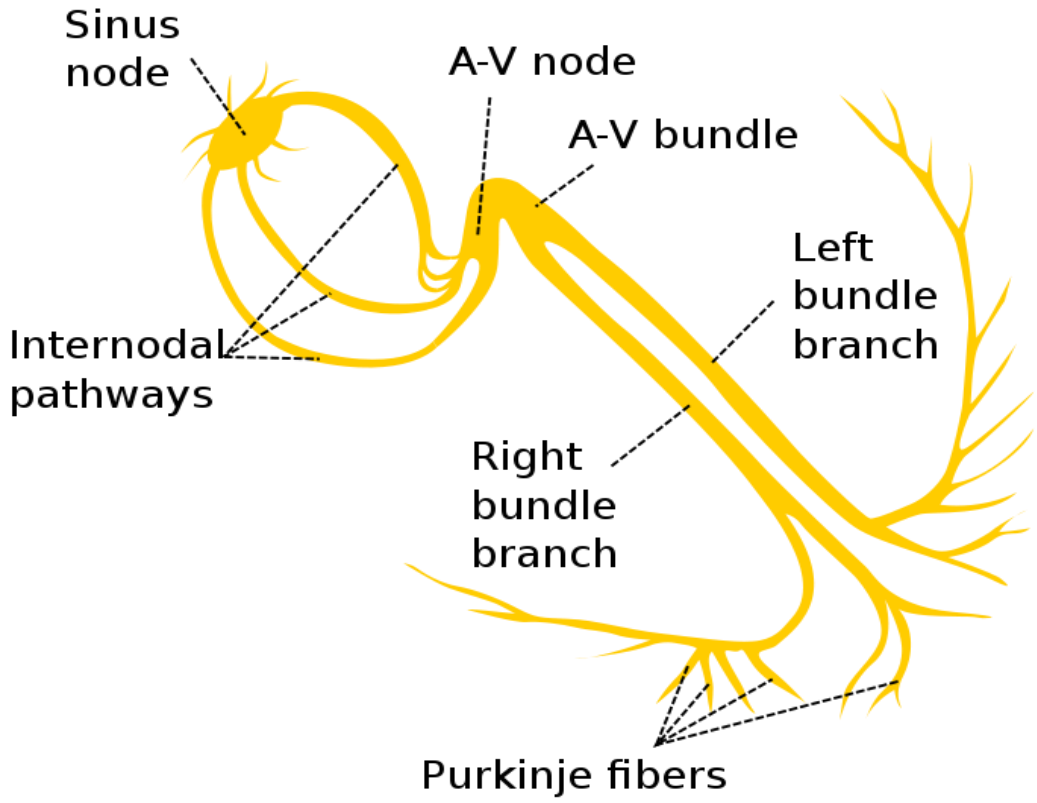
(1)SA node .

(2)AV node .

(3) AV bundle .

(4)bundle branches (left and right AV bundle branch)

(5)purknje fibers .



-Approximately 1% of cardiac muscle cells are autorhythmic rather than contractile, despite that, they are very important; because they are able to produce intrinsic impulses (without any stimulation) that spread all through the heart and cause contraction with different rates .

-SA node produces impulses, they spread through the atrial muscle to the AV-node (which is emerged in the atrial muscle), so AV-node picks the impulse and conducts it to the AV-bundle (bundle of His), then through right & left bundle branches, to Purkinje fibers to the ventricular muscle cells.

There is NO direct connection between SA-node & AV-node; AVnode receives the impulses from the atrial muscle (since it is part of it).

-Normally, the SA-node produces (70-80) action potential/min, which is conducted through AV-node to AV-bundle to Purkinje, so the heart is working with that rate also (70-80) beats per minute.

- SA-node : 70-80 (highest rate)
- AV-node : 40-60
- Purkinje : 15-40 (lowest rate)

-As a result, intrinsic rates of AV-node and Purkinje fibers have been suppressed by the higher intrinsic rate from SA-node (they are not working with their own rates), this is called Overdrived suppression.

* By removing SA-node : working by the rate of AV-node (40-60)

* If AV-node is blocked : no direct connection between the atrium and the ventricle, therefore, ventricles beat by the rate of Purkinje (15-40), whereas atria beat by the rate of SA-node (70-80), this is called AV block or Heart block.

Episode 3 : Conduction speed

(how fast they conduct the impulse or action potential)

- AV-node has the slowest conduction speed
- Purkinje fibers have the fastest conduction speed (4-5 m/sec)
- Ventricular & atrial muscle cells have moderate speeds

Now :

1) The AV-node conducts the impulse very slowly, why?
   Normally, the atria and the ventricles should NOT contract together (the atria should contract and finish their contraction then the ventricles start to contract), to assure this, there should be a delay in the impulse so they will not overlap.

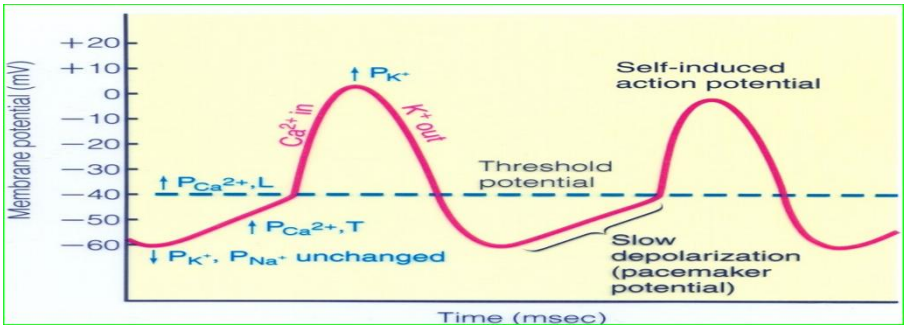
2) Purkinje fiber conducts with the highest rate, why?

In order to conduct the impulses to all ventricular muscle cells almost at the same time, so that they can contract simultaneously as one unit. (Purkinje is wider)

Mechanism of the two responses (Slow & fast) :

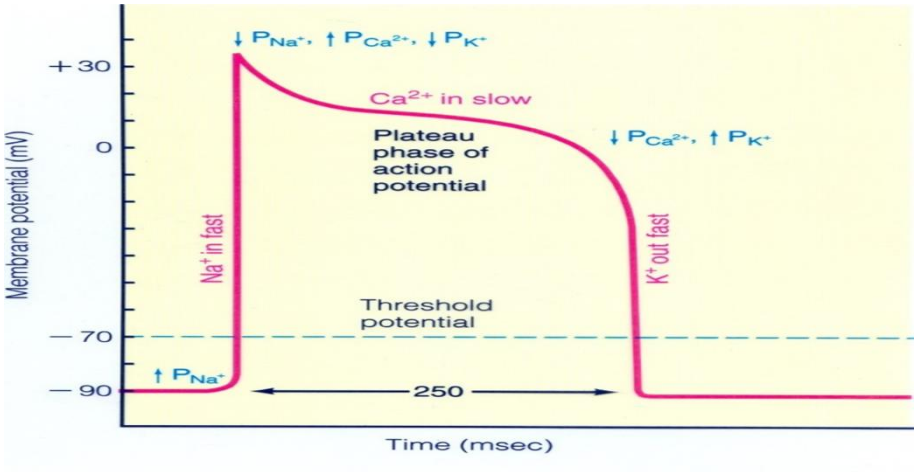
1) Slow Response Action Potential (pacemaker potential)

- Because these cells are leaky to Na+ , the resting membrane potential will never reach -90mV (it reaches -60mV)
- Slow depolarization due to Na+ influx (because it is slowly depolarized, the inactivation gate of Na+ channels close before the activation gate opens
- so Na+ gated channels are closed), and then Ca++ channels open causing Ca++ influx (depolarization) phase zero
- Slow Depolarization due to Na+ influx through leakage channels phase 4
- Repolarization due to K+ efflux in phase 3
- There is NO (1 or 2) phases (no Plateau)



2) Fast Response Action Potential

- Resting membrane potential is much more negative
- Fast depolarization due to Na+ influx phase zero
- There are phases 1 & 2 (Plateau)



-Ectopic pacemaker: abnormal site of pacemaker (ex: AV-node).

Episode 4 : Innervation of the Heart

-The heart is supplied by Autonomic nerves

-They are working for <u>regulation of the impulse not initiation</u>

بالعربي الفصيح : شو الفرق بين عصب رايح لعضلة هيكلية و بين عصب رايح لعضلة القلب ؟ الأول يجي يحكيلها للتراي مثلا انو والله تقلصي , هون راح تبلش تعمل جهد فعل **بسبب العصب** و تتقلص , بينما اللي رايحين للقلب وظيفتهم انو بس يرتبوا شغل القلب مش انو يشغلوه (ارتفع يخفضه , انخفض يرفعه) , بكلمة ثانية : هم مثل صمامات الأمان للقلب , بالحالة الطبيعية ما بشتغلوا بس لما يصير شي غير طبيعي " لا سمح الله " ..

-They are two types : Sympathetic and parasympathetic

Important terms :

-Chronotropic effect: change in the rate

-Inotropic effect: change in force of contraction in atria and ventricles (contractility)

-Dromotropic effect: change in rate of conduction of impulse (speed)

Positive : increase Negative : decrease

1) Sympathetic Extrinsic Innervation of the Heart :

- From the cardiac plexus
- Supplies all parts of the heart (atria, ventricles, SA & AV nodes, AV bundle and Purkinje)

- Affects either directly or indirectly through its neurotransmitters which are epinephrine and norepinephrine (AKA: adrenaline and noradrenaline)
- Causes increase in permeability of cardiac cells to Na+ & Ca++
- Positive Chronotropic , positive Inotropic , positive Dromotropic

Mechanisms :

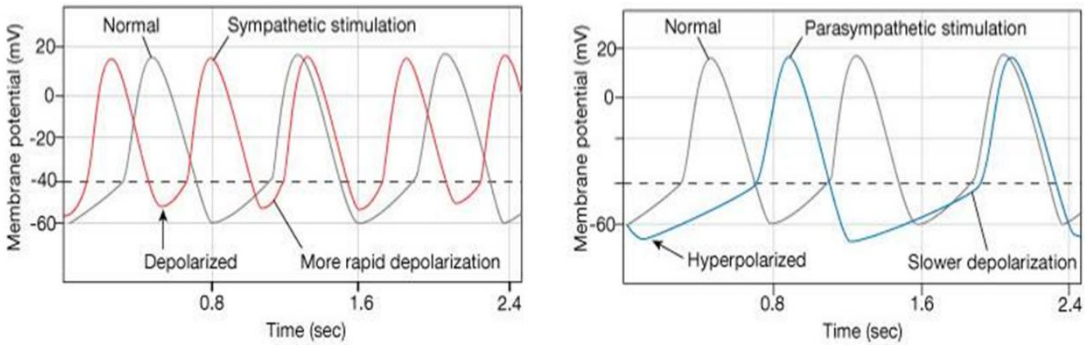
- ✓ Increasing permeability to Na+
  - The resting membrane potential will not reach (-60mV) less negative (ex. 55mV) due to Na+ influx (more positive charges enter these cells)
  - Faster depolarization we reach the threshold earlier, so that we have higher rate
  - Positive Chronotropic effect (increase in the rate)
- ✓ Increasing permeability to Ca++
  - This will affect the contractile cells _especially the ventricles_ (Ca++ does not affect conductor cells)
  - Increasing in the force of contracting (due to Ca++ influx, so more Ca++ would be inside) more contractility
  - Positive Inotropic effect (increasing contractility)
  - Positive Dromotropic effect (faster rate (speed) of conduction of the impulse)

2) Parasympathetic Extrinsic Innervations of the Heart :

- From Vagus nerves (العصب الحائر , مش عارف وين رايح)
- Supplies only the SA & AV nodes and the atria (does not supply the ventricles)
- Affects either directly or indirectly through its neurotransmitter which is acetylcholine
- Causes increase in permeability of these cells to K+ and decrease of permeability to Na+ & Ca++
- Negative Chronotropic , negative Drpmotropic , NO Inotropic effect

Mechanisms :

- ✓ Increasing permeability to K+
  - The resting membrane potential will be more negative due to K+ outflux
- ✓ Decreasing permeability to Na+
  - Slower depolarization longer time to reach the threshold, so that we have slower rate
  - Negative Chronotropic effect (decrease in the rate)
- ✓ Decreasing permeability to Ca++
  - Has almost NO effect on contractility; because the ventricles are not supplied by parasympathetic Vagus nerve
  - Almost NO Inotropic effect



For your information :

When we come to the regulation of sympathetic, how do you think our brain senses the blood pressure? For example if we want to do exercise and increase the Blood pressure, how the brain knows that the blood pressure must be increased?

The Only way by which the brain knows that the blood pressure is low or high is by SIGNALS that come from the major blood vessels :

Ex: in the arch of aorta there is baroreceptors " baro means pressure, so it senses pressure " ..

Another ex is the carotid sinus in the common carotid artery in the neck ..

Clinical case : There is something called the carotid sinus syndrome , for example a young male during his engagement party is under stress , usually males wear tuxedoes and a neck tie (girls have no problem because they usually wear dresses , so they have nothing pressing on their neck) so the

carotid sinus syndrome is for males , some of the males are very sensitive on the neck area , so this is a warning specially for you guys when you are laughing or fighting with your younger brother , do NOT chock them from the neck because it is a very dangerous area ,here we have the two carotids , if you press on them in some people that are very sensitive , the receptors will get a wrong information that the blood pressure is rising from the external pressure , but actually it is not, so these information goes to the brain and will understand that blood pressure is dangerously increasing so it will call immediately the **parasympathetic** and cause decreasing in heart rate , so when you see a handsome young man wearing a neck tie and he suddenly faints, just open the first button and remove the neck tie and he will get better, this is what we call it carotid sinus syndrome, it's kind of external pressure that simulates high blood pressure. This needs to be treated, and this is a warning to you , even sometimes they put a pacemaker in the heart of the old people to treat this condition, when too much fainting trifler on the brain. (و هيك مات المغني ناظم الغزالي , كان كاعد يحلق ذقنه و ركز على هالمنطقة من رقبته لحتى انخفض ضغطه و وقف قلبه , لهيك جد ما حدا يعملها ! انا جربتها و كان رحت فيها)

Now think about these questions :

1) In the SA nodal action potential which phase should be faster to cause tachycardia ?
2) In the action potential for the SA node, in which phase the number of positive charges entering is more than the number of Positive charges leaving ?
3) During the action potential for the SA nodal cell in the heart, the permeability changes for which ion/ions ?
4) In the SA node, phase 4 depolarization (pacemaker potential) is attributable to which process ?
5) At which stage are the sodium channels mostly closed and not capable of opening?

" You have chosen the most difficult career in life , your error will lead to death , so , you have to be knowledgeable and understand how dangerous you could be if you have half knowledge "

كل التوفيق و شدولنا حيلكوا
وآسف على أي خطأ بس ماكو وقت
Husain physiology ☺