The Cardio-VASCULAR System

- ○ Anatomy
- ○ Histology
- ○ Pathology
- ○ Pharmacology
- ● Physiology
- ○ Microbiology

Lec #: **10**

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Done By: **Nedal Al Sabatin**

- ○ Handout
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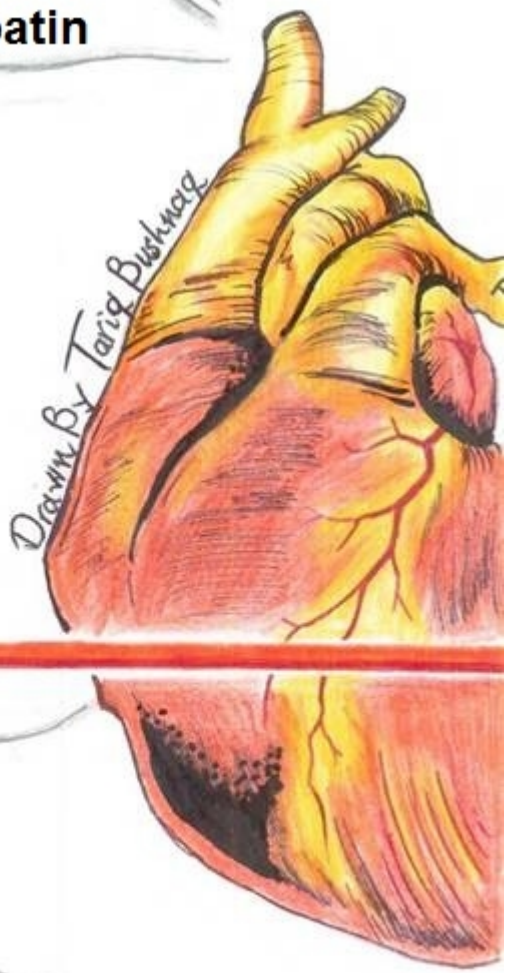

CARDIAC OUTPUT REGULATION

Factors that affect stroke volume:

1. Preload
2. Contractility
3. Afterload

Cardiac output=stroke volume*heart rate

Stroke volume=EDV-ESV

Ejection fraction=SV/EDV

The **preload** is the amount of pressure found in the ventricle before it contracts, so the preload is caused by the passive tension. It can be called the end diastolic pressure. If the end diastolic volume "EDV" increases, the passive tension in the ventricle would also increase, which results in the increase of end diastolic pressure (the preload). So the preload is proportional to EDV. According to Frank-Starling law, as the length of the cardiac muscle increases (which happens as the EDV and the preload increase), the contracting force (active tension) of the cardiac muscle would increase. This causes an increase in the contractility of the heart which causes an increase in the stroke volume and the ejection fraction of the heart (as discussed later).

The **afterload** is the minimum amount of pressure that has to develop in the ventricle in order to eject the blood from the heart (through the semilunar valves). This pressure is determined by the **diastolic pressure** of the aorta in the case of left ventricle, and the pulmonary artery in the case of right ventricle. The diastolic pressure in these main arteries is the back pressure being applied on the semilunar valves which must be overcome by the ventricular pressure in order to open these valves; ejecting blood.

The **contractility** is the measure of the inotropic effect. It is the force developed by the cardiac muscle, and is determined (mainly) by the end diastolic volume (EDV). Contractility is measured by the ejection fraction "EF", which is the percentage of the blood ejected from the total blood volume in the diastole (stroke volume/EDV). In order to measure the contractility using the ejection fraction, the **EDV must be fixed**, then, the stroke volume would be measured, and the EF could be calculated. For e.g a negative inotropic effect results from a decrease in the the SV when the EDV is held constant.

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Frank-Starling Law:

It states that the preload (which is proportional to EDV) is the critical factor that determines the stroke volume of the heart. This is because the contractility of the muscle increases, as its optimal length for contraction is yet not attained.

Slow heartbeat and regular exercise increase the venous return to the heart, thus, increase the EDV, so the stroke volume increases.

Blood loss causes a decrease in blood volume, which decreases the heart's venous return and the EDV, so stroke volume is decreased. Extremely rapid heartbeats also cause a decrease in stroke volume; this occurs because the rapid heart rate decreases the time of the cardiac cycle, this decrease in the cardiac cycle period mainly occurs on the account of diastole's time, thus, the decrease in the time of the diastolic period is less than that of the systolic period, eg: if there was a decrease in the cardiac cycle time from 0.8 sec to 0.6 sec, the systole's time decreases from 0.3 sec to 0.28 sec (a 0.02 sec decrease), while diastole's time decreases from 0.5 sec to 0.32 sec (a 0.18 sec decrease). The diastole's time is important as it determines the amount of blood that enters the heart; if it was reduced, then, the heart will receive less volume of blood, EDV decreases, and the stroke volume decreases. As the stroke volume (volume of blood ejected per heartbeat) decreases, the cardiac output (volume of blood ejected per minute) might also decrease, and that is although the heart rate is increasing!

This is explained as follows: when someone wants to make an exercise, he is advised not to exceed 90% of the maximum heart rate of the person, which is calculated by "220 - age of the person", because after exceeding 80% of the maximum heart rate, cardiac output starts to decrease, that is because diastole's time is highly decreased, so there is no enough time for the heart to fill with blood, and the stroke volume will be highly decreased, thus, decreasing the cardiac output.

Cardiac Output:

Cardiac output is increased either by increased heart rate or increased heart's stroke volume or increased both.

Heart rate is increased by extrinsic factors, eg: the sympathetic nervous system increases heart's rate (while parasympathetic system decreases heart rate), some chemicals like calcium ions, catecholamines increase the heart rate (while acetylcholine decreases the heart rate). Thyroid hormone also increases heart rate like what occurs in hyperthyroidism diseases, while hypothyroidism decreases heart rate.

Stroke volume is increased by increasing the preload and contractility as discussed previously, also, decreasing the afterload increases the stroke volume. As the afterload decreases, blood would start to be ejected from the heart at a lower pressure, allowing

for a higher blood volume to be ejected from the heart. On the other hand, hypertension causes an increased afterload, which causes the heart to contract harder in order to overcome this high overload, and at the end, less stroke volume would be ejected from the heart.

Thus, the hypertension causes two problems to the heart:

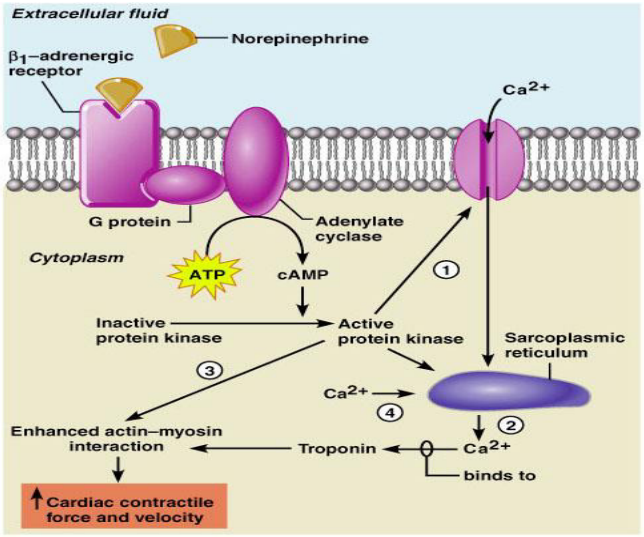
1) It increases the work needed to be done by the heart, so it increases oxygen demand

2) Less oxygenated blood would reach the coronary arteries, as the stroke volume of the heart decreases, this even exacerbates the first complication. These complications lead to infarctions in the heart and ischemic heart diseases.

In a nut shell: you affect the heart rate by affecting the preload, afterload, contractility and heart rate.

Extrinsic factors that affect the stroke volume include:

- ✓ Sympathetic nervous system, which causes a positive inotropic and chronotropic effect that increases contractility and stroke volume. Parasympathetic nervous system does not affect heart's contractility as it does not supply the ventricular musculature.
- ✓ Calcium ions, positive inotropic drugs and certain hormones like thyroxine increase heart's contractility and stroke volume.
- ☒ Acidosis (decreased pH) decreases contractility (negative inotropic effect)
- ☒ Increased extracellular potassium (hyperkalemia) decreases contractility.
- ☒ Calcium channel blockers decrease contractility by decresing intracellular Calcium.

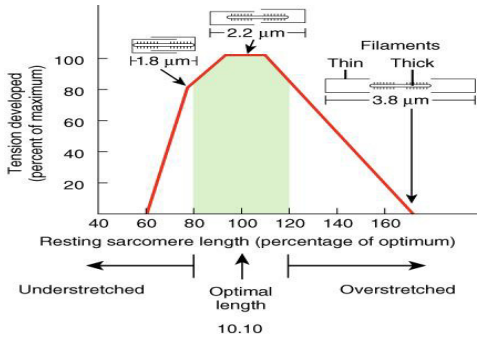


Mechanism of sympathetic nervous system on cardiac muscle cells:

Norepinephrine is released at the nerve endings, it binds to β1 adrenergic receptor, which is a G-protein associated receptor, the activated G-protein activates adynelate cyclase that produces cAMP. cAMP activates protein kinase A, which activates two transporters,

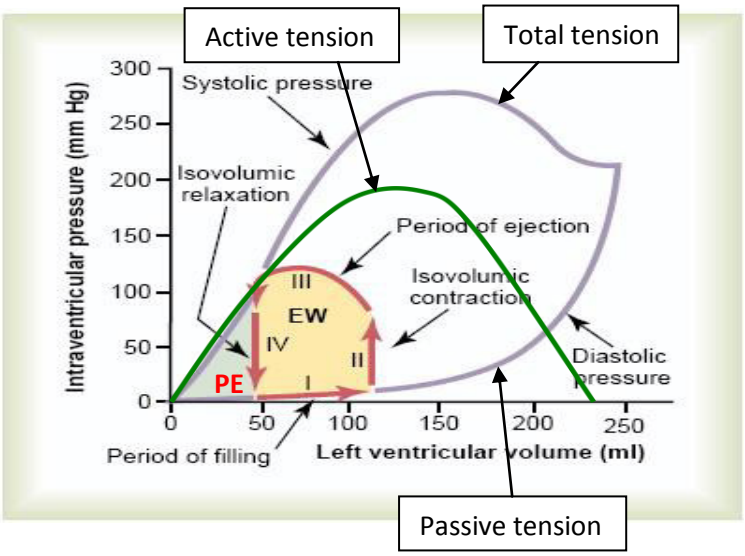
1) Ca++ transporter on plasma membrane, which increases the influx of Ca++ into the cytoplasm, more Ca++ in the cytoplasm means higher Ca++ released from SR and thus higher contractility force of the cell.

2) Phospholamban is activated, it activates calcium-ATPase pump on the sarcoplasmic reticulum "SR", so Ca++ will be removed more quickly from the cytoplasm, which decreases the relaxation time and the heart rate increases. Also more Ca++ will be stored in the SR for contraction.



So, the effects of norepinephrine on muscle cells (which are different from conducting system of the heart), is increasing contractility of the heart **and** contributing in increasing the heart's rate.

Graphical presentation of heart cycle:



In Frank-Starling law, the x-axis was the length of the muscle, while y-axis was the force of contraction, while in the heart, x-axis is EDV, and the y-axis is intraventrecular pressure (before the contraction).

As shown on the graph, total tension is the sum of passive and active tensions. The cardiac cycle starts from the end systolic volume, then, at line I, there is ventricular filling. After that, systolic phase starts, the atrioventricular valve closes, and isovolumic contraction occurs, where volume is constant while pressure is increasing, represented by line II. Pressure increases until it reaches 80 mm Hg (diastolic pressure of aorta/ afterload), at this point, the afterload is overcome, semilunar valve opens, and the ventricular volume starts to decrease as the blood is ejected. At line III, volume stays decreasing and pressure stays increasing until it reaches 120 mm Hg then systole ends, and semilunar valve closes. Diastolic phase starts by isovolumic relaxation at that point, and pressure keeps decreasing at line IV (while volume is constant) until pressure is almost zero mm Hg, less than atrial pressure, thus, the atrioventricular valve opens, and the cycle repeats itself again.

So,

Phase I: ventricular filling

Phase II: isovolumic contraction

Phase III: ejection phase

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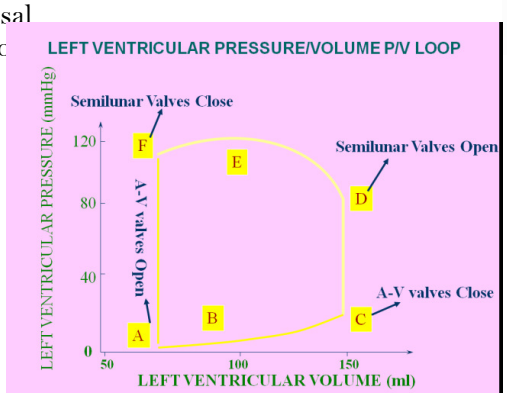
Phase IV: isovolumic relaxation

See valves' opening and closure here ⟶



Work & energy:

The area under looped curve represents the **external work** done to move the blood through the circulation. It is calculated by multiplying the stroke volume (distance between line II and line IV) by the mean change in pressure (pressure at systole – pressure at diastole).

The area to the left of the loop represents the **potential energy** "PE", this energy could be used to increase the contractility of the heart at a constant EDV by increasing heart's contractility (inotropic effect)and thus stroke volume, so the left line of the graph moves more to the left.

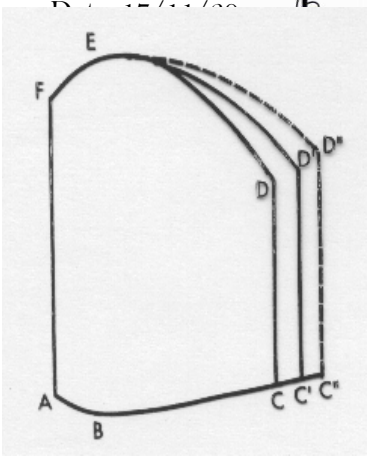
The **total energy** produced by heart's contraction is the **external energy + the kinetic energy**. The kinetic energy =1/2*mass*v^2. In the normal case, the kinetic energy makes only 1% of the total energy. In the case of a stenosed valve, a lot of kinetic energy would be needed to pass the blood through the stenosed valve (aortic or pulmonary valves), this can reach to 50% of the total energy of the heart, this causes the heart to work harder in order to pump the blood through the valve, which increases heart's demand for energy and oxygen, that may subject the heart to infarction and ischemia.

In a nutshell: Kinetic energy can be neglected exept in the cases of aortic or pulmonary stenosis.

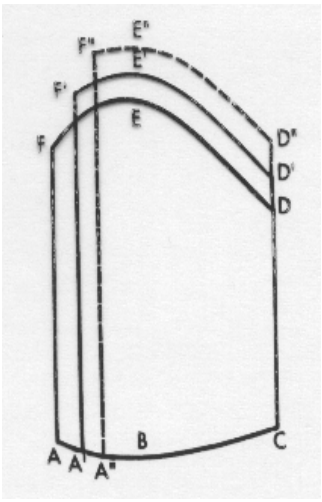
For the following three pictures:

A) AV valve opening
B) Ventricular filling
C) AV valve closes
D) Similunar valve opens
E) Ejection phase
F) Semilunar valve closure

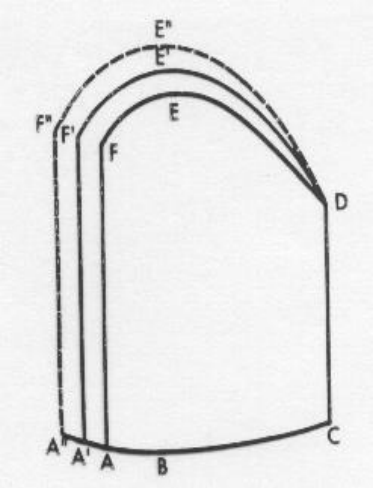
When the EDV (**preload**) of the heart is increased, line II of the volume-pressure graph would shift to the right, increasing the stroke volume (the distance between line II and line IV). This coincides with Frank-Starling law that says if the preload (which is proportional to EDV) is increased within the physiological limit, the stroke volume would increase.



If the **afterload** increases, the stroke volume would decrease, and thus the heart would need a higher force and so more energy to pump the same volume of blood. These complications are associated with hypertension as were discussed previously.

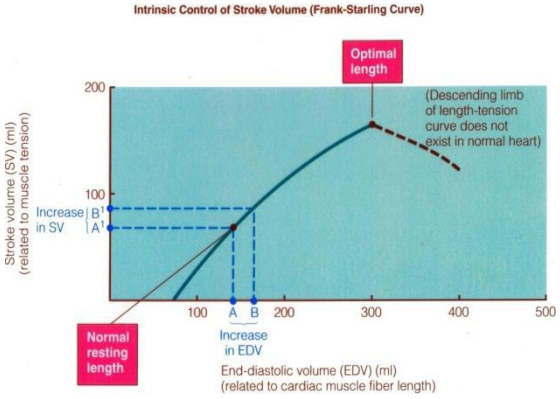


If the **contractility** of the heart increases, the stroke volume of the heart increases, this is when the EDV is constant. The increase in stroke volume comes from the end systolic volume



Heart failure:

As has been said before, an increase in EDV causes an increase in stroke volume, this is because the optimum length (of the muscle cells) is not yet reached and because of the elastic of elements in cardiac muscle. However, if the



optimal length of the muscles is reached, **heart failure** occurs, which is that the heart fails to eject the amount of blood that it receives, so more blood stays in the heart after each contraction.

Regulators of the heart rate:

They are either positive or negative chronotropics.

Autonomic nervous system: as known, sympathetic stimulation increases heart rate, and parasympathetic stimulation decreases the heart rate. What is to be added to this is that the heart rate is mainly affected by the parasympathetic stimulation, and that the contractility of the heart is stimulated by sympathetic stimulation. Based on that, if the autonomous nervous supply to the heart was cut, the heart rate would **increase** (no parasympathetic stimulation) and the contractility would **decrease** (no sympathetic stimulation).

Hormones like thyroxine and epinephrine increase the heart rate, and the ions concentrations intra- and extracellularly also affect the heart rate.

Cardiac output concepts:

Cardiac index=cardiac output/surface area of the body; is 3 L/min/m^2 in normal people.

Cardiac index allows us to compare the heart's functioning in different people.

When compared with the physical equation of Ohm's law, C=V/R, were C: electric current, V: voltage, R: resistance; the cardiac output "CO" is equivalent to the current, and the pressure is equivalent to the voltage, so the equivalent formula would be:

CO= (mean arterial pressure – right atrial pressure)/total peripheral resistance

The right atrial pressure is almost zero, so it can be negligible so the final equation would be:

CO= mean arterial pressure /total peripheral resistance

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Dedicated to: Moath alBalawi, Qusai alSharif & **Qs**