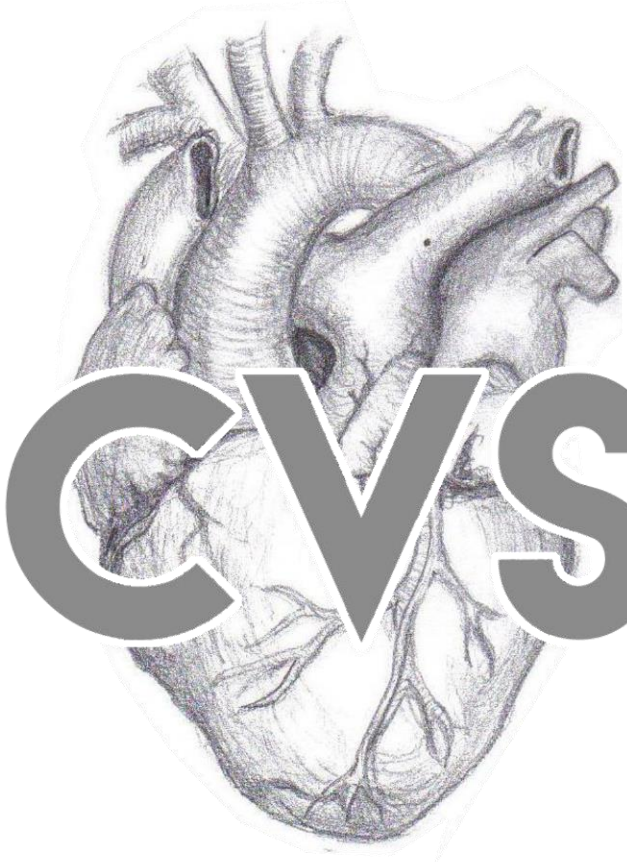

CVS

PHYSIOLOGY

☑ Sheet ○ Slide ○ Handout

Number

9+10

Subject

Cardiac cycle-2

Done By

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Corrected by

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Date: 00/00/2016

Price:

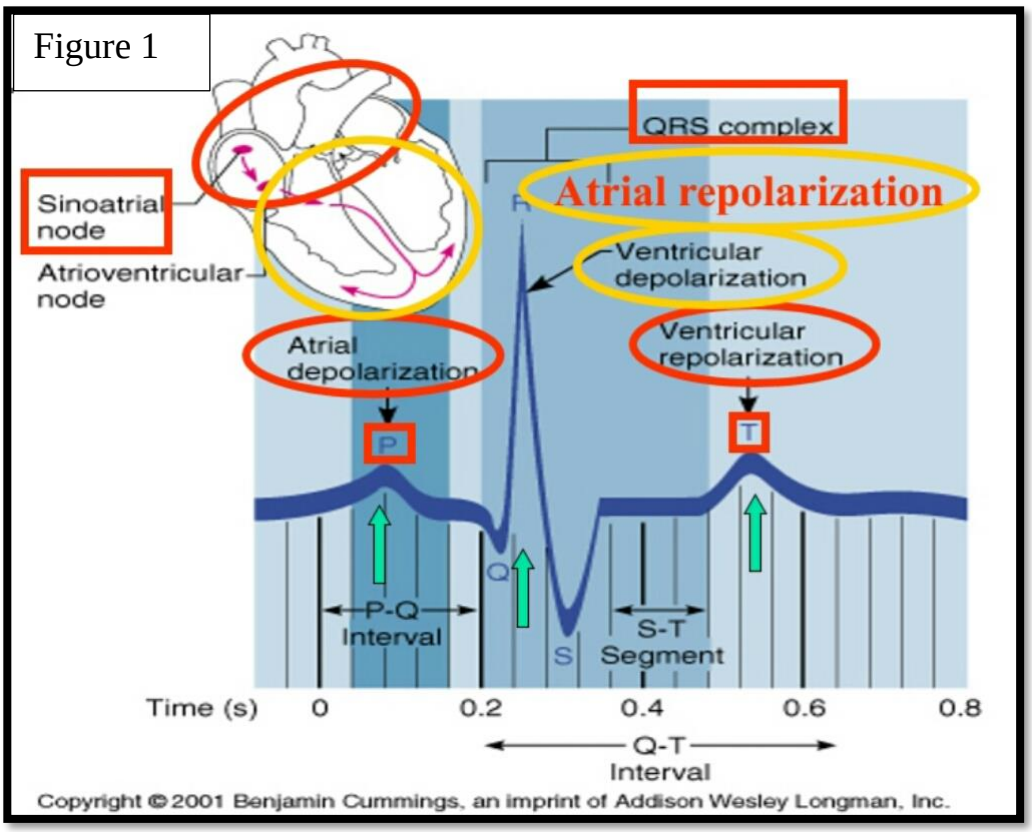
Before we start ..

- This sheet was written according to the recording that belongs to section 3.
- This sheet includes two lectures; 9 and 10.
- Topics of lecture 9:
  - ECG deflection waves irregularities.
  - Review of the Cardiac cycle.
  - Pressure Changes in the cardiac cycle.
  - Heart sounds.
  - Cardiac output and reserve.
  - Factors affecting stroke volume.

I. ECG deflection waves irregularities

- ***figure 1*** represents main electrical events detected by ECG:

Figure 1



- By now, you have to be familiar with this figure.
- As you know, **the first electrical event in the heart is atrial depolarization**, that's initiated from SA node, represented by upward deflection, called ***P wave***.
- **Atrial depolarization is followed by ventricular depolarization**, which is presented by ***QRS complex***. Atrial repolarization co-occur with ventricular depolarization, but it doesn't have any wave in ECG as it is masked by QRS complex.
- **The third electrical event is ventricular repolarization**, that's represented by an upward deflection, because it starts from pericardium toward the endocardium. This deflection is called ***T wave.***
- We have also segments and intervals in ECG. **a segment represents an isoelectric line**, we have tow important segments in ECG; PQ segment and ST segment. While interval is any area between two points that contains at least one wave, we have two important intervals in ECG; PQ interval and QT interval.
- Any irregularity in the sequence, timing or intensity of these values reflects abnormality in the heart muscle itself.

●The length of **PQ interval represents the time that's required to transmit action potential from the atria toward the ventricles through AV node**:

- The normal duration of PQ interval is between 0.16 to 0.2 Seconds (*160 to 200 mSeconds*).
- If it exceeds 0.2 seconds, this means that there's ***AV node*** conduction failure (AV block), there are three degrees of AV block.
- In ***1st degree AV block***, P-R interval is > 0.20 sec, and each P is followed by QRS-T complex.
- In ***2nd degree heart block*** P-R interval increases to 0.25 - 0.45 sec. Moreover some impulses will pass through the A-V node while others don't thus causing "dropped beats" or palpitations . However there is a rhythm that develops 2:1 or even 3:2…etc. This is called regular irregularity.
- ***3rd degree heart block*** Occurs when there is dissociation (no relation between) the P wave and the QRS- T complex. There is complete block of conduction in the AV junction, so the atria and ventricles form impulses independently of each other.

● QRS complex represents ventricular depolarization:

- ***Enlarged QRS complex occur when there's ventricular hypertrophy*** (*larger muscle mass means more currents, and thus higher reading*), common causes of ventricular hypertrophy are ***hypertension***, ***mitral valve stenosis*** or we may simply find it in athletes.
- ***Prolonged QRS complex occur when there's a problem in ventricles, like bundle branch destruction***.

●T wave represents ventricular repolarization.

- This wave is potassium dependent, But why?
  - *Remember that T wave represents repolarization wave that migrates from pericardium toward endocardium, and repolarization is basically efflux of K+*.
- When there's hyperkalemia, T wave will be peaked.
- In cases of hypokalemia or ischemia, T wave will be flattened.
- ***Extra Note***: Nobody exactly knows why does this occur, some argue that K+ Channels conductance is affected by ECF K+. Others say that blood supply is the main cause of difference in endocardial and pericardial action potential as it brings K+ with it, thus affecting the rate repolarization.

●we know that the normal ECG electrical changes occur with the range of 1 to 2 mV, but what does it mean if this voltage is changed?

- If the sum of voltages of Leads I-III is greater than 4 mV, this is considered to be a high voltage EKG. Most often caused by increased ventricular muscle mass (**hypertension, marathon runner**).
- Decreased Voltages in Standard Bipolar Limb Leads occur due to Cardiac muscle abnormalities (***old infarcts causing decreased muscle mass, low voltage EKG, and prolonged QRS***). The following Conditions surrounding heart that make it further away from the chest (***fluid in pericardium, pleural effusions, emphysema***).

●And by that, we finished everything about ECG, you need to be familiar with ECG and every thing related to its 12 leads by now (you must know the axis, angles, which side is positive and which is negative….etc.)

II.Cardiac cycle

●***The cardiac cycle*** is the time between one beat and the next one. If we look at the ECG it would be between one R and the next R, or one P and the next P, it takes 0.8 Seconds in average.

●our purpose of studying cardiac cycle is to know the timing and sequence of **electrical events**, **mechanical events, pressure changes, volume changes** and **sound changes** in one cardiac cycle, or basically understanding ***figure 2***. By the end of this topic you have to be able to identify which event co-occur with which event, and when do they occur.

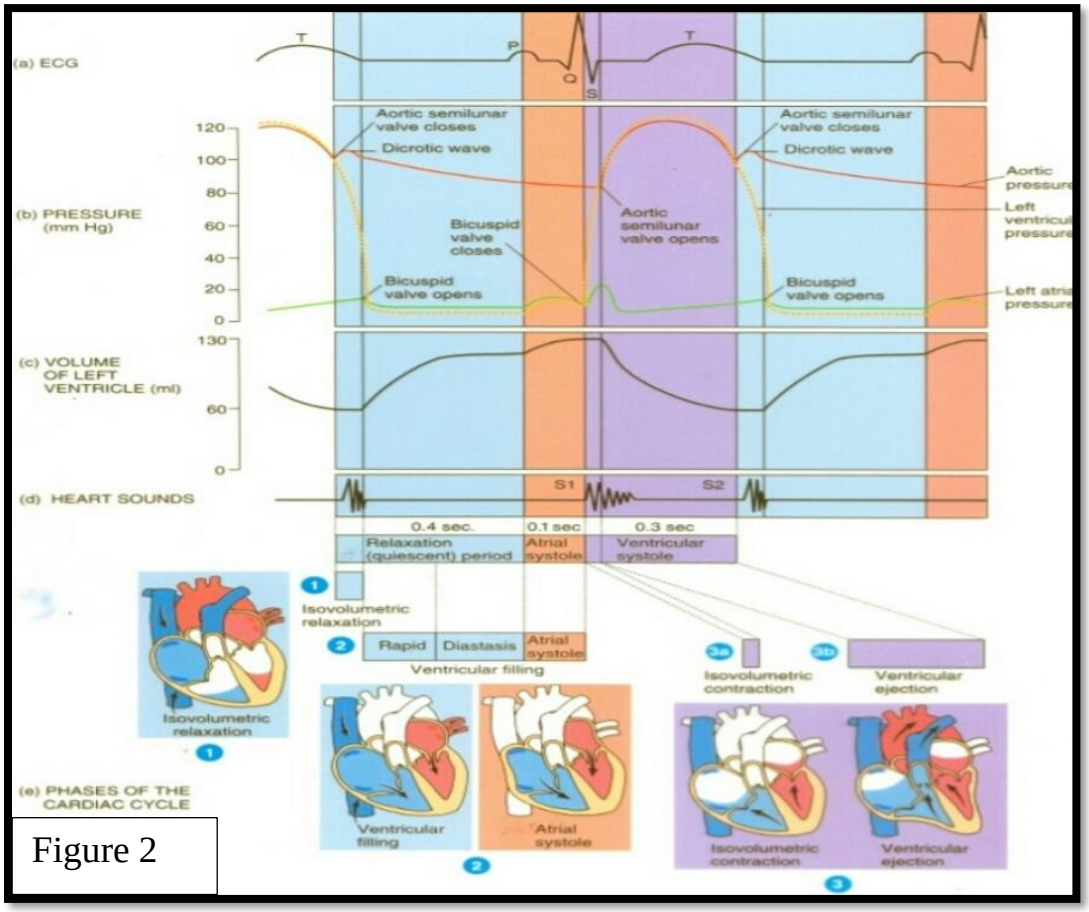


Figure 2

a) Electrical changes

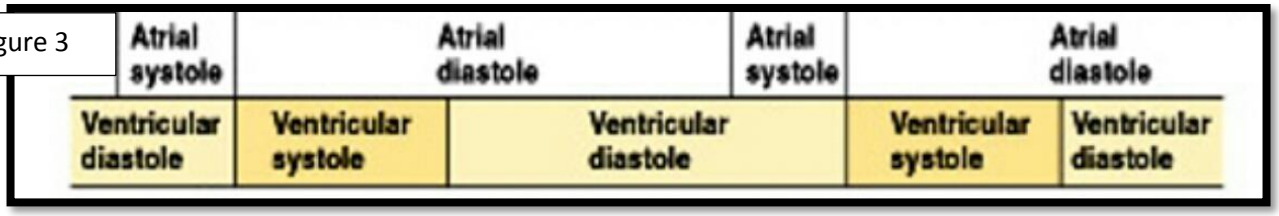
●Electrical changes are basically the ECG, and you should know it by heart by now.

b) Mechanical changes

●Mechanical changes are contraction and relaxation, or simply, systole and diastole. (***Figure 3***)

- We said that the atrial systole takes 0.1 seconds and that atrial diastole lasts 0.7 seconds.
- After atrial systole, ventricular systole begins and lasts 0.3 seconds. Finally, ventricular diastole lasts 0.5 seconds.

Figure 3



c) Volume changes

●We are concerned here with volume changes in ventricles.

- We discussed ***end diastolic volume (EDV)***.This is the volume of blood remaining in the ventricle, at the end of atrial systole (which is also at the end of ventricular diastole).
- This is followed by ***Isovolumetric contraction***, contraction during a short period in which the four valves of the heart are closed. During this period, there is no change in volume, only a change in pressure.
- Pressure increases very quickly, to the extent of the pressure of the ventricle being greater than the pressure in the aorta, in the left side, and greater than the pressure of the pulmonary artery on the right side. When the pressure in the left ventricle exceeds the pressure in the aorta, the aortic semilunar valves will open and blood is ejected from the left ventricle into the aorta. When the pressure in the right ventricle exceeds the pressure in the pulmonary artery (which is around 8mmHg), the pulmonary semilunar valves will open and blood is ejected from the right ventricle into the pulmonary artery.
- The first part of ejection is called **rapid ejection**.
- Then, because the valve is open and blood goes from the ventricle to the arterial system, the ejection is slow until we reach the end of systole.
- At the end of systole, there's still a certain volume of blood in the ventricle. This is what we call ***end systolic volume (ESV)***.

- Diastole starts with a short period of **<u>isovolumetric relaxation</u>** (both the AV and semi-lunar valves are closed). The pressure in the ventricles drops, and is much less than the pressure in their corresponding major vessels (the aorta on the left and the pulmonary artery on the right).
- Then <u>once the atrial pressure becomes higher than the ventricular pressure, the AV valves open</u>, allowing rapid filling (due to the collection of blood in the atria during ventricular systole) of the ventricles with blood. This is ventricular diastole.
- The second stage of blood flow into the ventricles is slow filling and is referred to as **<u>diastasis</u>**.
- The last stage is due to atrial systole.
- We've mentioned previously that atrial systole is not that important, as it contributes less than 25% of ventricular filling.

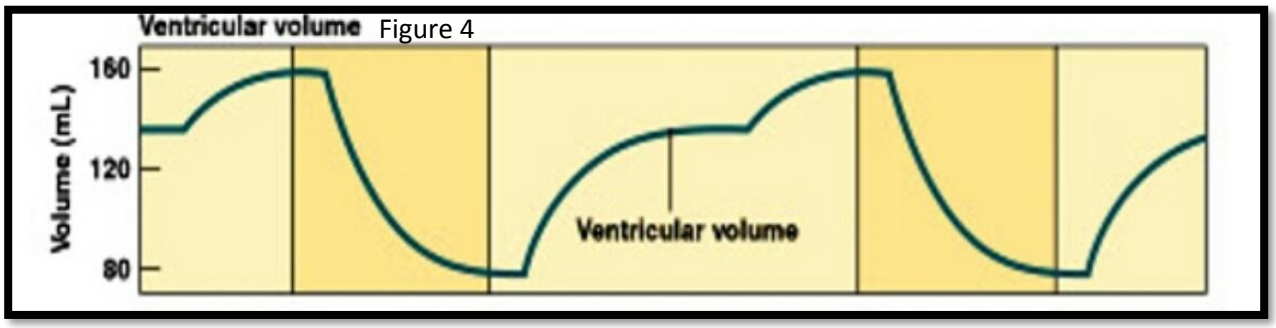
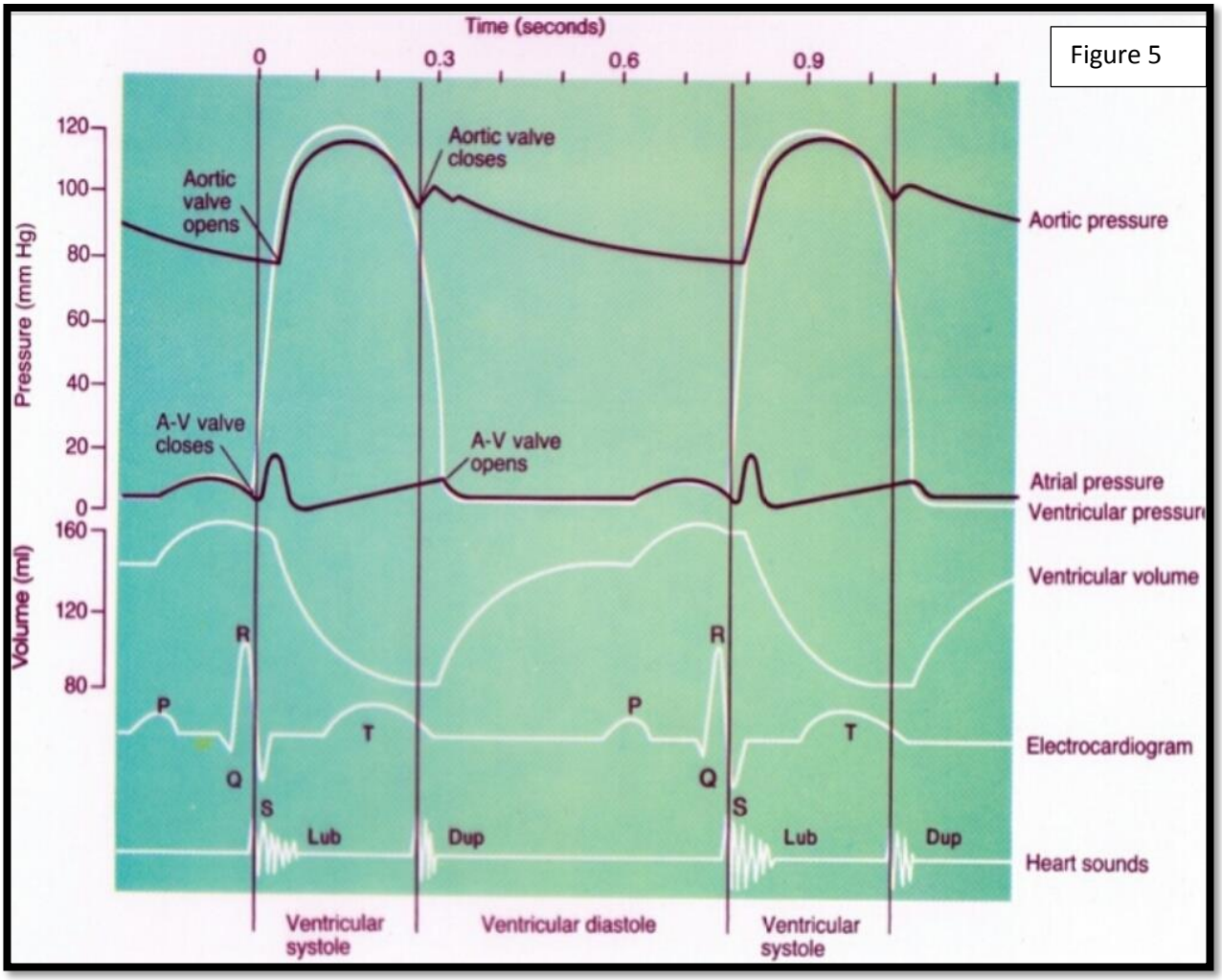


Figure 4

d) Ventricular and aortic pressure changes

●The pattern of the waves in different pressures is the same. However, the scale (value) of the waves is not the same.

- On the right side of the heart, the pressure in the pulmonary artery varies between **8-25mmHg**.
- The pressure in the aorta varies from **80-120mmHg**.
- We use these numbers as textbook values, but in reality, every individual is different from the next.



●**figure 5** represents normal events in the cardic cycle. Here, we are concered with the aortic pressure, which is represented by the black lines. The white lines represent the ventricular pressure.

- now look at the ***atrial diastole***, at the atrial diastole the ventricular pressure has to be less than the atrial pressure. So, if the atrial pressure is 0, the ventricular pressure should be less than 0.
- When the atria push blood into the ventricles rapidly (***systole***) , the ventricles increase in their pressure, but the atrial pressure is still higher than ventricular pressure during that period.
- When ***ventricular systole*** begins, the pressure starts to build up in the ventricle. The first increase in pressure in the ventricle raises its pressure above 0. When the pressure in the ventricle is higher than the pressure in the atrium, the AV valve closes.

Note: The closure of the AV valve prevents the blood in the ventricle from returning to the atrium. Since, the AV valve is closed, what does the blood do?

- It starts to move around the closed AV valve. This movement of blood gives us the 'Lub' sound (low-pitched) or S1, which we hear with a stethoscope. So, S1 coincides with the closure of the AV valve

- During isovolumetric contraction, when the 4 valves are closed and the ventricle is contracting, the pressure in the ventricle gets very high, very rapidly.
- When the pressure of the ventricle rises above the pressure of the aorta during diastole (which is 80mmHg), the aortic semi-lunar valve opens and the blood flows into the aorta.
- At this moment, aortic pressure increases since we are pushing blood through this tube, which is placing pressure on the walls of the aorta.
- The ventricular pressure, however, is still higher than the aortic pressure.
- At the end of the ventricular contraction, the pressure in the aorta exceeds the ventricular pressure, but the blood still flow from the ventricles toward the aorta, this is due to the **momentum** or **inertia**.

●Why should the pressure in the ventricle remain higher than the pressure in the aorta?

- For blood to flow, there must be a pressure gradient, which is from an area of higher pressure to an area of lower pressure.
- If the aortic pressure is higher than the ventricular pressure, the blood will regurgitate into the ventricle.

●Notice in the figure, that the ventricular pressure In the last stage of ventricular systole is slightly lower than the aortic pressure although blood is still moving from the ventricle to the aorta. How does this work?

- Remember that the direction of movement of an object is determined by the resultant of forces exerting on it. The pressure is force per unit area, so we use it usually to determine the direction of movement of the blood. However, there are other forces that affect the blood, such as inertia or momentum (الزخم). The blood ejected from the ventricles has high inertia, and therefore flows from the ventricle toward aorta.

- When the pressure overcomes this momentum, the aortic semi-lunar valve closes.
- After that initial increase in aortic pressure, the pressure in the aorta gets even higher and the pressure gradient is restored, causing blood to flow back into the ventricles and the semi-lunar valves to close. *The second heart sound, or the 'Dub' sound (high pitched) is the sound of the blood trying to flow back to the ventricles after the semi-lunar valves have closed.*
- This blood exerts pressure on the semi-lunar valve creating a notch in the curve (*rapid increase and fall in the pressure*). This forms what we call a ***Dicrotic Notch*** or ***Incisura***, and is due to the closure of the semi-lunar valve.

●**Note:** The highest pressure in the ventricle as well as the aorta during systole is around 120 mmHg, During diastole, the aortic pressure is 80mmHg, while the ventricular pressure reaches 0.

- This is why when we measure blood pressure we get a value of 120/80.
- 120 representing systole and 80 representing diastole.
- In the left ventricle, the pressure varies from 0-80mmHg.
- In the right ventricle, the pattern of the wave is the same, but the values are different. The pulmonary artery's diastolic pressure is around 8 mmHg. The systolic pressure in pulmonary artery is around 25 mm Hg, The right ventricle pressure varies between 0 and 25 mmHg.

e) Atrial pressure changes

● This pressure is most significant in cases of abnormal pressure, because it can exert pressure on the jugular vein. *Back to figure 5 and notice the changes in atrial blood pressure*.

- The atrial pressure is usually zero.
- During ventricular diastole, AV valve is open so blood flows from the atrium to the ventricle according to the pressure gradient, increasing ventricular pressure.
- Atrial systole occurs during late ventricular diastole. During atrial systole, the atrial pressure increases slightly, and gives us what we call the **A wave**. So, the A wave is due to atrial systole.

- During ventricular Systole, the high pressure in the ventricle pushes the cusps of the closed AV valve upwards, which causes an increase in the atrial pressure. The pressure in the atria also increases because blood is still flowing into the atria. The atria then give us a wave which coincides with isovolumetric contraction (of the ventricles), This gives us the ***C wave***.
- After the isovolumetric contraction, the pressure that pushes AV valves is relived, thus decreasing atrial pressure.
- When the ventricular systole ends, the semi-lunar valves will be closed, while the AV valves are closed. This is the isovolumetric relaxation. The atrial pressure is Belding up here due to venous retain, This gives us the ***V wave***.
- At the end of isovolumetric relaxation, the AV valve opens. When the AV valves open, the pressure in the atria drop suddenly. Blood passes to the ventricles rapidly (rapid filling), followed by slow filling (diastasis), then atrial systole once again.

●So to sum up, ***we have 3 atrial pressure waves***, **A wave** occur due to atrial systole, **C wave** is due to ventricular isovolumetric contraction, and **V wave** occur with ventricular isovolumetric relaxation.

f) The Heart sounds

●The ***first heart sound (S1, lup)*** coincides with the QRS wave of the ECG (the beginning of isovolumetric contraction).

●The ***second heart sound (S2, dup)*** coincides with the end of the T wave (the beginning of isovolumetric relaxation).

- These sounds occur due to turbulence of the blood around the closed valve, not due to closure of the valve.
- Because of that, there are two more heart sounds, S3 and S4.
- The slow filling of the ventricles from the blood in the atria makes the heart sound, S3.
- The rapid filling of the ventricles from the blood in the atria makes the heart sound, S4, due to atrial contraction.
- S3 and S4 are more pronounced in valve stenosis (narrowing of the valve) or during the regurgitation of blood. We don't usually hear these two heart sounds. You can only hear these if you have what's called a good musical ear.

●You may hear an abnormal "split" second sound (S2) when the aortic and pulmonary valves don't close at the same time, this is called ***murmur of the heart***.

●The important thing to know here is the time between S1 and S2. The time between these two sounds represents ventricular systole, which is around 0.3 seconds. The time between S2 and the next S1 is 0.5 seconds, which represents ventricular diastole.

●How can we detect the heart sounds?

1- Using a stethoscope, here, you have to detect the heart sounds by your ear. There are certain places that can we hear heart sound from them, summarized in **figure 6.**

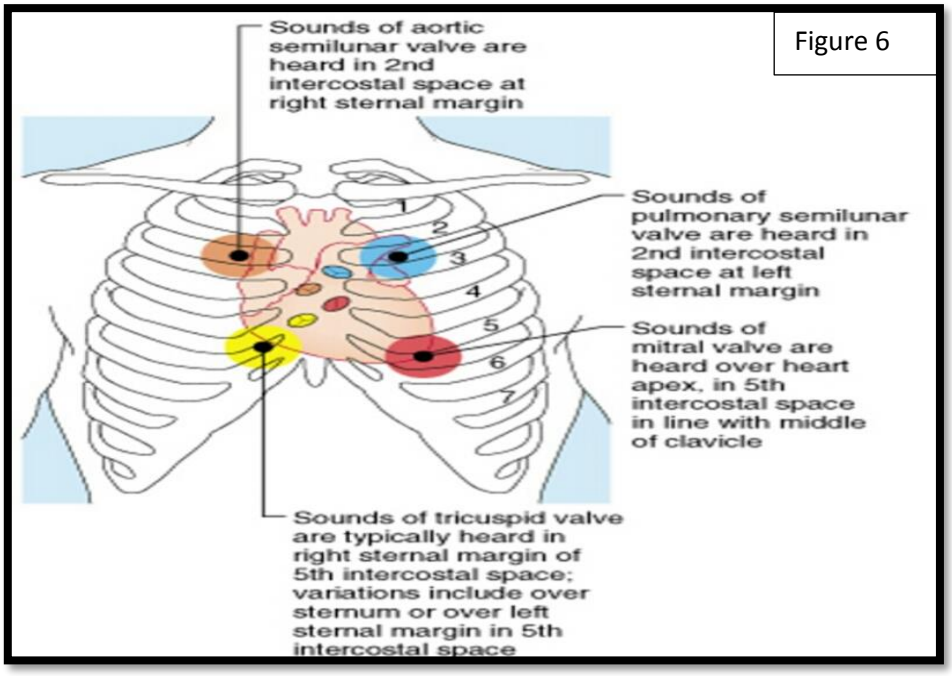


Figure 6

2- Using phonocardiogram, that converts heart sounds into waves on a computer screen.

III.Cardiac Output and Cardiac Reserve

●Remember that the maximum volume of blood that's achieved at the end of the diastole is called **end diastolic volume (EDV)**, which equals normally 125mL. while the volume of the blood inside the ventricle after contraction is called **end systolic volume (ESV)**, which equal normally 55mL.

- From that, we can calculate the ***stroke volume (SV)*** , which equals ***EDV-ESV***, stroke volume represents the amount of the blood that's bumped by the heart per beat, which equals normally 70mL.

SV = EDV – ESV……(1)

- We can also calculate the ***ejection rate***, or ***the efficiency*** of the heart, that equals ***SV/EDV***.

Ejection rate =SV/EDV…….……(2)

●The amount of blood pumped by each ventricle per minute is called cardiac output, which equals stroke volume multiplied by the heart rate.

C.O = SV×HR…….……(3)

- Now we said that the cardiac output for the right ventricle must equal the cardiac output of the left ventricle.
- Actually the cardiac output on the left side is a bit higher than on the right side. Why?
    - *This is a result of the drainage of the blood supply of the bronchi into the pulmonary veins.*

●**Cardiac Reserve (Intrinsic Regulation)**: the difference between maximum and resting cardiac output.

- According to ***frank-starling law***, an increase in the length of the muscle increases its tension (active tension), within physiological limits.
- The length of the muscle is proportional to the end Diastolic Volume (volume of blood found in the heart before it contracts).

- So, we can say that <u>any increase in the end diastolic volume will increase muscle length and therefore increasing strength of contraction, stroke volume as well as cardiac output.</u>
- We can keep increasing the stroke volume until the optimum length of the muscle (optimum length of sarcomere) is reached.
- The <u>*difference between the maximum cardiac output and the actual cardiac output is called* ***cardiac reserve***</u>.

●The maximum cardiac output that can be reached is around 15 liters/minute, in athletes, maximum cardiac output may reach 35 liter/minute.

●The normal (resting) cardiac output In our body is 5 liters/minute, the cardiac output can be increased from 5 to 15 liters/minute intrinsically without any sympathetic stimulation.

●The difference between 15 and 5 (10) is the Cardiac Reserve, the Cardiac Reserve in athletes is much higher than that of an average person.

IV. Cardiac output regulation

A) Regulation of the stroke volume

● Factors that affect stroke volume are:

- Preload
- Afterload
- Contractility

●<u>***The preload*** is the amount of pressure found in the ventricle before it contracts, so the preload is caused by the passive tension</u>.

- So It's proportional to the end diastolic pressure **(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.
- <u>This causes an increase in the strength of contraction of the heart which causes an increase in the stroke volume and the ejection fraction of the heart.</u>

●***The afterload*** is <u>the minimum amount of pressure that has to develop in the ventricle in order to eject the blood from the heart</u> (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.
- Therefore, ***afterload*** is inversely proportional to ***stroke volume***.

●***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 increases stroke volume but doesn't affect EDV, how?
  - By ejecting more blood, therefore decreasing ESV.
- This will increase also the ejection fraction, which is used actually to measure the contractility of the heart.
- ***Positive inotropic effect***: *increases ejection fraction, stroke volume, cardiac output. And decreases ESV, but doesn't affect EDV and heart rate.*
- ***Negative inotropic effect:*** *decrease ejection fraction, stroke volume, cardiac output. And increases ESV, but doesn't affect EDV and heart rate.*

B) Frank-Starling Law of the heart :

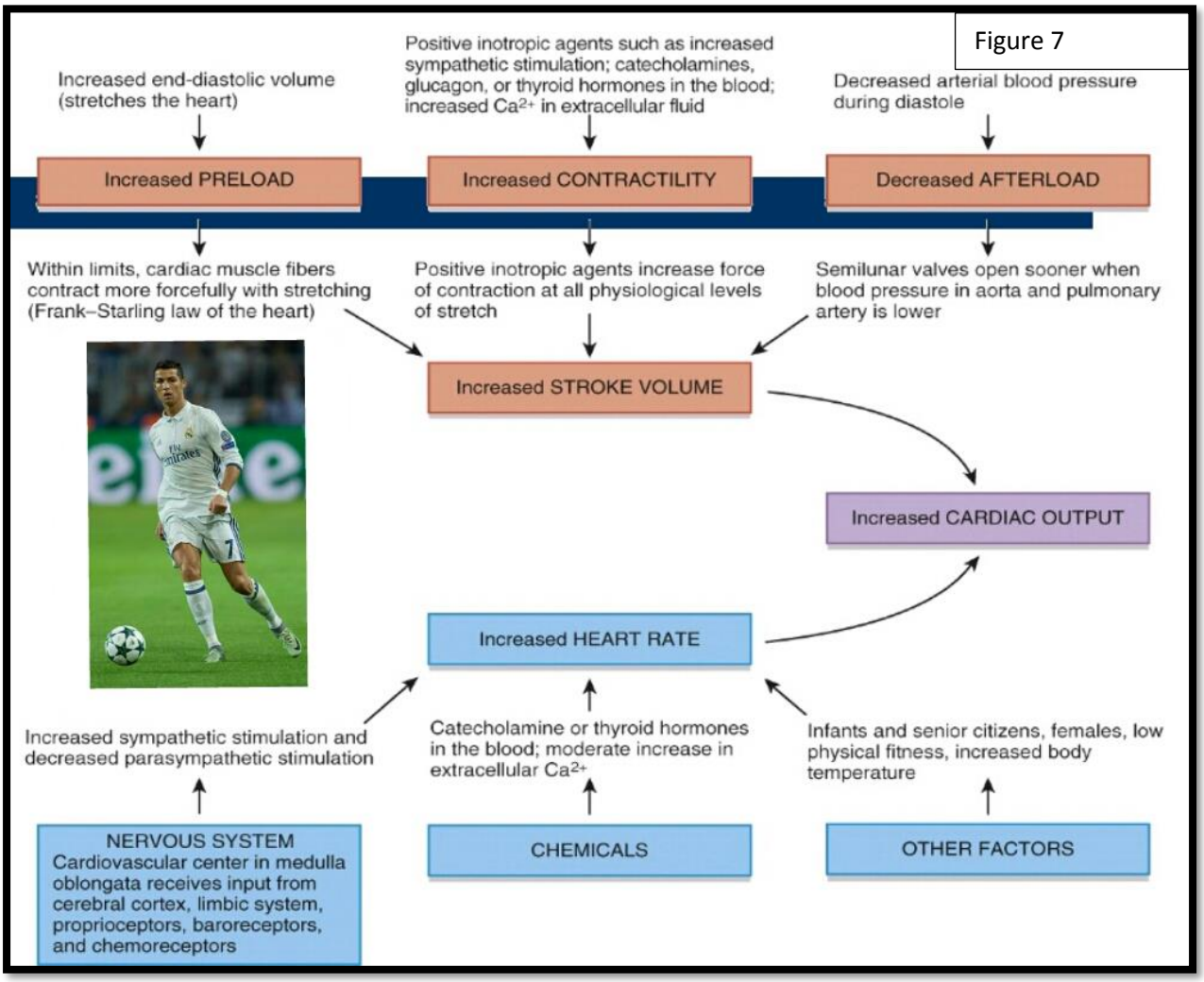
●It states that the preload (which is proportional to EDV) is the critical factor that determines the stroke volume of the heart.

- This is because the active tension 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.
- So, 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!

C) *Cardiac output*

Figure 7



●in ***figure 7***, we can see Cristiano Ronaldo trying to shoot the ball :P, this excessive physical effort requires higher cardiac output, but how can we increase 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, (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.

●and by that, we have finished lecture 9 :p

مفاجأة الموسم ....

يقال أن اللحظة التي تجد فيها صفحة فارغة في منتصف الشيت من أجمل لحظات الحياة ☺ ☺

شايفين ما أحسني 😂😂..

يلا خذلك بريك صغير و فتح مخك و أقلب الصفحة .. ما ظل شي

●Topics of lecture 10:

- Extrinsic factors that affect the stroke volume.
- Work and energy calculations.

D) Extrinsic factors that affect the stroke volume

●Extrinsic factors that affect the stroke volume include:

- ***Sympathetic nervous system***, which causes a positive inotropic and chronotropic effects, increasing contractility and stroke volume, while 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, angiotensin and glucagon 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 decreasing intracellular Calcium.

●***Important note***: in general, heart rate is controlled mainly parasympathetic tone, while contractility is controlled mainly by sympathetic tone.

- Because of that, blocking parasympathetic stimulation will increase the heart rate. While blocking sympathetic stimulation will decrease contractility.

g) **Mechanism of sympathetic nervous system action on cardiac muscle cells**:

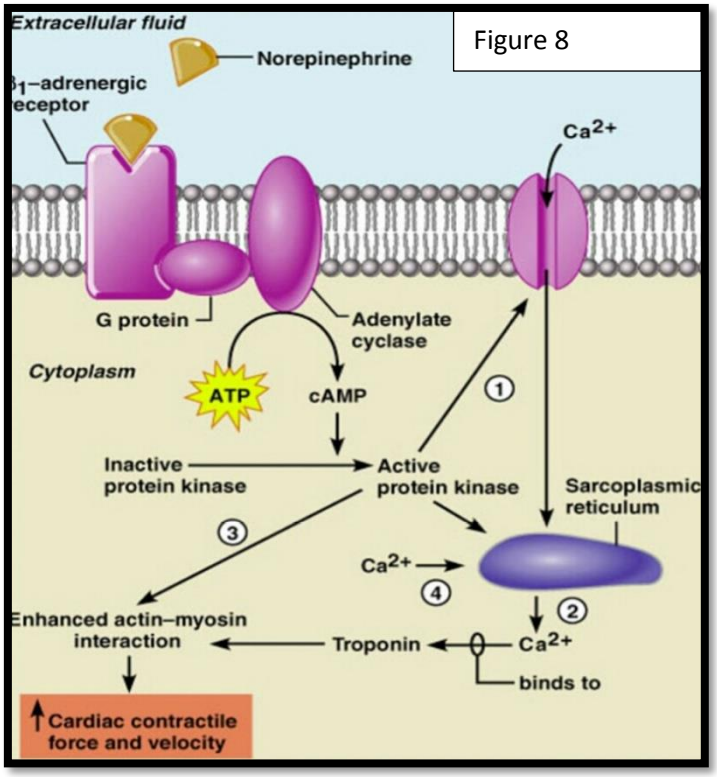


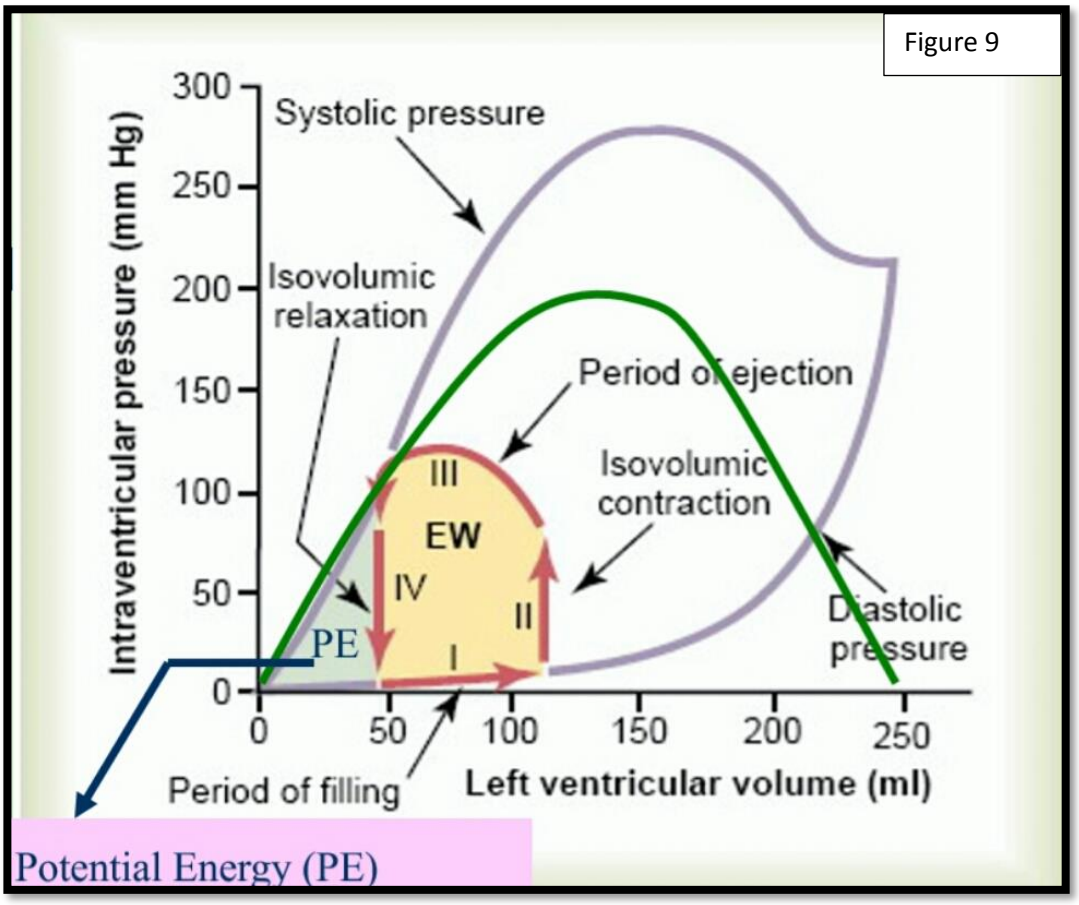
Figure 8

- Norepinephrine is released from ***sympathetic*** 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:
  - A) ***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.
  - B) ***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***.

V.Work and energy calculations of the heart :

●Here, we ae going to present work an energy changes in heart during one cardiac cycle as seen in figure 9, don't panic, follow me and you'll understand it, I promise :p

Figure 9



●We know that the Frank-Starling law, studies length – tension relationship in the heart

- If we presented length – tension relationship by a curve, ***we put length of the muscle on the X-axis***, and ***the tension on the Y-axis***.
- But if wanted to presented these values in terms of cardiac cycle in the left ventricle, we can ***replace "muscle length" by left ventricular volume***, and the ***tension by interaventricular pressure***.
- now in this figure, we are presenting two data; the first one ***is simply length tension relationship according to Frank-Starling law***, the second is ***pressure – volume changes in one cardiac cycle***.

- But why do we put both of them together?
    - Normal cardiac cycle is a small part of length - tension relationship according to Frank-starling law, so it's better to put them together in order to compare them and to know were does these events occur actually.

●Frank-starling law is presented by three curves; ***passive tension***, ***active tension***, and ***Total tension***. (Go back to the curve and try to identify them, if you face any difficulty, compare this curve to length - tension relationship curve in previous sheets.

- ***Passive tension*** could by measured and presented by EDV, as we mentioned previously.
- ***Active tension*** is measured and presented by interaventricular pressure.
- And ***the total tension*** could be measured and presented by systolic pressure**.**
- As shown on the graph, total tension is the sum of passive and active tensions.

●The cardiac cycle is represented in this curve in terms of pressure and volume only, so we can't know the duration of these events from this figure, however, these events are labeled by (I, II, III, IV) according to there sequence.

- 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.

●To sum up, ***Phase I: ventricular filling. Phase II: isovolumic contraction Phase. III: ejection phase. Phase IV: isovolumic relaxation.***

●Cool, true? Let's make it harder :p

●think about it, what's the importance of the curve? Why we are wasting our time drawing this meaningless curve?

- The main purpose of this curve is to calculate work and energy changes during one cardiac cycle.
- 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).

●***Note:*** the area under the curve represents the work done by the heart to pump the blood, but why?

- Remember that unit used to express work is ***joule***, which equals ***N.m*** (***Newton.Meter)***
- The area under the curve presents the result of multiplying stroke volume by pressure changes.
- The volume is measured by ***liters*** or ***meter*** ^{3}, and the pressure is actually Force/Area = N/m^2.
- By multiplying Volume by pressure, we are multiplying m^3 by $N/m^{2.}$ $m^3 \times N/m^2 = N.m =$ ***joule.***
- As a conclusion V×P =Work

- 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 =$1/2 \times mass \times V^2$.
- 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.

●There are few slides that talk about the regulation of cardiac output and heart valves functions, we talked about these previously.

●Now let's test our understanding of the curve:

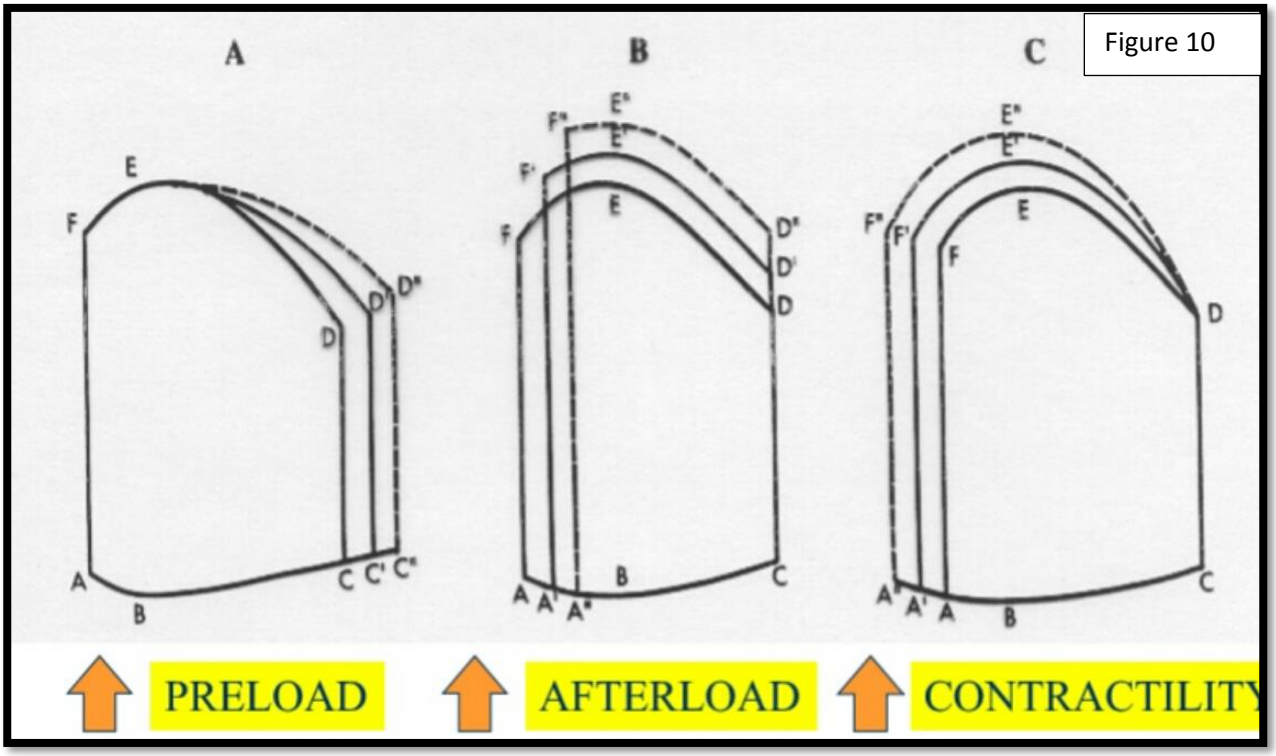


Figure 10

- 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, ***(See curve A).***
- 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, ***(See curve B)***

- 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. **(See curve C)**

●The concept of heart failure:

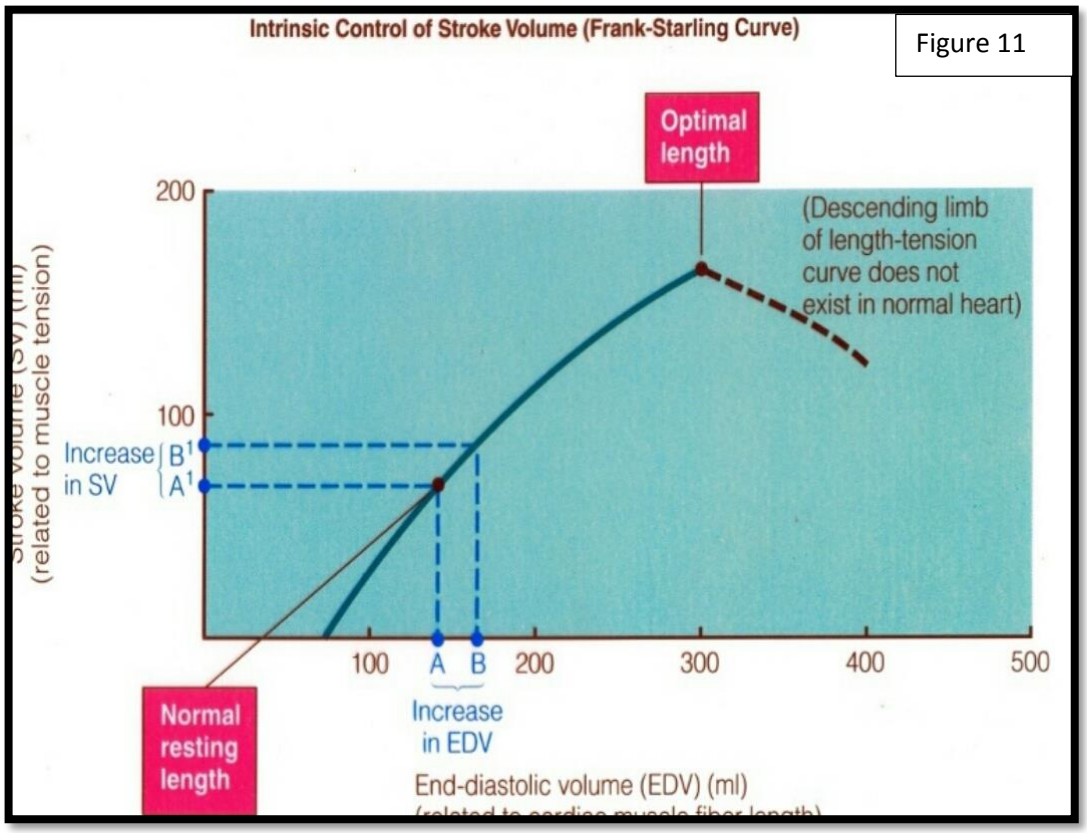


Figure 11

- 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.

VI. Cardiac output concepts and regulators:

A) Heart rate regulators

● They are either positive or negative chronotropics.

- Autonomic nervous system: as known, sympathetic stimulation increases heart rate, and parasympathetic stimulation decreases the heart rate.

- 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.

●Atrial (Bainbridge) reflex: ***a sympathetic reflex initiated by increased blood in the atria.***

- Increased blood returning to the atria pressures on SA node, stimulating it, thus increasing heart rate.

B)Cardiac output

●We know that the Cardiac Output is the amount of the blood produced by the heart per one minute, it equals also the sum of all tissue flows and is affected by their regulation:

- CO is proportional to tissue O_2 use.
- CO is proportional to 1/TPR when AP is constant.
- According to ohm laws of electrical currents, currents flow according to voltage changes. The value of this current equals voltage change over total resistance.
- Same thing applies here, Cardiac output equals pressure gradient over total peripheral resistance.
- Pressure gradient equals the difference between mean arterial pressure and the right atrial pressure.
- Mean arterial pressure is the mean of systolic and diastolic pressure, calculated by integration.
- CO = (MAP - RAP) / TPR
- Right atrial pressure equals zero, so we can neglect it
- CO=MAP/TRP

CO = MAP/TPR……(4)

●Cardiac index = cardiac output/surface area of the body.

- is 3 L/min/m2 in normal people.
- Cardiac index allows us to compare the heart's functioning in different people.

Cardiac index= Cardiac output/Surface area of the body……(5)

●In figure 12, we can see the relationship between right atrial pressure and the cardiac output:

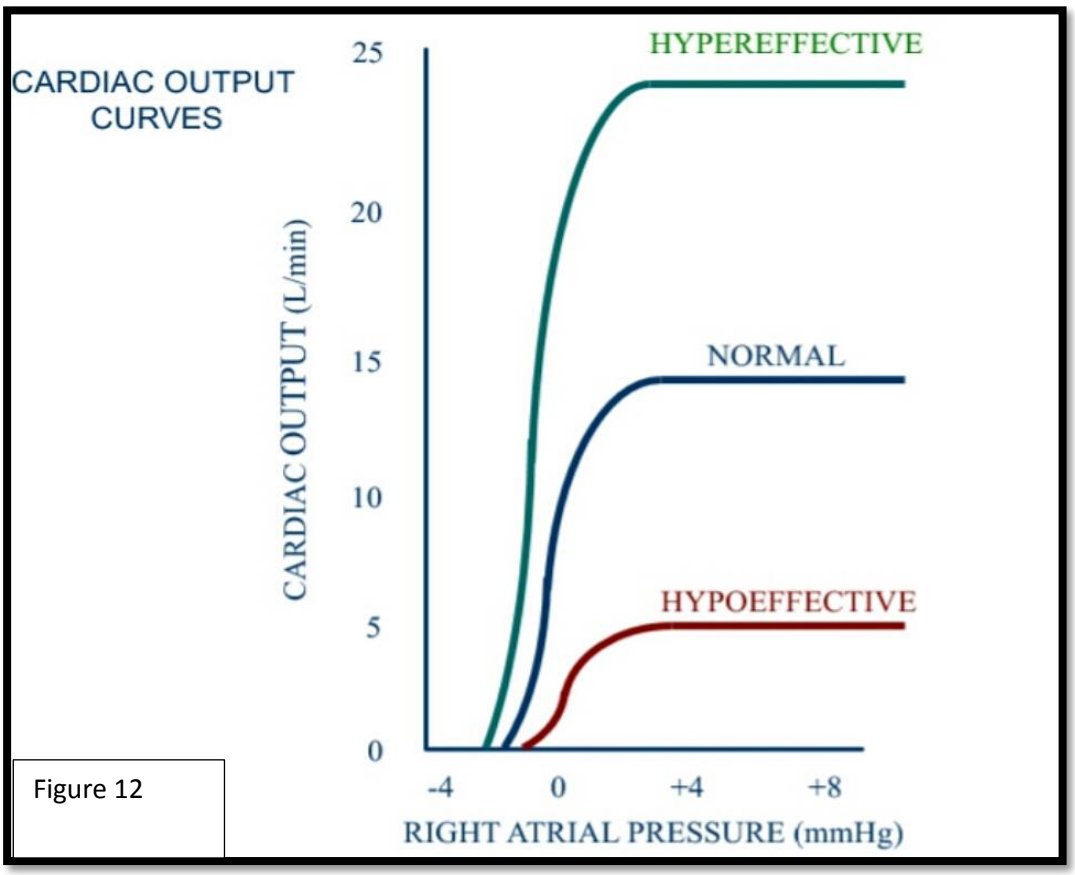


Figure 12

- The higher the right atrial pressure, the more that ventricular EDV is, and the more we have passive tension.

- As we increase right atrial pressure, Cardiac output increases, as we increasing contractility according to frank-starling law.
- After we reach the maximum value of active tension, we will observe a brief plateau in this curve, as the increase in the EDV won't increase contractility.
- If we increased right atrial pressure more and more, the cardiac output will decrease, leading to heart failure. (Not seen in the figure)
- In causes of cardiac hyperactivity (in athletes, sympathetic stimulation.. etc), the curve will be higher as we are increasing stroke volume.
- In causes of cardiac hypoactivity (in MI, sympathetic block.. etc), the curve will be lower as we are decreasing stroke volume.
- ***figure 13*** shows the difference in work done between two ventricles, the curves have similar pattern, but the left ventricle do higher work (10 times) as it pumps the blood against higher resistance.

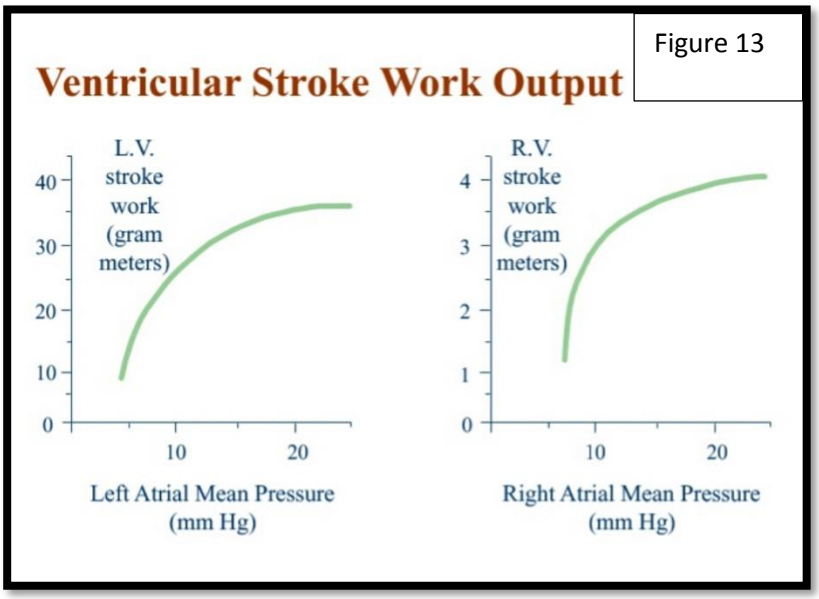


Figure 13

●The end ☺ ☺ ☺ ☺

●Sorry for this very long sheet 😊.. I'm sure it is the longest physiology sheet ever.

● "If you really want to do it, you'll find a way. If you don't, you'll find an excuse."

●Good luck

●Mohammad Qussay Al-Sabbagh