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Lec 1 (CVS)

-The heart is a muscular involuntary organ

(الاوامر بتيجي من القلب نفسه مش من عصب فنقدر نقول ان اللي بيتحكم في القلب هو ال autonomic nervous system)

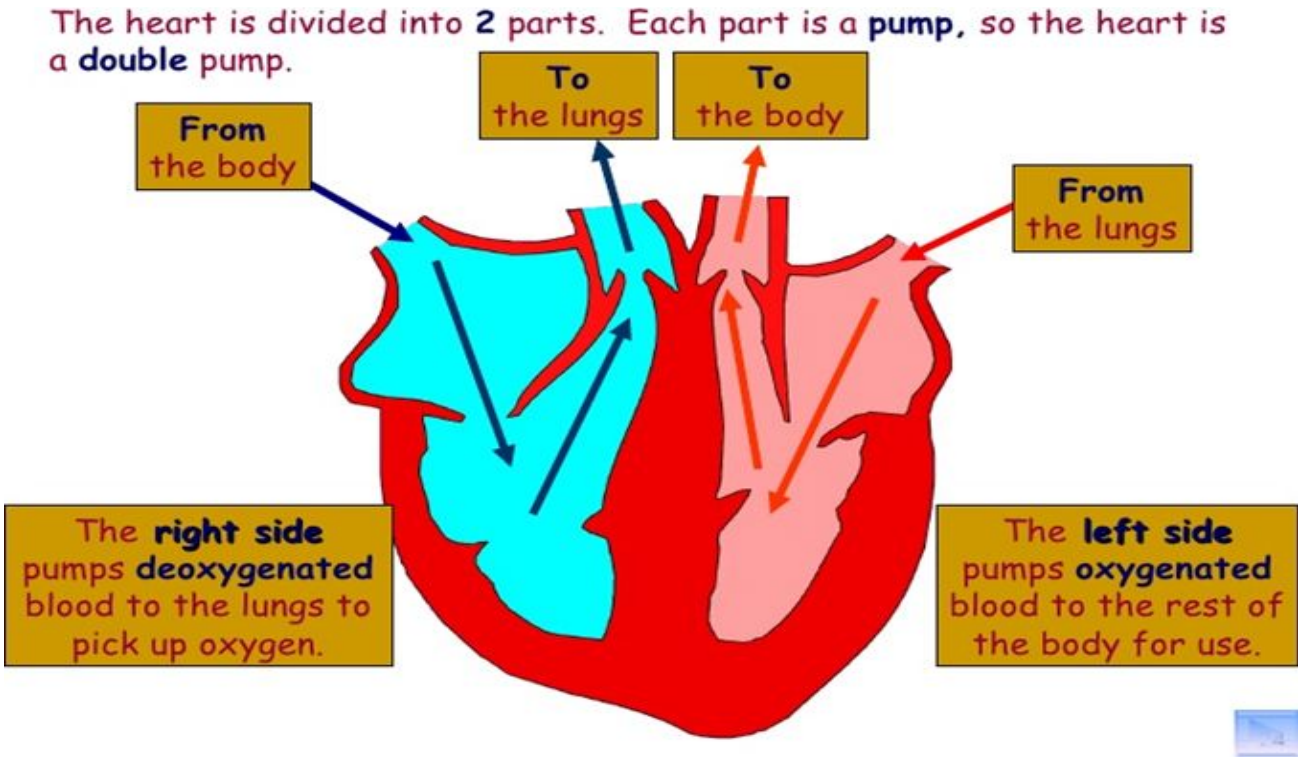
*autonomic nervous system (A.N.S) is divided into sympathetic and parasympathetic nerves

-**Location**: in the thorax behind sternum, it's an inverted (مقلوب)cone with base at top and apex beat located towards the left (below the left nipple)

*heart located at the middle in mediastinum (منطقة في نص الصدر) but its apex only directed towards the left

*few of people are dextrocardia (their apex of the heart directed towards the right)

-pumps of the heart:



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*the right-side pump is called **volume pump** (لان الجدار بتاعها رفيع ف مش محتاج ضغط عالي عشان ينقل الدم) that pumps blood to lung against low resistance (Because the pulmonary vascular resistance is very low هتتشرح كمان شوية)

*The left-side pump is called **pressure pump**
that pumps blood to rest of body (aorta بيحتاج ضغط عالي عشان يتغلب علي الضغط بتاع ال) against high resistance

*الاختلاف بين ال2 pumps دول عشان يحافظوا علي ال cardiac out يعني كمية الدم اللي داخلة تساوي الكمية اللي خارجة من القلب

-Each pump is composed of:

1. Atrium: -has thin muscular wall

لان اول م الصمام اللي بين الatrium و ال ventricle يفتحوا, الدم بيضخ لوحده من الatrium لل ventricle بال pressure gradient ف مش محتاج جدار سميك

-Acts as blood reservoir (خزان)

-contract weakly to pump blood to ventricles

2. Ventricle: -thick muscular wall

-pumps blood at great force through the arteries

-Valves of the heart:

1.The Atrio-ventricular valves (A.V)

-permit the passage of blood from atrium to ventricle in one direction

-composed of right AV valve that called tricuspid valve and left AV valve that called bicuspid valve (mitral valve)

2. The semilunar valves (SL)

-Permit the passage of blood from ventricles to arteries in one direction

-composed of aortic valve (that separates left ventricle from the aorta) and pulmonary valve (that separates right ventricle from pulmonary artery)

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*Pulmonary artery is divided into 2 parts (right and left) toward the 2 lungs

*Aorta is composed of جزء صغير طالع لفوق اسمه ascending aorta, وبعدها بيلف وبيتسمي aortic arch, وبعدها ينزل لتحت جوا ال thorax and abdomen وبيتسمي descending aorta

-The circulation:

1. General or systemic circulation

-Heart pumps oxygenated blood through aorta of the left ventricle (pressure pump) to the all body organs. The blood is distributed to all body organs through arteries, arterioles then capillaries.

-Than gas and nutrients exchange will occur

الدم بياخد ال waste products وبيدي للجسم ال nutrients وبعدها يتجمع الدم جوا small venules
وتتجمع بعد كده في veins اكبر ف اكبر لغاية م كل ال veins تصب في ال

superior vena cava (upper part of the body) and inferior vena cava (lower part of the body) which will open in the right atrium

-Then blood will be ejected from right atrium to right ventricle through the tricuspid valve

2. lesser or pulmonary circulation

-Right ventricle (volume pump) pumps deoxygenated blood to pulmonary artery through pulmonary valve. The blood is distributed into pulmonary capillaries in lungs

-Then gas exchange will occur by getting rid of excess CO_2

-Then the oxygenated blood will return back through the pulmonary veins to the left atrium

-Then blood will be ejected from left atrium to left ventricle through the bicuspid (mitral) valve

*The pulmonary capillaries are the junction points between the pulmonary arteries and the pulmonary veins

*Pulmonary veins (4 veins) carry oxygenated blood (unlike the rest of veins), while pulmonary arteries carry deoxygenated blood (unlike the rest of arteries)

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-Functional histology of cardiac muscles:

1. fibrous skeleton of the heart

2. ordinary cardiac muscle fibers

-cardiac fibers are striated as skeletal muscle fibers but it's involuntary unlike the skeletal

-Cardiac muscle fibers are arranged in a branched network

-The branches of muscle fibers are connected by **intercalated discs** which have a lot of gap junctions with low electric resistance (so the cardiac excitation waves spread between fibers very fast due to the low resistance)

-Cardiac muscle acts as a functional syncytium, atria and ventricles have a separated functional system (they act as single muscle fiber)

3. Junctional tissue (ALL OF THE UPCOMING STRUCTURES ARE ILLUSTRATED ON THE NEXT DIAGRAM, THANKYOU!)

-They're specialized cardiac muscle fibers that initiate and propagate the cardiac excitation

-القلب بيطلع ال impulse بتاعته بسبب ال electrical activity يعني بيحصل ف action potential بيحصل ال contraction فيضخ الدم وده وظيفة القلب الاساسية

-طب البداية بتاعت ال excitation في القلب عشان يضخ بتيجي منين؟... بتيجي من اجزاء في القلب specialized or modified fibers حصل فيها تعديل وبتتسمي conducting system to heart وبتقدر تولد الاشارة الكهربية وهما 3 اجزاء

(AVN, SAN and purkinje)

a) Nodal tissue (autonomic pacemaker fibers هيتشرح الاسم ده كمان شويه)

-initiate cardiac impulse

-composed of:

1- Sino-atrial node (SAN)

-Opens in the posterior wall of the right atrium below and medial to the opening of the superior vena cava

-the impulse starts in it then moves into AVN

2- <u>Atrio-ventricular node (AVN)</u>

-Opens in the right side of the inter-atrial septum at the junction of the atrium and ventricle

*The waves move from a node to another node through inter-nodal fibers

<u>b) Conducting system:</u>

-conducts cardiac excitation wave from atria to ventricles

-composed of:

1-<u>Atrio-ventricular bundle (AV) (Bundle of His)</u>

-Arise from AV node

-The only electrical connection that transmits the impulse from atria to ventricles

-pass through the fibrous skeleton of the heart to the upper part of the interventricular septum then it divides into 2 branches right and left branches, one for each ventricle

2-<u>Bundle branches</u>

-these branches pass down in interventricular septum under endocardium (الغشاء المبطن للقلب من جوا) to the apex of the heart then branch up to the base of the heart (in the lateral wall of the ventricles)

-then the branches become very small and called purkinje fibers

<u>3-Purkinje fibers</u>

-These purkinje fibers arise from each bundle branch that enters into the ordinary ventricular muscle fibers and also pass from endocardium to the epicardium (اول طبقة تحت الغشاء الخارجي للقلب)

الfibers ده بتختلط مع ال interventricular muscle fibers لانها سميكة ف لازم fibers تدخل بينها عشان تنقل الاشارة الكهربية جواها

***The conclusion:** The impulse moves from SAN → AVN → Bundle branches → purkinje

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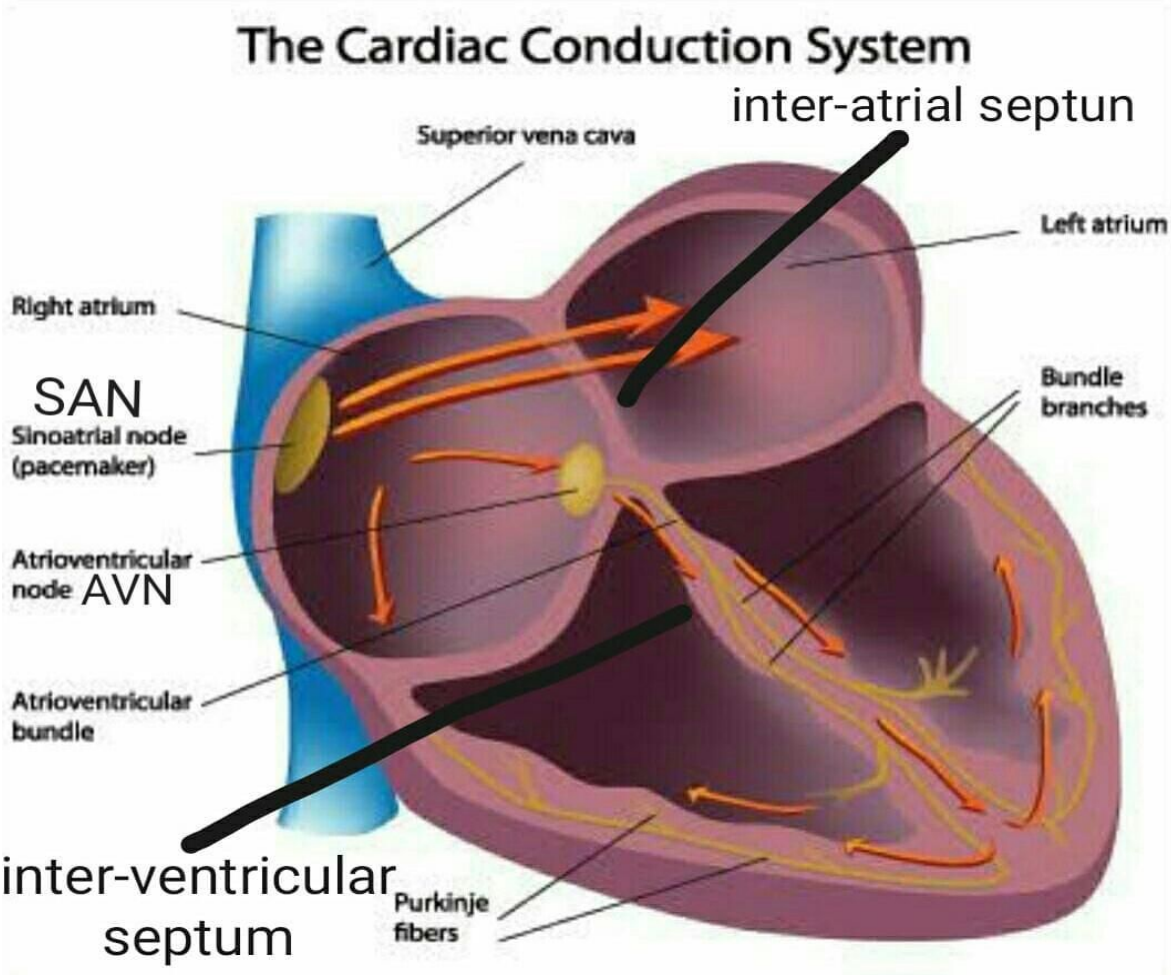

Cardiac properties

1)Rhythmicity

2)conductivity

3)excitability (when impulse leads to action potential)

4)contractility

1)Rhythmicity (automaticity):

● it's the ability of cardiac muscle to beat regularly and initiate its own regular impulses independent of any nerve supply

(يعني قدره عضله القلب ان ضرباتها تكون منتظمه وتخلق هي الضربات دي من غير اشارة عصبية)

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● it's a property of the cardiac muscle so, it's myogenic (عضلية))in nature
● it is present in certain fibres of the heart (not all the heart fibers), these fibers can initiate the cardiac impulses at different rates,
and they are:-
1)Sino-atrial node (S.A.N): produces 90 impulses/minute (highest rhythm)
2)Atrio-ventricular node (A.V.N): 60/minute
3)Purkinje fibers: 30/minute

The pacemaker of the heart:

●It's the part of the heart that has the highest Rhythm, and all the heart obeys it. under usual conditions it's the S.A Node (because its rhythm is the highest)
● but in pathological conditions, if the S.A node stops functioning, the A.V node will be the pacemaker and the producer of the heartbeat, this is called "AV nodal rhythm"
●And if both A.V and S.A nodes stopped functioning, the purkinje fibers will be the pacemaker
Q)Give reason: The normal heart rate under resting conditions is about 70/ minute although the normal rhythm of S.A node is 90/minute.
Due to the vagal tone, which is continuous impulses from the vagus nerve that decreases the high rate of sinoatrial node to about 70/minute
Q)Why if the vagi is cut or blocked by drugs,the heart rate will increase up to 120/ minute?
due to the sympathetic tone which will increase the heart beat (as mentioned before)

- so under resting conditions,, the parasympathetic has a higher effect on the heart then the sympathetic

● if we cut the sympathetic supply too, the heart becomes **denervated** (not supplied with nerves), so the heart rate will be 90/minute (the rhythm of S.A.N)

Q) T or F:-

1) during rest, the heart is supplied by parasympathetic nerves only ? (F)
Why False?
Because whether the heartbeat is 60 or 120, it is supplied by both sympathetic and parasympathetic nerve supply, but during rest, the vagal tone is much more powerful and predominant than the sympathetic tone, so the heart beat is decreased (والعكس صحيح))

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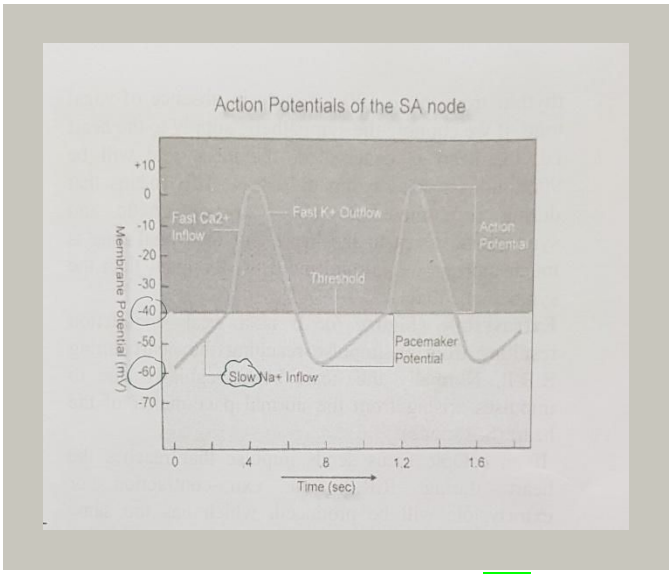
Properties of the Pacemakers:

1)They have unstable membrane potential (because it doesn't reach R.M.P) and they can produce impulses without the need for nerve supply, this ability is called **prepotential** or **diastolic depolarization** (because it takes place in diastole)

2)There is no plateau in their A.P

Prepotential or pacemaker potential (A.P of pacemakers):



●It is slow partial depolarization starting from -60 which occurs during diastole (relaxation) of the heart, and when the firing level is reached ,A.P will be produced and will spread over the cardiac muscle to contract (Systole)

●It is due to small increase in Na+ inflow, with no K+ outflow. It continues until reaching firing level (-40)

●once -40 is reached, Calcium channels on the membrane called "**voltage regulated(or activated) fast-calcium channels**" are opened, to allow the rapid inflow of Calcium

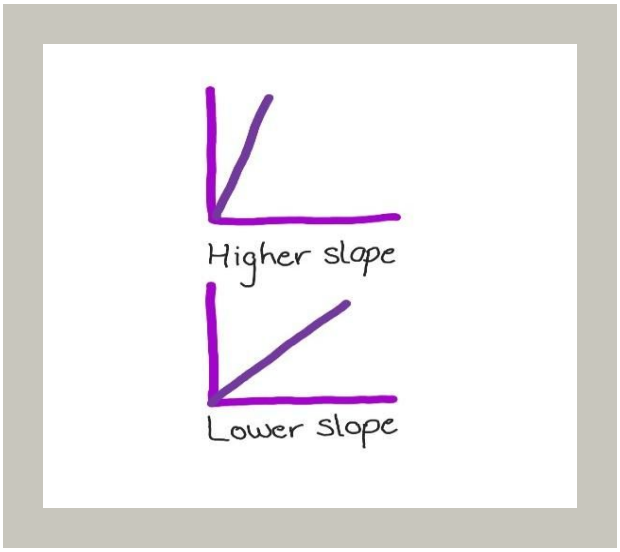
●Q)Give reason for the importance of the opening of voltage regulated fast-Ca channels.

To produce the rising phase (depolarization phase) of the A.P, to make the peak (قمة))of the curve slightly above 0

●Then repolarization takes place by K outflow (as mentioned before) till the membrane potential reaches -60 only (not the R.M.P which is -90)

●Then Na channels open slowly to cause depolarization from -60 to -40 and then Calcium channels open (Na first then followed by Ca) and so on...

The slope of diastolic depolarization determines the heart rate:



1)when the slope decreases, the heart rate decreases (bradycardia)

2)when it increases, the heart rate increases (tachycardia)

2)conductivity:

● it is the ability of the cardiac muscle to conduct the excitation wave

(قدرة عضلة القلب علي نقل الاثارة)

●the rate of conduction of cardiac impulse is different over different parts of the heart (slowest at A.V.N and fastest at purkinjie fibers)

Q) Give reason for the slow conductivity of A.V.N

1)To give a chance for the cardiac impulse to cover both atria before it reaches the ventricles so that the atria contract and empty their blood content before the ventricular contraction

(لازم الاثاره وهي بتعدي على ال A.V.N تبطأعلشان تلحق تغطي كل الatria قبل ما توصل لل venteicles علشان ما يحصلش contraction للاثنين مع بعض علشان ما تبقاش حاله مرضيه)

2) to prevent abnormal high rhythms originating in the atria from reaching the ventricles

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For illustration:

(ساعات كده ممكن تحصل حاجه مش طبيعيه ان ال atria جزء منها يبدا يبعت impluses to A.V.N
الحته دي بيكون اسمها ectopic focus و ممكن تبعت حوالي 300/الدقيقة فال A.V.N بيحمي القلب منها،
ويعدي منها 150 بس مثلا، النبضات هاتبقي سريعة اه بس مش مميتة زي ال 300)

Q) Give reason for the fast conductivity of A.V bundle of his, it's branches and purkinje fibres

Because the ventricular muscles are thick, and the excitation wave must cover both ventricle muscles in very short time, so that they contract in 1 time as one syncytium (one unit), to pump the blood against the pressure resistance

(لان العضلات بتاعت ال ventricles تخينه فا المرور من خلالها بسرعه بيكون صعب فلازم ال
conductivity بتاعت الpurkinje و كده تكون عاليه جدا علشان تلحق تمر خلال ال 2 ventricles في
نفس اللحظه عشان مايحصلش contraction في حته قبل حتة)

3)Excitability:

●It's the ability of cardiac muscle fibres to respond to an adequate (threshold) stimulus (from S.A node for example)

● it's response رد فعلها))is the action potential that is conducted along the membranes of muscle fibres, and is followed by mechanical response (contraction) of the muscles

(رد فعلها انها تولد الaction potential اللي هايتبعها الcontraction)

● the cardiac muscles are present in polarized state (as mentioned before), the negative charges inside while the positive outside

●their resting membrane potential is between -80 and -100(approximately -90)

● **R.M.P is due to:-**

1)selective permeability of membrane

2)sodium potassium pump mechanism

(as mentioned before)

4)Contractility:

-It's the main function of the heart that occur during systole to pump blood against the peripheral resistance

-This contraction causes pressure gradient in the cardiovascular system فرق الضغط
ده بيحصل عشان يساعد الدم انه ينتشر في الاوردة والشرايين

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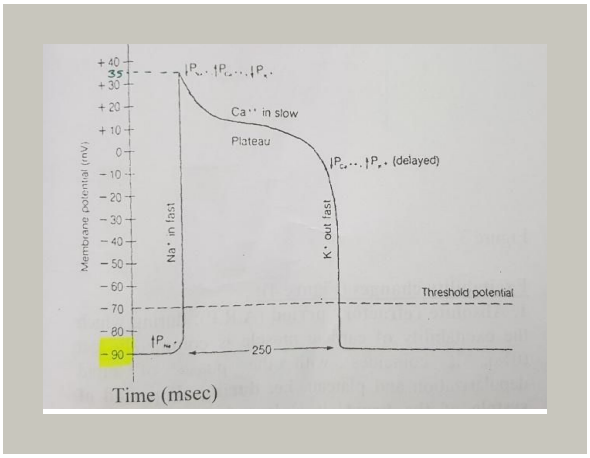
-Mechanism of heart contraction is nearly the same as the skeletal muscle (excitation-contraction coupling)

-Cardiac contraction is affected by extracellular ca^{+2} because the spread of AP over cardiac muscle fibers stimulates Ca^{+2} movement from outside of the fibers to inside

الCa^{+2} مش كله جاي من القلب فيه شوية بيجوا من بره ف ده بياثر علي عضلة القلب, فلو نسبة الCa^{+2} قليلة (hypo) ف ده هيسبب tetany وعلاجه Ca^{+2} intravenous بس لو اديتهاله مرة واحده ممكن يسبب cardiac arrest , ف ده دليل علي ان ال Ca^{+2} extracellular بياثر علي القلب

Action potential of cardiac muscle:



When the cardiac muscle is excited:

1)The potential difference between the inside and outside of the membrane will decrease gradually then lost (partial depolarization then **complete depolarization)** to reach 0

2)Then **reversal of polarity** occurs (outer -ve and inner +ve) to reach +35 mV

Q) Why the depolarization and Reversal of polarity forms the rapid ascending limb of the action potential ?

due to rapid increase permeability to Na which flows rapidly from outside to inside according to concentration and electric gradients (due to opening of fast Na channels)

3) After Reversal of polarity, repolarization starts and it has three phases:-

●**Phase 1:** first small rapid repolarization,Why?

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due to entry of Cl- ions which helps in repolarization(as it is -ve) and outflow of K+

●**Phase 2:** the repolarisation slows down forming a plateau (balance between outer and inner +ve) near 0 mv, Why?

Due to balance in small inflow of calcium and sodium ions ,and small outflow of potassium ions

(يعني الموجب اللي جوه بيكون تقريبا قد الموجب اللي بره)

* the A.P in atrial fibers have less prominent plateau, and lasts for 150 ms, while in ventricular fibres it's prolonged to about 300 ms

●**Phase 3:** rapid repolarization takes place till membrane potential reaches the resting level,why?

Due to the delayed مؤجل)) increase in K outflow from inside to outside of the fiber to complete the Repolarization process

(كان متعطل في ال plateau بعدين طلع كله مره واحده بسرعه)

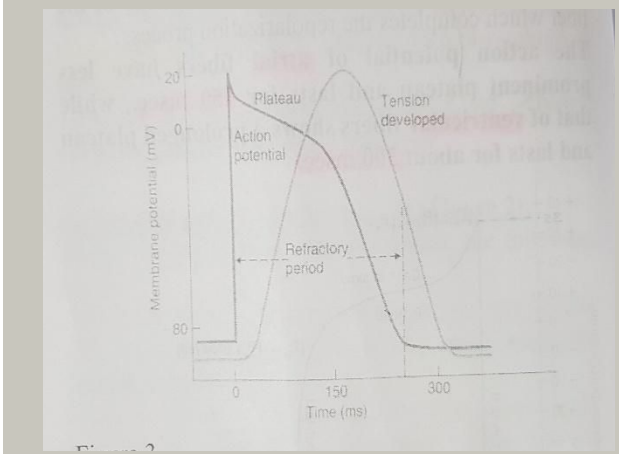
Q)what are the only differences between A.P of skeletal and nerve,and A.P of cardiac muscle fibers?

1) the entry of -ve chloride ions that helps in rapid repolarization

2) the small inflow of calcium and sodium during repolarization which forms the plateau

3) there is no hyperpolarisation

Relation between mechanical response and A.P of the heart:



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●**The mechanical response consists of:**

systole (contraction) followed by **diastole** (relaxation)

●It lasts 1.5 times as long as the action potential
(يعني الانقباض و الانبساط مدتهم اد ال A.Pمرة) ب 1.5

●The **systole** starts **after depolarization** and ends by the end of the plateau

●The **diastole** starts **at the end of the plateau** (the rapid phase of repolarization)

●A.P contains all systole, but only the first half of diastole, so, the repolarization is completed **by the end of first half of diastole**

●while the **second half** of diastole continuous after the ending of A.P

To conclude:

●The mechanical response starts just after depolarization ends and it is completed by the end of the second half of diastole (which is after the A.P), and that's why it equals 1.5×A.P

●The peak of the systole in the mechanical response curve is found at nearly the same level of the ending of the plateau in the A.P curve (as shown in the above figure)

(يعني اعلي حته في curve ال mechanical بتكون تقريبا على نفس الخط الطولي اللي بينتهي عنده ال plateau اللي في curve ال A.P (ال2 curves في الصورة))

Excitability changes:

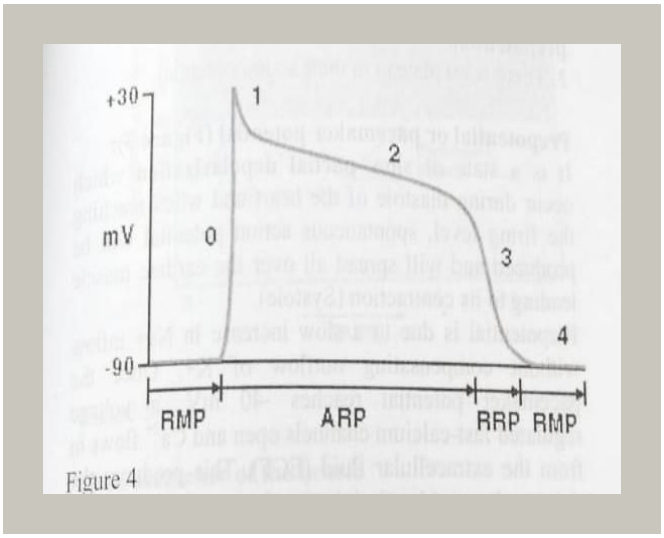

Figure 4

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1)Absolute refractory Period (A.R.P):-

●During ARP, the excitability of cardiac muscle is completely lost (dropped down to 0%), it coincides with the rapid rising depolarization phase and plateau (during all Period of systole of the heart)

● it's duration is longer than that of skeletal muscle

● if any stimulus reaches the heart during this period, there will be no response

Q)What is the significance of long A.R.P of the heart?

To prevent tetanic contraction (relaxation اللي كان بيمنع العضلة من ال) of the heart which is fatal, as the main function of the heart is pumping, it contracts to eject blood then relaxes to be filled again to re-pump it and so on....,so, continuous contraction (tetanus (تشنج)) will stop the circulation

ربنا خلق ال A.R.P في القلب تكون مدتها طويلة عشان القلب مايستجبش لاستثارة جديدة و هو لسا في حالة الانقباض ، لأن دا هيخلي فترة انقباضه الاضعاف و دا هيمنع انه يتملي تاني عشان يرجع يضخ الدم تاني ...فا دا هايخلي الجسم مجالوش oxygenated blood لمدة كبيرة فا يموت)

For illustration:

The A.R.P makes the time between first response and a second response 300 ms minimum, which protects the heart from tetanus which causes cardiac arrest (death), it coincides all systole, and it contains a small part of diastole

2)Relative refractory period (R.R.P):

●During it, the excitability recovers again gradually from 0% to 100% . so, strong stimulus can produce weak response

●It coincides with the rapid repolarization phase of action potential (the first half of diastole)

-Factors affecting contractility:

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1. All or none rule

-It means the cardiac muscle contracts maximally or doesn't contract at all

-The minimum stimuli will stimulate **all** cardiac muscle fibers (due to the functional syncytium of the heart as mentioned before)

لان ماينفعش احصل علي gradient response وده لان ال cardiac muscle fibers كلها متداخلة مع بعضها, يعني اول مايجي الاشارة هاتنتشر كلها بسرعه عالية عن طريق ال intercalated disc and (purkinje fibers (as mentioned before

-Changing of stimuli strength will not affect the strength of contraction

-The contraction strength can be changed by mechanical, nervous (sympathetic of parasympathetic) or hormonal factors under natural conditions

2-Tetanic (continuous) contraction

-It's fatal to the cardiac muscles due to its long ARP (as mentioned before)

-It **can't occur in cardiac muscles** (القلب بيحمي نفسه من انها تحصل) because the cardiac muscles during systole don't respond to any other contraction except after diastole of the heart to be refilled with blood

فترة ال ARP في القلب هي من كل ال systole وجزء من ال diastole, و زي ماقولنا قبل كده ان الفترة ده القلب مش بيستجيب لاي اثارة...طب ده ليه؟

لانه لو القلب استجاب لمؤثر تاني وهو في فترة الانقباض ده هيخلي ال circulation بتاع الدم في الجسم يقف و ده لان القلب هو مضخة الدم للجسم وبيملي في فترة الdiastole ف لما يخلص فترة الsystole ويجي مؤثر علي طول بعدها كده مش هيكون دخل في فترة الdiastole اللي بيملي فيها الدم , ف كده مش هيلاقي دم يضخه ف هيقف ال circulation

3-Length-tension relationship (starting law)

-It states that: there is directly proportional relationship between the cardiac contraction force and initial length of the cardiac muscle fibers **within limits**

-increasing initial length of cardiac muscle fibers gradually causes increase in force of contraction, till the length reaches its maximum (called L-max)

ومثال علي ده لو قطعنا عضلة الbiceps اللي في الدراع هيقل طولها فتقل قوتها والعكس صحيح

-After L-max, the increasing of length will decrease the contraction force

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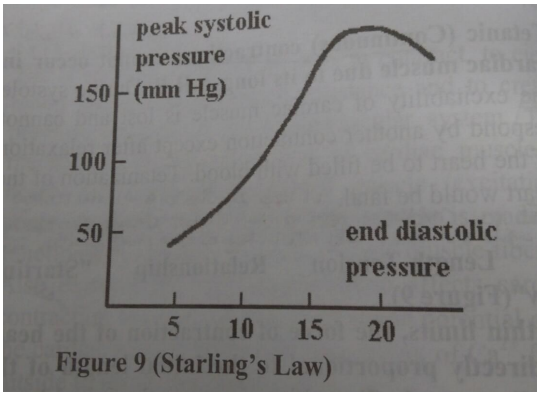

Figure 9 (Starling's Law)

-the reason of being the contraction force at L-max is the maximum is due to the sarcomere length (=2.2 micron), at which the number of cross bridges between actin and myosin are increased to maximum so the contraction will be at the maximum

ولو زاد طول الساركوميرعن طوله ده هتبعد ال cross bridges عن بعضها في مش هيتشابك الاكتين بالمايوسين ف هتقل الcontraction force

*Wisdom of the heart

-under normal conditions, there is a relation between the initial length of ventricular muscle fibers and the amount of venous return in ventricles(EDV end diastolic volume)

-So, increasing of venous return will increase the initial length and cardiac contraction force too to be able to pump all blood coming to it

بدل كلمة initial length of the muscles هنحط كلمة end diastolic volume (وده معناها كمية الدم اللي موجودة جوا الventricles في نهاية ال diastole), و ده بيزيد اول يقل علي حسب كمية الدم اللي داخل ليها وكل مابتزيد كمية الدم بيزيد قوة انقباض عضلة القلب عشان تضخ كمية الدم الزيادة اللي داخلالها و لو ده محصلش وخزنت شوية دم ممكن يحصل heart failure

4-Frank-starting relationship

A) Positive inotropic:

It's an effect of factors that increase the cardiac contraction force

EX. 1-increasing of sympathetic stimulation

*Ventricles are not supplied by parasympathetic (mentioned before)

2-Drugs as digitalis بيحسن اداء عضلة القلب

B) Negative inotropic:

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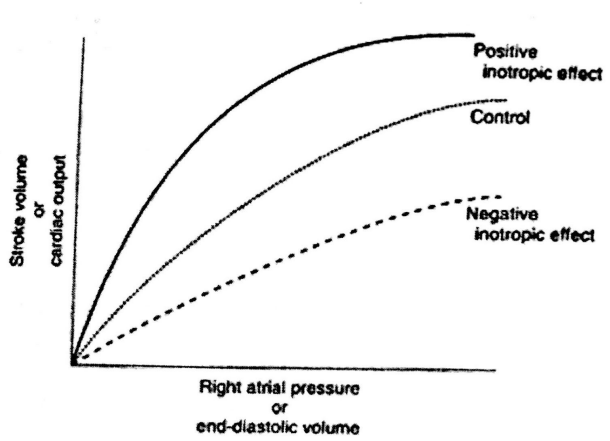
It’s an effect of factors that decrease the cardiac contraction force

EX. Vagal activity of atrial muscle (parasympathetic which affects atria only)



*عند نفس الطول لو ال curve حصله shift لفوق ده معناه ان عند نفس الطول (end diastolic volume)
ال force بقيت اعلي وده اللي بيعمله ال positive inotropic والعكس صحيح