Physiology | Lecture 18

Conduction System of the heart Pt.1

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Heart is part of the excitable tissue in the human body

To eject blood, the muscle cells should receive electrical excitation

Human cells:

1. Excitable, performs its function only upon excitation

For example: Heart, smooth muscles, skeletal muscles, nervous system cells which can't perform their function unless excitation occurs.

2. Non excitable, performs its function without any need for excitation like endocrine cells that can secrete hormones without excitation.

What is excitation?

Reversal of membrane potential which means turning the negative potential inside cells into positive potential (ex. Turning the inner potential from -70 mV to 10mV)

How does it occur? By introducing positive charges to the interior of the cells like Na+ or Ca++or both.

Plasma is about 92% water. **The concentrations of substances in the interstitial and plasma (in the capillaries) are similar except for proteins because the capillary endothelium is permeable for many substances** unlike the plasma membrane of target cells which have some sort of selective permeability.

The channels can be in 4 conditions

closed and ready to open

Closed and not ready to open

Opened totally

Opened partially

We have about 1% of heart muscle cells, even though they are a part of the heart, there function is conduction not contraction (they lack actin and myosin).

SA node generates the impulse, and this impulse is transduced to:

1- left atrial myocytes; to contract and empty its content in the left ventricle

2-right atrial myocytes; to contract and empty its content in the right ventricle

Atrial contraction is not essential for living because blood can go to the ventricles without contraction (many people have Atrial Fibrillation and are alive).

3-av nodal cells that transduce the action potential to the ventricles (the only way to let the action potential reach the ventricles because there is an electrically insulator fibrous ring between the atria and the ventricles)

Ventricular contraction is essential for living.

Cells in the heart are connected **via gap junctions** (you can't stimulate a cell without stimulating the others) **(atrial syncytium and ventricular syncytium, because of the fibrous ring). two syncytia in the heart (between the two atria and between the two ventricles)**

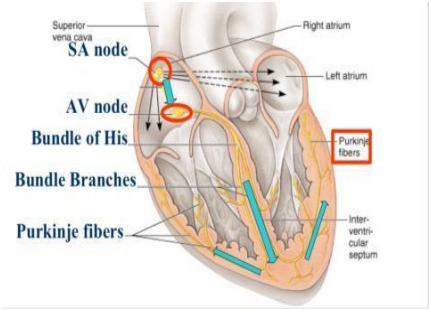
Excitation of the **ventricular** myocytes heart:

1. Excitation begins in the SA nodal cells (in the right atrium)
2. Excitation then travels to the atrioventricular

(AV) node (in the right atrium) by conductive pathways.

3. Then to the atrioventricular (AV) bundle (bundle of His)
4. Then to the left and right branches (in the inter ventricular septum) followed by Purkinje fibers
5. Lastly to the myocardium itself (the heart muscle)

This is the sequence of events produced by electrical behavior of the heart.



**** approximately 1% of cardiac muscle cells are autorhythmic rather than contractile**

- If SA node was the pacemaker of the heart (deciding its rhythm), heart rate would be between 70-80 beat per minute.
- If AV node was the pacemaker the speed rate would be 40-60 beat/min (less leaky to Na than SA node at resting potential)
- Purkinje fibers: 15-40 beat/min (less leaky to Na than AV node at resting potential)
- Normal heart rate (in adults) is between **60-100 beat/min.**

  Bellow 60 bpm is bradycardia and above 100 bpm is tachycardia

SA nodal cells are the fastest in reaching threshold therefore it is the pacemaker, but in some conditions, it doesn't function properly because of damage (inflammation or if the node is ischemic (dead)).

In this case, the AV node becomes the pacemaker and as a result, heart rate decreases and becomes **40-60 beat/min,** and people are **still able to live normally.**

If we stop communication between the atrium and ventricle (complete AV block (a cut in AV bundle for example)) Purkinje fibers become the pacemakers (The doctor said that but actually in this case the left and right branches should become the pacemakers) with a heart rate of **15- 40** which is **not enough for people to live** therefore an **artificial** pacemaker (we put battery with appropriate voltage beneath the skin and a we extend a wire to any cell in the ventricles, usually a cell in the right ventricle) is needed which gives impulse every 0.8 seconds which results in 75 beat per minute.

An example of damaged SA node is SSS (sick sinus syndrome)

**Note* SSS is a disease in which the heart's natural pacemaker (SA node) located in the upper right heart chamber (right atrium) becomes damaged and is no longer able to generate normal heartbeats at the normal rate.

- SA node is the pacemaker.
- AV node, AV bundle, Left and right branches, Purkinje fibers can be pacemakers, respectively. (They are named **latent pacemakers**, because they will not be pacemakers unless there is damage to the pacemaker before them. (For example, the bundle of his will not be the pacemaker unless the AV node is damaged. Also, the Purkinje fibers will not be the pacemaker unless the left or right or both branches are damaged)
- However, ventricular myocytes should never ever be the pacemaker (life threatening condition) if they become the pacemakers; they are named ectopic pacemakers.
- Ectopic pacemakers may be abnormal cells that become faster than the SA node, so it takes the pace making even if the SA node is intact.
- **Ectopic focus: An abnormality (due to ischemia for example) in which the heartbeat is driven by an ectopic pacemaker. (it can be treated by DC shock)**

Intrinsic Conduction System's Function: Initiate & distribute impulses so heart depolarizes & contracts in orderly manner from atria to ventricles.

SA node:

Also known as Sinus Node (Sinoatrial node):

- Specialized cardiac muscles
- small diameter (3 micro meter)
- connected to the atrial muscle.

Has Na leaky channels which produces the impulse for action potential (depolarization)(impulse is born in the node) therefore the SA node doesn't need external stimulus from neither the nervous nor the hormonal system.
SA nodal cells' Membrane potential increases to the threshold on its own, then complete depolarization and repolarization.
This means that SA nodal cells excite themselves by themselves, which is called autorhythmic, this means that the cell can bring the membrane potential towards threshold by itself… intrinsic ability to stimulate itself and generate action potential.
Intrinsic Automaticity: The ability to initiate its own beat.
Intrinsic Rhythmicity: The regulatory of such pace making activity.

Question: What is so special about SA nodal cells?

its resting membrane potential is unstable with respect to time (slow depolarizing wave) (slope is more than zero) because they are leaky to sodium at rest (without stimulus) autorhythmic.

It is the pacemaker because of its special membrane properties.

We already know that excitation is through the entry of positive charges to the cell like Na+ current or Ca++ current, then it moves to the neighboring cell and to next cells by gap junctions which transmit action potential between neighboring cells (**syncytium**) syn means together while cytium means cells, this means once a cell is stimulated neighboring cells all are stimulated (think of domino pieces) , there is also low electrical resistance between cells which in turn leads to excitation easily transferring between cells.

In short, once a cell in the heart is excited, the entire heart is excited. **Not entire heart but entire atria or entire ventricles.** This is important for the heart to contract as one piece to have an effective contraction. Unlike skeletal muscles where force of contraction is great, for example if you are holding something in your hand, the number of muscles used is different depending on what you are holding. In skeletal, in weak contraction, few fibers are contracted; others are relaxed. Contraction is graded not as syncytium.

This is called graded contraction in skeletal muscle and is possible due to the absence of syncytium (no gap junctions) each cell is on its own.

Na concentration outside the cell is 140 inside 14 moves by simple diffusion in the cell bringing positive charges inside. If the channels stay open Na will keep entering until the electrical force inside the cell starts repelling Na.

When chemical force of Na = the electrical force but opposite to each other then Na moving inside= Na moving outside.

*Movement never reachs zero only the net is zero.

Ion channels for the same ion on the cell membrane have different behaviors Voltage, ligand, …

How positive does the cell potential need to become in order to stop Na entry to the cell? (How much electrical force do we need?)

=-61log (in/out)

-61log (14/140) = -61 * -1=61 mV

This is the potential that when reached stops sodium entry. If the

resting membrane potential= -60

In depolarization membrane potential becomes 10 How much

sodium enters the cell ?

A very small amount that is not measurable.

What is the sodium concentration outside and inside the cell at the end of depolarization ? The **same** as before.

If you want equal concentration on both sides you will need 500000 depolarization, 1 action potential doesn't change the concentration, and still the increase in Na inside is sent back outside by the Na k pump to maintain the same gradient.

Na keeps entering the cell trying to achieve E_{Na} to reach **equilibrium where no forces would be affecting sodium ions or pushing it in any direction.**

(net movement of ions is zero)

Chemical forces = electrical forces only in quantity but **have opposite directions**

Calcium concentration inside cell is 10^-7 and outside the cell is 10^-3

Outside is 10000 more times than in the cell

E_{ca} (When the electrical gradient is equal to the chemical gradient and opposite to it) =

-61/**2(valence)** * log (10^-7/10^-3) = -30.5 *-4 =~ +120

K+ in is 150 outside 4

E_k= -61 * log (150/4) = -90 mV

Na+ 140 out and 14 in

E_{Na}= -61 * log (14/140) = +61mV

Each ion tries to get the membrane potential close to its own equilibrium potential.

The movement or flow of each ion inwards or outwards is called a current and is represented by the letter I.

I = DF / R

R=resistance

Flow is directly proportional to DF and inversely proportional to the resistance.

Flow means anything happening or moving per unit time.

Resistance tells you about the difficulty of the process, but it is a vague expression so to make it easy to calculate we take the permeability instead

I=DF * K where K is the permeability.

Permeability tells you how easy the process will be and is used for non charged molecules like aminoacids and glucose.

For the charged ions it is called conductance (g), g could be 0 when channels are completely closed ,1 where channels are complete open or any number between 0 and 1

I= DF * g

The driving force might be 10000, but the current would be zero because the conductance is zero.

What is the driving force?

Em is the membrane potential

Ex is the resting membrane potential for the certain molecule. (Ex: is the equilibrium potential for that specific ion)

The Driving Force (DF) = Em-Ex

For example, if the membrane potential is –90:

I_k = (-90-(-90)) * g_{k+}= 0 the net movement of K+ is zero

So to generate a current we need both a driving force and conductance. If there is no conductance for Calcium ions

for example: I_{Ca++}= (-90-120) *0= 0

Resting membrane potential

What is common between excitable and non-excitable cells?
Both have resting membrane potential

Even though all these cells are surrounded by the same concentration of ions, they have different resting membrane potential, why?

The ion conductance is different, and the ion with the highest conductance (highest current) determines the resting membrane potential.

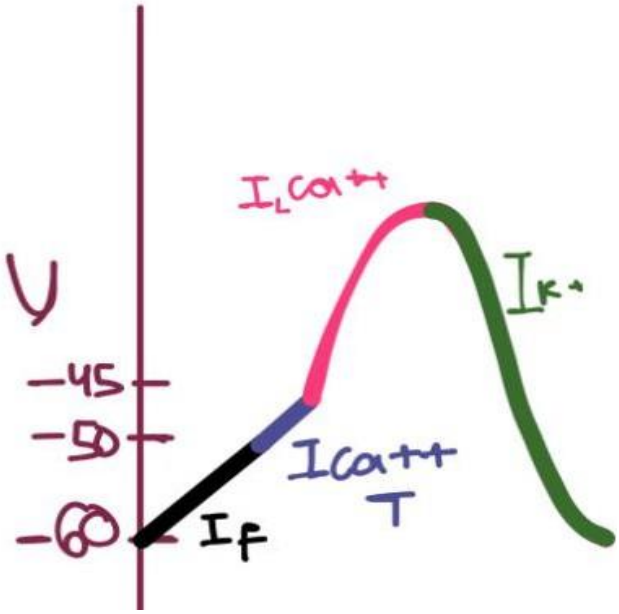
For example, when the resting membrane potential is -80, we can tell that potassium has the highest conductance and is very low for Ca and Na ions.

In SA nodal cells, potassium has the highest conductance, but it is also affected by sodium conductance.

The resting membrane potential is about -60mV

1. In SA nodes I_{Na} is called **funny I_f because it only opens till the potential reaches -50mV.**
2. There are also transient calcium channels (T-type) which open when the potential is -50mV and close when it reaches -45mV.
3. Finally, long lasting calcium channels (L-type) open, and depolarization occurs until it reaches +10mV then it closes and potassium channels open leading to repolarization until reaching resting membrane potential.

From –60----> -45 phase 4
-45----> +10 phase 0
+10----> -60 phase 3



**T-type is slow, which means that the change in voltage related to time is low when comparing it to L-type. However, the L-type is long-lasting because it opens For a longer time.

Additional Resources

رسالة من الفريق العلمي:

For any feedback, click the code.

Versions	Slide #	Before	After
V0 → V1	4 6	Less clear -	More clear and precise Addition of the diameter of SA node cells
V1 → V2			