Cardiovascular System

Sheet 4

Subject | Physiology

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Last time:

-we introduced the conduction system of the heart, which is composed of modified cardiac muscle cells, that give intrinsic impulses to the heart, followed by contraction and relaxation cycles.

-when transplanting a heart to a faraway patient, transport medium must contain calcium, why calcium? Because it can enter muscle cells through slow calcium channels, this in turn induces more calcium influx and calcium release from ER overall increasing intracellular calcium concentration causing the contraction cycle.

Contraction of muscle cannot take place unless proceeded by an action potential (electrical signal), which in the heart is produced intrinsically by THE CONDUCTION SYSTEM OF THE HEART

Components of this system: (the SA node, AV node, bundle of His, bundle branches, and Purkinje fibers.)

-SA node, sinoatrial node in the posterior wall of the right atrium just below the entrance of the superior vena cava

-AV node, atrioventricular node found between the right atrium and right ventricle .

Since the atrium and ventricle are not connected to each other muscularly, impulses from the atrial muscle won't reach ventricular muscle unless there's a way to transmit impulses between them, this way is through the AV node

Then from AV node to a wire like connection called the AV bundle (bundle of his), then dividing into right and left bundle branches, both of which run in the sub endocardium, finally dividing into the last division of this conduction system, the Purkinje fibers

It is said that there are additional internodal fibers between SA and AV nodes (ant, post and middle internodal fibers), doc however believes that atrial muscle cells conduct the signal from SA to AV node.

Cardiac muscle cells of this conduction system represent only 1% of the total muscles of the heart, and are modified, How?

1- Anatomically: By lacking the contractile proteins (actin and myosin), and by - having a rounded instead of rectangular shapes.

2-Physiologically: they are leaky to sodium, have special channels called **leaky sodium channels (If channels, (f)for funny as their leakiness seemed funny to scientists)** which allow sodium to diffuse in according to its concentration gradient. Enabling them to generate intrinsic impulses.

Since 1% of heart muscle cells are noncontractile comp of the conduction system the other 99% of heart muscle cells are contractile cells .

Differences between the diff comp of the conduction system in the following:

a-Intrinsic rate (the number of impulses- action potentials- generated per minute) as follows: SA node 70-80/min, AV node 40-60/min and Purkinje fibers 15-40/min.

The cells of this system are **autorhythmic cells**: this means that they can discharge (generate an action potential) without a stimuli or external innervation.

All these comp have the ability to generate their own intrinsic impulses, but since SA node has the fastest intrinsic rate ,thus its rate will be the one conducted

through to AV→AV bundle →purkinje fibers→ contractile muscles of the heart , setting the pace (speed) of the heart thus SA node **called PACEMAKER** .

Think of this system as train having multiple carts, and of course the cart with the highest rate leads, so: that's why heart rate measures (that of atrial and ventricular contraction) will be that of SA intrinsic rate =70-80bts/min

All the other rates of the other comp will be suppressed by the higher rate they receive from the top (SA node), this is called **overdrive suppression**

They can however still generate their own rate in case the normal pacemaker is destroyed resulting in the absence the upper rate, thus absence of the overdrive suppression .

-SA rate absent: heart rate=40-60 bts/min(rate of the AV node)

However the AV node is an abnormal site for the pacemaker , thus called Ectopic pacemaker. **(ectopic pacemaker**-any pacemaker other than the SA is ectopic**-)**.

-AV rate absent: heart rate=15-40bts/min, this is called AV block (heart block)

Scenarios that could lead to ectopic pacemaker formation:
Example 1: a myocardial infarction that resulted in the formation of a focus in the ventricle that transmits a very high intrinsic rate of 120bts/min, higher than the normal heart rate .→ ectopic pacemaker in the ventricle.
Example 2: part of atria started beating at a higher rate than that of SA node, SA node is suppressed →ectopic pacemaker in the atrium.
-notes:

-Ectopic pacemaker can result in a both higher and lower heart rates, not necessarily lower

-absence of AV node rate could either be due to a dysfunctional AV node or dysfunctional AV bundle→ point is: impulses don't reach Purkinje

-What if only AV node is dysfunctional but SA node and purkinje are still working? there will be two rates in the heart, atrial (70-80) and ventricular rate (15-40)

b- Conduction rate (It is the **speed** at which an impulse propagates, how fast they conduct action potential) as follows:

Tissue	Conduction rate (m/s)
Atrial muscle	0.3
Atrial pathways	1
AV node	0.05
Bundle of His	1
Purkinje system	4
Ventricular muscle	0.3-0.5

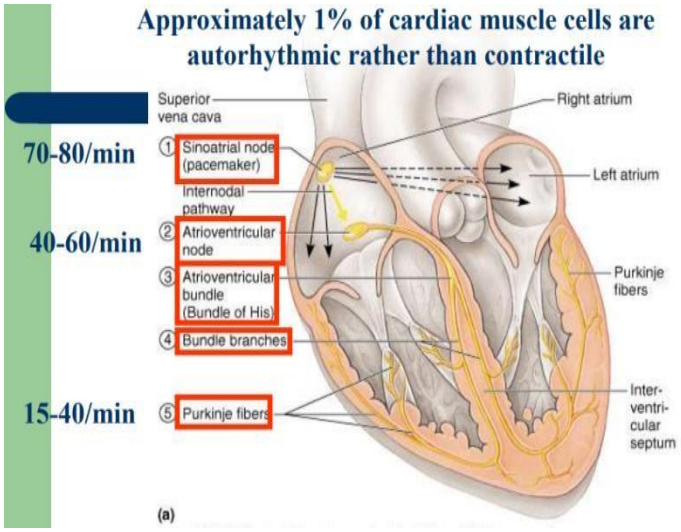
-SA node: slow speed of conduction.

- Ventricular and Atrial muscle: Moderate speed of conduction.
- AV node: slowest speed of conduction.
- Purkinje fibers: Fastest speed of conduction, slowest intrinsic rate as notes earlier.

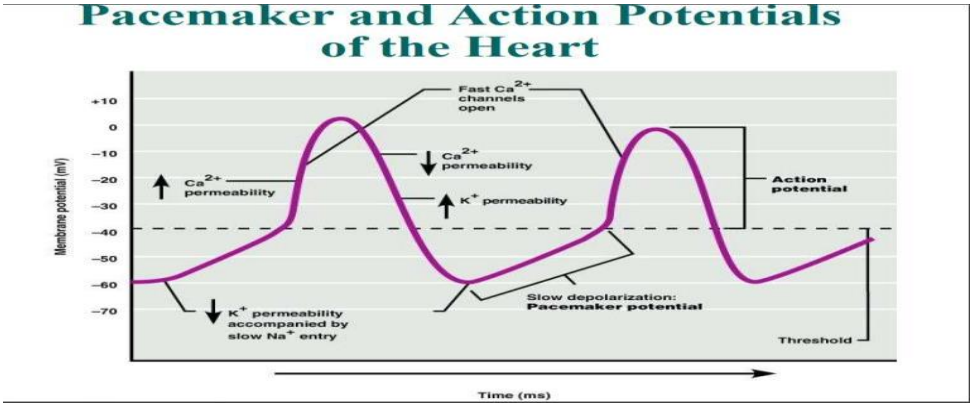
- The conduction is **unidirectional**, due to refractory periods (anything recently repolarized won't be depolarized again for a while, so the wave can't go back). - **Why the conduction rate in the AV node is the slowest**? To ensure that the atria and ventricles do not contract at the same time; atria systole finishes, followed by ventricular systole, this is mediated through **AV** node which **delays the impulse**. this delay is called **AV delay**
- The conduction rate is the fastest in the Purkinje, 4m /sec, due to ,high number of gap junctions, large diameter and low resistance, all to make sure that ventricular muscle cells receive the impulse at the same time and contract at the same time as a one unit(one pump),within milli seconds the entire ventricle will have contacted. Otherwise, each ventricular fiber contracts independent from the others, this is called **ventricular fibrillation** which is **lethal**, and the physician should interfere to relief the condition by defibrillation, either defibrillation shock or drug.

Risk of ventricular fibrillation is why all MI patients are referred to the hospital, for control and monitoring

-clinical scenario: if there is a Right Bundle branch block(it is either Cut or cannot transmit signal to right ventricular muscle cells),right ventricular muscle will receive impulse through ventricular muscle(the onces that got stimulated on the left) instead of through purkinje ,ventricular muscles conduct impulses at a moderate speed by means of gap junction ,but at a lower rate than that of purkinje ,this can be seen on ECG and diagnosed accordingly as right bundle branch block.



- **We said that the pacemaker can generate action potential intrinsically, this action potential is different from the cardiac muscle AP as we will see:**



Extra note:The cells of the conduction system have No resting potential, we call it Pacemaker potential or slow response potential, why? As the membrane potential does not stay the same due to leaky sodium channels.

1-Phase 4 (slow depolarization phase)

-The membrane potential will be **less negative reaching -60**, and does not reach -90,(typical cardiac muscle cell resting membrane potential) , the cause behind this reduced negativity is that the cell membranes of SA nodal cells is naturally leaky to sodium and calcium ions,(more to sodium) ,

These Leaky channels allow entry of sodium raising the potential to a less negative value, allowing slow depolarization to take place ,this is phase (phase 4) slow depolarization phase ,threshold is reached slowly ,(-40 millivolts), since the threshold was reached slowly the inactivation gate will be closed so despite activation gate being open no more sodium will enter.
-This is the longest phase of SA node action potential.
-This phase is an imp determinant of the heart rate

2-Phase 0 (depolarization)
Once threshold is reached, voltage gated calcium channels open , **(long lasting calcium channels)**. These channels open at threshold of -40 millivolts, also called slow voltage gated calcium channels.

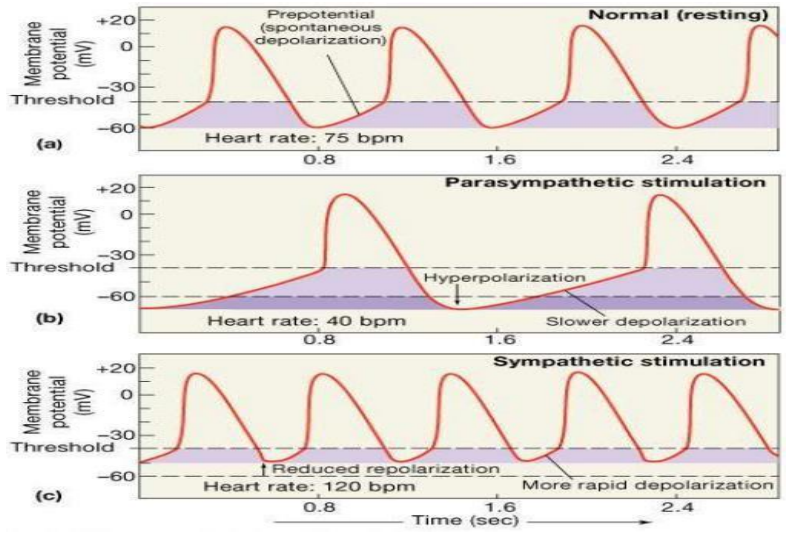
3-Phase 3 (repolarization)
-Occurs due to increased permeability and efflux of K ions. Returns membrane potential to its pacemaker potential of -60 but not -90 as membrane Is leaky to na+ so only reaches -60

-**There is no phase1 (partial repolarization) nor phase 2 (plateau)**
- This cycle continues. Remember that we said that it occurs intrinsically without any stimulation.

Note: the rate of the impulses depends on
1-**the slope** of the Phase 4 (-60 to the -40 ,threshold). Higher slope means less time to reach the threshold thus, a higher rate .
2-the **extent of negativity** of the membrane potential, the less negative it is ,the shorter the time needed to reach the threshold.
→Steepness of the slope and membrane potential depend on the permeability of the membrane to sodium, potassium and calcium.

Finally, this is what creates the difference in the rhythmic rates between SA, AV nodes and Purkinje. It is due to the difference in their sodium permeability (sodium leakiness), AV node less permeable to sodium than SA so membrane

potential more negative, more time needed to reach the threshold, intrinsic rate is less than that of SA node.



SYMPATHETIC AND PARASYMPATHETIC INNERVATION OF THE HEART :

<u>Sympathetic</u> fibers of thoracolumbar origin, from last cervical and first thoracic , supplying all parts of the heart (both ventricles and atria) through way of cardiac plexus .-mediated by epinephrine and norepinephrine results in :

→Increase permeability to sodium and calcium

a- Increase the rate (**positive chronotropic effect)**

- Increasing the permeability to sodium(influx) and calcium , the resting membrane potential become less negative, the slow depolarization occurs faster (increasing the slope of phase 4) reaching threshold faster , the heart rate increases.

b- Increase the strength of contraction **(positive inotropic effect)**

- Increasing the permeability to calcium, calcium not imp for conduction system (ex.SA node) but is imp for contractile cells (ex. ventricular cells,) Force of contraction increases.

c- Increase the rate of conduction **(positive dromotropic effect)**

<u>Parasympathetic</u> fibers of craniosacral origin from the vagus nerve (10^{th} cranial nerve,runs close to trachea), supply only the atria (SA node and AV node), and has no effect on the ventricles.-Mediated release acetylcholine which :

→Increase permeability to potassium and decreases permeability to calcium and sodium

a-Decreases the heart rate **(negative chronotropic effect):**

-Increasing the permeability for potassium (efflux) and decreasing it for sodium and calcium, the resting membrane potential becomes more negative, the slow depolarization occurs slower (decreasing the slope of phase 4) takes more time to reach thresh hold ,the rate decreases.

b- negative inotropic and dromotropic effects on the atria only.

c-Has no effect on the contractility of ventricles. As vagus nerve does not supply ventricle only atria, so only atrial contractility is affected.

-In either type of stimulation (sympathetic or parasympathetic) the peak doesn't change as it follows "**the all or none principle**".

What if both sympathetic and parasympathetic get stimulated together ?

Sympathetic has predominant effect on contractility and parasympathetic on heart rate. contractility increases, and heart rate decreases.

What if both sym and para stop working ?

Both contractility and heart rate decrease

Lastly, Continuous parasympathetic stimulation of heart due to for ex.continuous pressure on vagi, Av node stops working, this is called heart block ,heart rate stops, no pumping, low blood supply to brain ,person faints and falls down (syncope) for 15 -30 sec, after which he wakes up although heart rate is still inhibited by parasympathetic stimulation ,how? within 15-30 seconds, the Purkinje fibers will generate the impulses which drive the ventricles. ,this is called **ventricular escape** as ventricles are not supplied by parasympathetic ,but because biological systems are not that fast it took 15 to 30 sec for for this to happen.

A-V block results in a syndrome called **"Stokes-Adams" syndrome**. What we usually do is that a new pacemaker (artificial) is implanted in A-V node, penetrating part of A-V bundle or in the right ventricular muscle.

"**Stokes-Adams" syndrome** refers to syncopal episodes that occur from cardiac arrhythmia