

# Cardiovascular System

Subject | Physiology

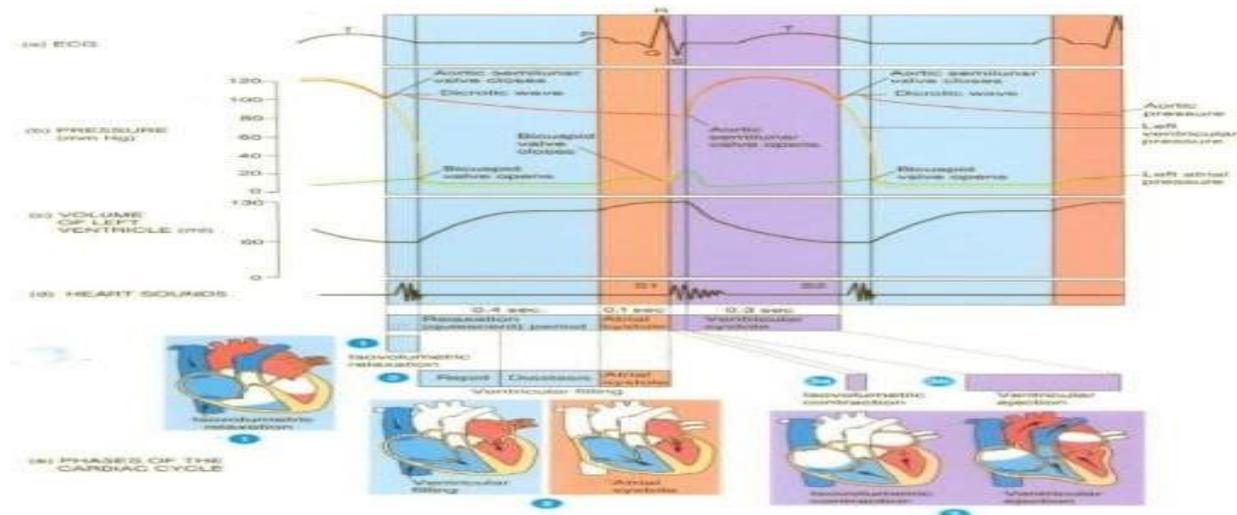
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## Cardiac cycle:



-The cardiac cycle takes 0.8 second to happen. This number is only for teaching and it is not fixed for all people. The atrial systole takes 0.1 second. The atrial diastole takes 0.7 seconds. Ventricular systole takes 0.3 seconds. Ventricular diastole takes 0.5 second

### -The ECG:



-the orange color represents the atrial systole. As you can see, the P wave starts before the contraction of the atria. The purple color represents ventricular systole. As you can see, the QRS wave starts before the contraction of the ventricles. The blue color represents relaxation. As you can see, the T wave starts before the relaxation.

### -The volume:



-this represents the volume of the left ventricle. the orange color represents the atrial systole. The purple color represents ventricular systole. The blue color represents relaxation.

- As you can see, the volume increased when the atrial systole started. The increase is not that much. The atrial systole gives the ventricle 25% of blood volume so it is not that essential.

-As you can see, the volume is fixed at the beginning of the ventricular systole because: 1- the AV valve closes when the systole starts, so no more blood will come to the ventricles from the atria 2-the semilunar valve is already closed so no blood will leave the ventricle. This is called isovolumic contraction.

-After that, the pressure in the ventricle is higher than the pressure in the Aorta, which opens the semilunar valve. Opening of the semilunar valve causes the blood to flow from the ventricle to the aorta. This is the cause of the high decrease in the volume of blood in the ventricle. This blood ejected from the ventricle to the aorta is called stroke volume.

- Stroke volume can be calculated: End-diastolic volume – End-systolic volume

- If you multiply the stroke volume by the heart rate, you get the cardiac output. So the cardiac output is the amount of blood ejected from the ventricle in a minute.

-After the contraction, the volume is fixed. This is called isovolumic relaxation. The reason is that the semilunar valve is closed because the aortic pressure is higher than the ventricular pressure and the AV valve is still closed so no blood will come from the atrium.

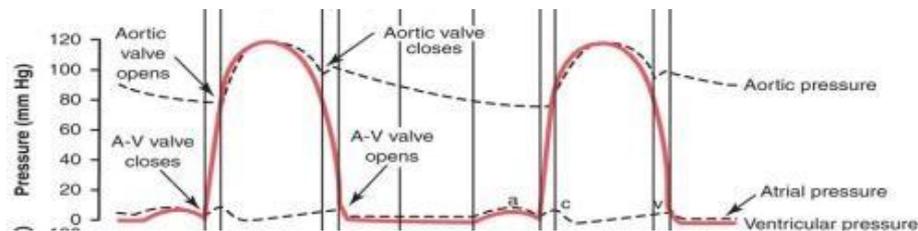
-The ventricular pressure continues to decrease which causes the opening of the AV valve. This then causes rapid filling of the ventricle which increases the volume of blood in the ventricle.

### The sounds:



-The first sound is the result of the AV valve closure and the second sound is the result of the semilunar valve closure

## Ventricular pressure:

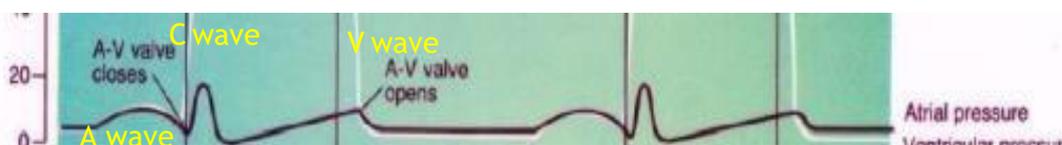


-The AV valve closes as a result of contraction of the ventricle to prevent blood flow from the ventricle to the atrium during systole. The AV valve is prevented from opening into the atrium during ventricular contraction by the chorda tendeneae that are pulled down by the papillary muscles in the ventricle. So the papillary muscles prevent prolapse of the AV valve. If myocardial infarction happens and the papillary muscles are damaged, this causes the flow of blood from the ventricle to the atrium during ventricular systole because of the AV valve prolapse. This is called **atrioventricular regurgitation**. In this case, you hear abnormal heart sounds. As mentioned before, the sounds are caused by the closure of the valves of the heart, so if the AV valve doesn't close the heart sound will be abnormal.

-The pressure in the ventricle continues to increase and it becomes higher than the pressure in the aorta, which opens the semilunar valve. Most of the systole the pressure in the ventricle is higher than the aortic until the end of the ventricular contraction. At that moment, the aortic pressure becomes higher than the ventricular pressure. This closes the semilunar valve. The closure of the semilunar valve prevents the back-flow of blood from the aorta back to the ventricle. When the valve closes, the pressure around the valve increases because the blood accumulate near the valve as it tries to go back to the ventricle, which increase the aortic pressure. So there is another increase in the aortic pressure which makes another wave called Dicrotic notch or Incisura.

The aortic pressure ranges from 80 to 120 mmHg and the left ventricular pressure ranges from 0 to 120 mmHg. On the right side of the heart, the right ventricular pressure ranges from 0 to 25 mmHg and the pulmonary pressure ranges from 8 to 25 mmHg.

## Atrial pressure:



-The black line is the atrial pressure.

-As you can see, there is a wave at the beginning; this is caused by the atrial systole. Systole means contraction and contraction means increasing the pressure. This is called the A wave.

-After the first wave, there is another wave caused by the ventricular pressure. The AV valve is closed because the ventricular pressure is higher than the atrial pressure.

While the valve is closed, it is pulled by the papillary muscles to prevent it from opening into the atria. Despite this, the ventricular pressure pushes the valve upward a little bit. This causes the increase in the atrial pressure. This wave is called the C wave. So the C wave is caused by the contraction of the ventricle.

- After that, the pressure in the atrium decreases because the semilunar valve opened and the ventricular pressure (which causes the C wave) decreased.

-The atrial pressure then starts increasing gradually as a result of the filling of the atria by the superior and inferior vena cava in the right atrium and by the pulmonary veins in the left atrium. This increase is slow because the atrial muscles are relaxed and they stretch. So the volume of blood increases without increasing the pressure a lot. This is called compliance. Remember that the AV valve is closed during this time which allows the increase in the pressure. If it was open the pressure will not increase because the blood will not accumulate in the atria and instead it will flow into the ventricles.

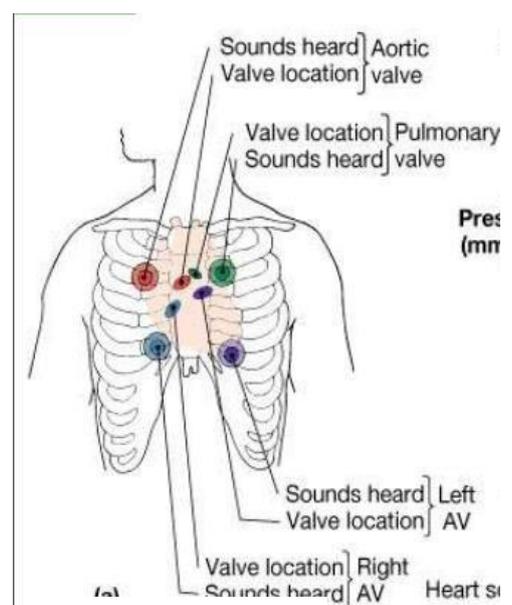
- With the diastole of the ventricle, the AV valve opens. This causes the flow of blood from the atrium to the ventricle. So the pressure in the atria is now zero. This third wave formed is called the V wave (I pointed it in the figure).

- You may hear a third or fourth sound in the heart. This is caused by turbulence (violent or unsteady movement of fluid, which is blood in our case)( all sounds are due to turbulence).

The third heart sounds are **caused** by a sudden and fast deceleration of blood flow into the ventricle from the atrium. The fourth sound is caused by atrial systole. Both of them are usually not heard. Abnormal heart sounds are called Murmur.

-Sounds summary: S1: caused by turbulence of blood around the AV valve. S2: caused by turbulence of blood around the semilunar valve. S3: caused by the rapid filling of the ventricle. S4: caused by atrial systole.

-You can hear these sounds from the chest. S1 and S2 are parasternal. The figure shows where you can hear each valve.



## Cardiac reserve:

-Normally, just by the Frank-Starling law (without any sympathetic effect), the cardiac output can be increased up to 15 liters per minute. By increasing the blood in the atrium during resting state, the muscles stretch more which causes a stronger contraction. So the maximal cardiac output without autonomic stimulation is 15 liters per minute in normal people.

-The normal (resting) cardiac output is 5 liters per minute. The difference between the maximal cardiac output (15) and the resting cardiac output (which varies from one person to another and it is usually around 5) is called cardiac reserve. So the cardiac reserve is around 10 liters normally.

-Cardiac reserve is only used in emergencies since it is neither that informative nor important. So it may be an indicator for something but it is not relied on.

-In athletes the cardiac reserve may be high since they might have ventricular hypertrophy and sympathetic stimulation during exercise. Their maximum cardiac output may reach 35 liters.

-Athletes normally have lower heart rate than other people. Because they might have ventricular hypertrophy their force of contraction is higher. If they are resting, they will only need 5 liters of blood per minute. So if their heart rate is as other people, their cardiac output will be high.

So the heart rate is lower to reduce the cardiac output( eg 50bpm)

## Factors affecting stroke volume:

-Preload: it is the end diastolic volume that stretches the right or left ventricle of the heart to its greatest dimensions. So it is basically the same as Frank-Starling law.

-Afterload: in order for the heart to open the semilunar valve, it has to exert pressure during ventricular contraction higher than the aortic pressure( during diastole which is 80mmhg) in case of the left ventricle and higher than the pulmonary pressure (8mmhg)in case of the right ventricle So the Afterload is the amount of contraction

that the ventricle has to develop in order to eject blood. A definition from the internet :

{ **Afterload** is the pressure against which the **heart** must work to eject blood during systole (systolic pressure). The lower the **afterload**, the more blood the **heart** will eject with each contraction}.

-Contractility: cardiac cell contractile force due to factors other than end diastolic volume. So if you fix the end diastolic volume and increase the stroke volume with decreasing ESV this is called contractility ( same as positive Inotropic effect). Positive inotropic effect increases the stroke volume and decreases the end systolic volume.

-Increasing preload increases the stroke volume so it increases the cardiac output

-Increasing afterload: increasing afterload means that you need more contraction. If contraction is not increased, then the stroke volume will decrease. So to keep the stroke volume, more contraction is needed and more energy is needed which means the need for more oxygen. So if a person has coronary stenosis and the oxygen amounts are not sufficient, all of the oxygen will be used in contraction and there will not be enough left for other cells so ischemia occurs. This is why you need to reduce

blood pressure in aortic/ pulmonary artery. High blood pressure increases the afterload because the aortic pressure is higher than normal and needs more contraction in order to open the semilunar valve.

-increased stroke volume doesn't necessarily increase the cardiac output because the heart rate might get lower.

And increasing the heart rate doesn't necessarily increase the cardiac output because the stroke volume might get lower. Since cardiac output= stroke volume\* heart rate, you have to increase both or increase one of them and fix the amount of the other in order to increase the cardiac output.

**A REDO/ YOU CAN SKIP THIS BOX IF U UNDERSTOOD WHATS ABOVE.**

**Stroke volume regulators:**

**1- Preload (Frank-Starling law):** within physiological limits, an increase in the passive tension increases the force of contraction.

\*Preload is an intrinsic factor.

-A breakdown of Frank-Starling Law>>

An increase in resting/passive tension = an increase in the end diastolic volume.

What's an end diastolic volume? the volume of blood in the ventricle BEFORE it contracts (also known as **PRELOAD** ).

\*\*Frank-Starling Law: stroke volume of the heart increases in response to an increase in the volume of blood in the ventricles, before contraction (the end diastolic volume), when all other factors remain constant (within physiological limits). \*\*

BUT keep in mind that if we **exceed the physiological limit** an INCREASE in the end diastolic volume causes a DECREASE in the stroke volume. (Heart failure)

**1- Contractility (inotropic effect):** with a fixed end diastolic volume, there's an increase in the stroke volume.

Positive inotropic effect: decreasing the end systolic volume, while maintaining the same - fixed- end diastolic volume, results in an increase in the stroke volume.

\*This is an extrinsic factor.

What causes a positive inotropic effect?

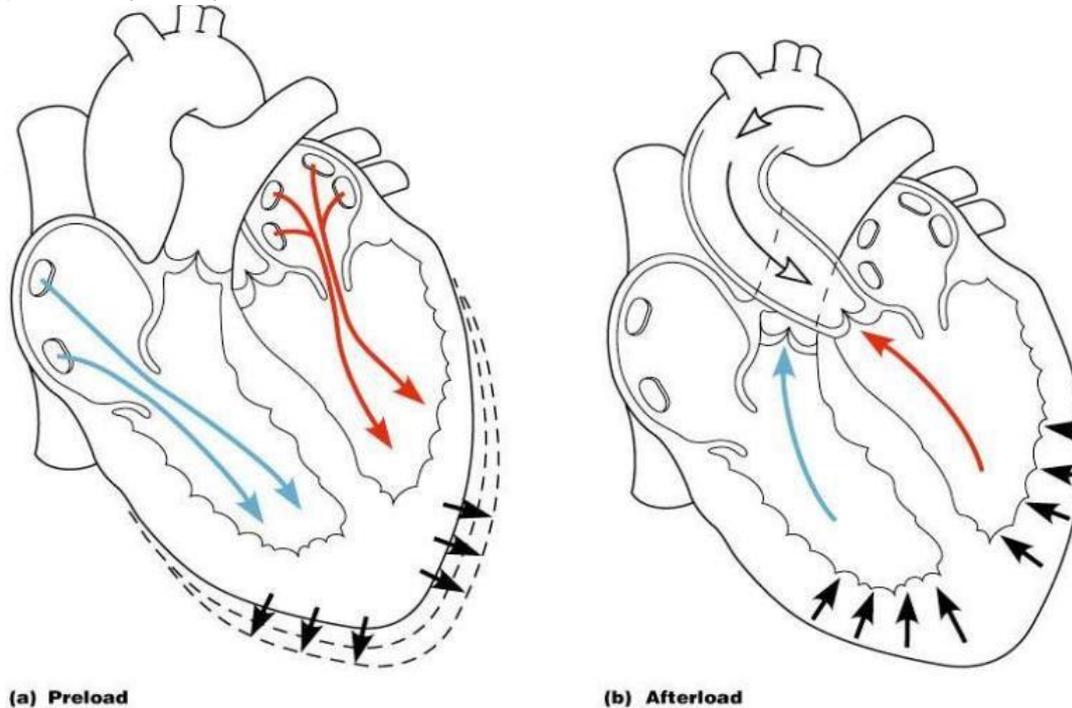
-Catecholamines (derived from tyrosine) - Sympathetic stimulation -Glucagon. -Certain hormones -  $Ca^{+2}$  and some drugs.

What causes a negative inotropic effect?

- Acidosis - Increased extracellular  $K^{+}$  - Calcium channel blockers

**2- AFTERLOAD:** the amount of tension the heart has to develop in order for it to eject blood. (HOW? when the pressure in the left ventricle exceeds 80 (diastolic pressure in the aorta) or it exceeds 8 in the right ventricle (diastolic pressure in the pulmonary artery)).

NOTE that in the afterload, we are talking about diastolic pressure in the aorta or pulmonary artery, not the ventricle itself!



Notes on the illustration above:

(a): The heart is "preloaded" and has reached the state of isovolumic contraction -the contraction hasn't occurred yet but it's about to occur-.

Black arrows show the tension/pressure that is being exerted on the heart's walls.

After contraction occurs we have "afterload";

(b): It occurs when the semi-lunar valves are about to open.

\*An increase in the preload results in an increase in the stroke volume.

\*An increase in the afterload means that the ventricles have to apply more pressure to open the semi-lunar valves so, if the energy exerted remains the same then the stroke volume decreases.

>> How to maintain a constant stroke volume? By exerting more energy on contraction (a stronger contraction)

Contraction needs energy, energy is provided by ATP and the (oxygen) needed for cellular respiration comes through blood flow

What if the person has coronary occlusion or blockage? Ischemia occurs, and it might proceed into myocardial infarction.

Cardiac output= Heart rate\* Stroke volume.

So, in order to increase **cardiac output** we have to increase:

1. stroke volume while heart rate is fixed.
2. heart rate while stroke volume is fixed.
3. both

To increase **stroke volume** we:

1. Increase the end diastolic volume (preload) within physiological limits.
2. Increase contractility (positive inotropic effect).

We call the change in contractility; inotropic effect, but how do we change it?

-Positive inotropic agents (increase contractility) include increased sympathetic stimulation, catecholamines, glucagon and thyroid hormones, increase in extracellular  $Ca^{2+}$ .

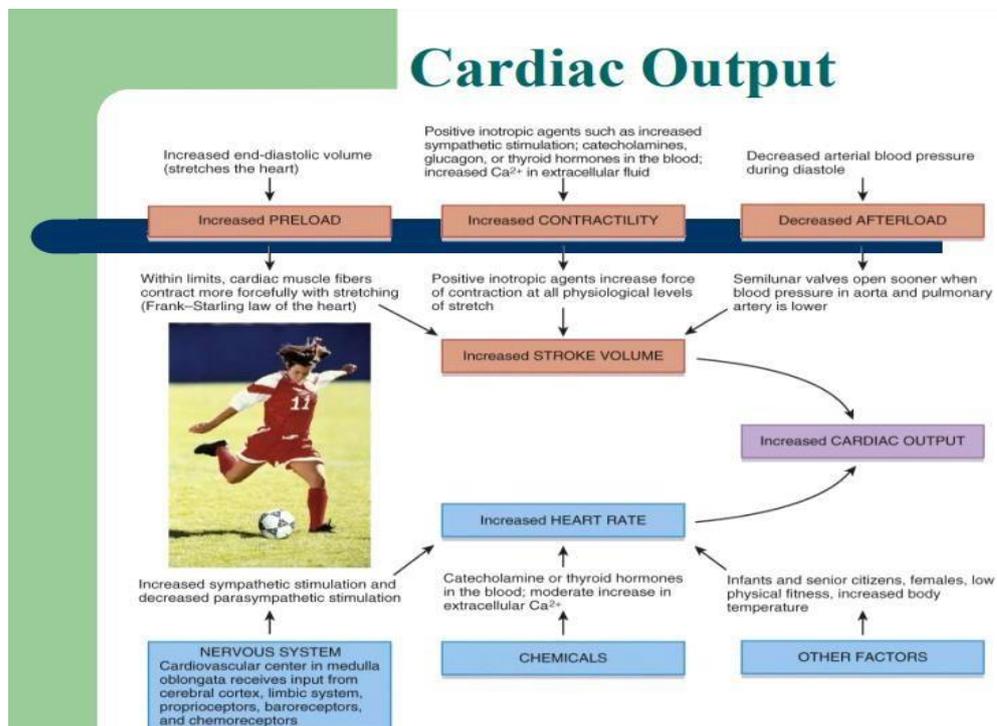
-Negative inotropic agents (decrease contractility) include  $Ca^{2+}$  channels blockers (less calcium entering the myocardial cell), hyperkalemia (affects the membrane resting potential) and acidosis (decrease in the pH) that can affect the enzymes activity.

. Increased the heart rate can lead to increased cardiac output, and we call the change in the heart rate; chronotropic effect

\*Positive chronotropic, increasing heart rate by sympathetic stimulation or also by catecholamines or thyroid hormones in the blood or due to increased temperature.

\*Negative chronotropic, decreasing heart rate by parasympathetic stimulation.

Decrease the afterload, the semilunar valves open sooner and the stroke volume increases.



\*\*This slide summarises all of the above and it's really important to understand, do not skip it.\*\*

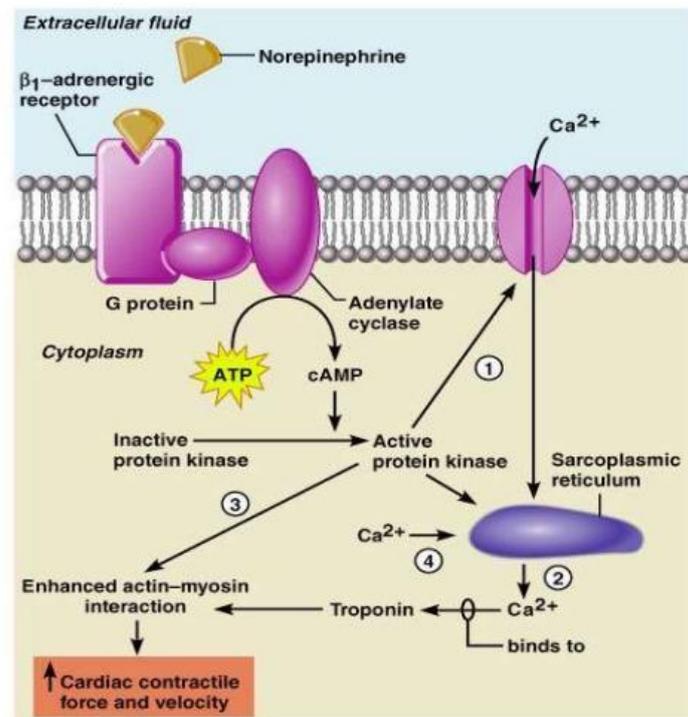
3. \*The parasympathetic system has a negative inotropic effect on the atria but not the ventricles.

**KEEP IN MIND THAT:**

An increase in the EDV leads to an increase in FORCE OF CONTRACTION (FRANK-STARLING LAW).

## Contractility and Norepinephrine

- Sympathetic stimulation releases norepinephrine and initiates a cyclic AMP second-messenger system



\*\*Norepinephrine is released from sympathetic nerve endings, then it binds to  $\beta_1$ -adrenergic receptors in the heart resulting in the activation of G-protein, the activated G-protein will activate adenylate cyclase, which will produce cAMP, that will activate Protein kinase A.

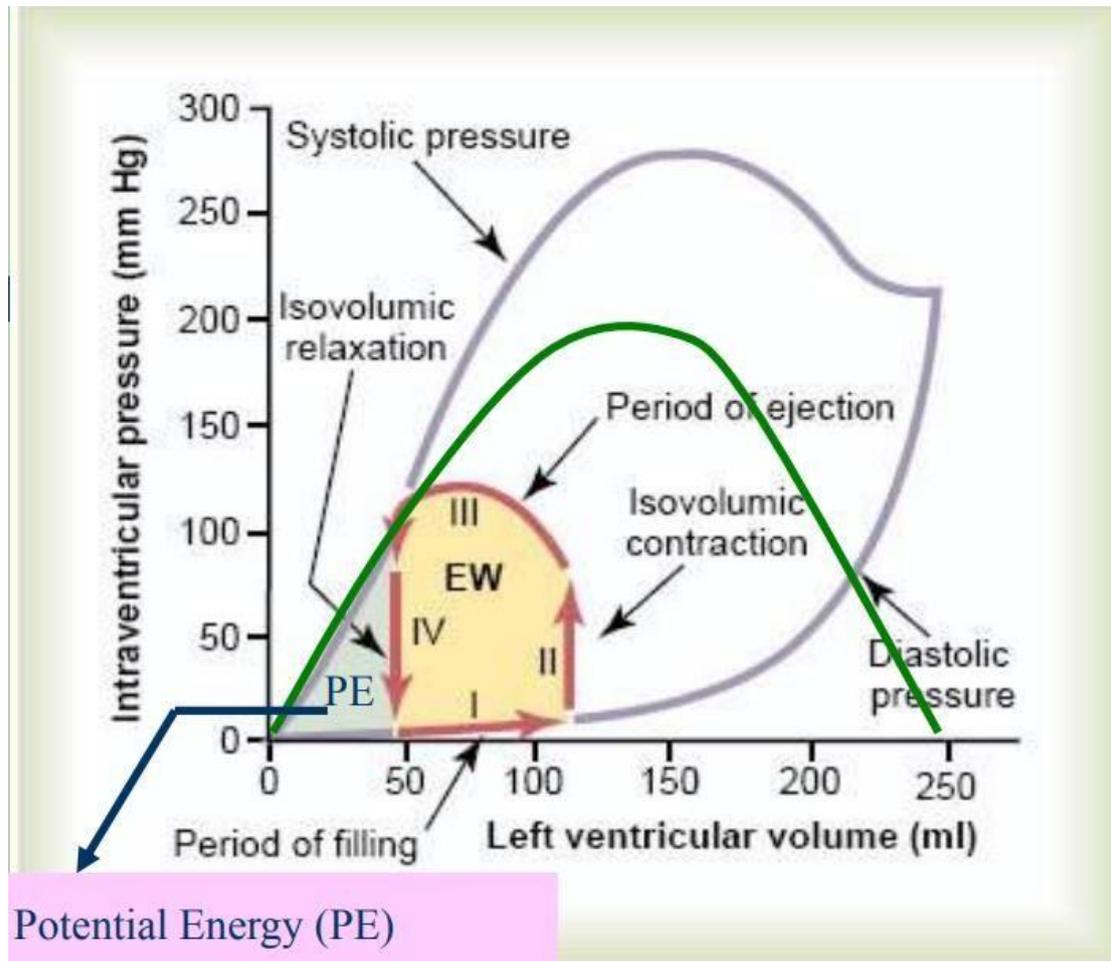
Protein kinase A will activate (via phosphorylation) phospholamban, which will activate the Ca<sup>+</sup>-pump of the SR, so we will have more Ca<sup>+</sup> stored in the SR.

In the following cycle, more Ca<sup>+</sup> will be released from the SR, resulting in increased contractility (positive inotropic effect).

Also, this activated Ca<sup>+</sup>-pump will return the Ca<sup>+</sup> to the SR faster, so the time of diastole will be decreased, when diastolic duration becomes less, the time a heartbeat takes will, in turn, be less and the heart rate will increase (positive chronotropic effect).

\*When the heart rate increases diastolic duration decreases significantly, the decrease in systolic duration is much less.

## Mathematical representation of the cardiac cycle.



To represent the cardiac cycle in terms of curves

- X axis: (left ventricular volume).
- Y axis: intra-ventricular pressure.

We start the cycle from the end systolic volume

**Phase I:** gradual filling of the heart in blood, the volume and pressure (insignificantly) increase because it's a slow increase, the ventricular muscles are relaxed and stretchy during the **FILLING PERIOD**.

\*\*In compliant tissues, very little increase in pressure occurs regardless of how much volume we add; unlike non-compliant tissues.

**Phase II:** we reached end of diastole and got to the beginning of systole, this phase stands for **isovolumic contraction** (the first stage of systole) where there's a change in pressure but no change in volume (fixed). The AV valves close and the pressure keeps increasing.

**Phase III:** Pressure keeps increasing until the semilunar valves are opened when the pressure of the ventricles exceeds the pressure of the aorta or pulmonary artery, and when

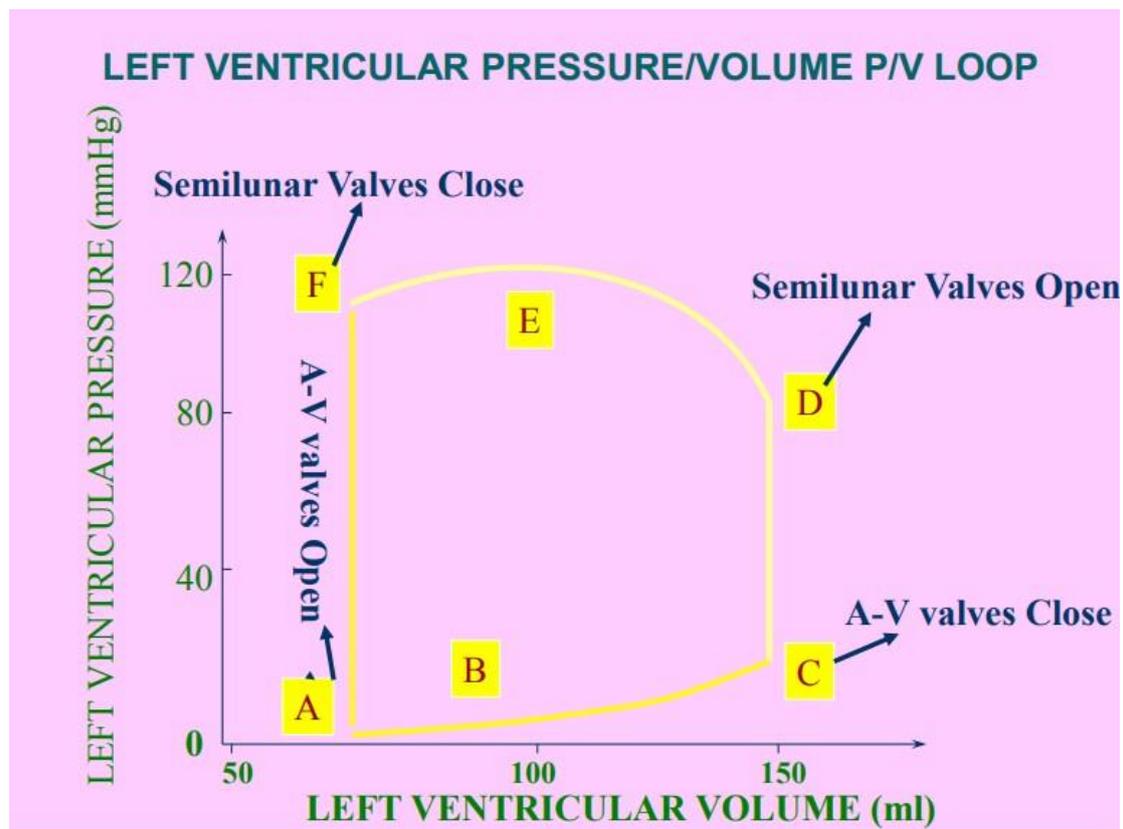
the valves open ejection occurs and the volume decreases. Note that the pressure keeps increasing. At this point we've reached the end of systole. And it's called **ejection phase**.

**Phase IV:** this represents the beginning of diastole which begins in **isovolumic relaxation**.

In cardiac cycle, we have three types of energy (work) spent by the heart during the cycle, and they can be calculated from the curve:

1/Using this curve, we can calculate the energy exerted by the heart. Now, how much energy (work) is spent is represented by the area under the curve **EW (external work)**.

External Work: represents the main energy spent by the heart to move the blood in the circulation



Y axis: Intra-ventricular pressure. X axis: Intra-ventricular volume

A: AV valves open

B: filling phase.

C: AV valves close, Isovolumic contraction (first heart sound)

D: Semi-lunar valves open

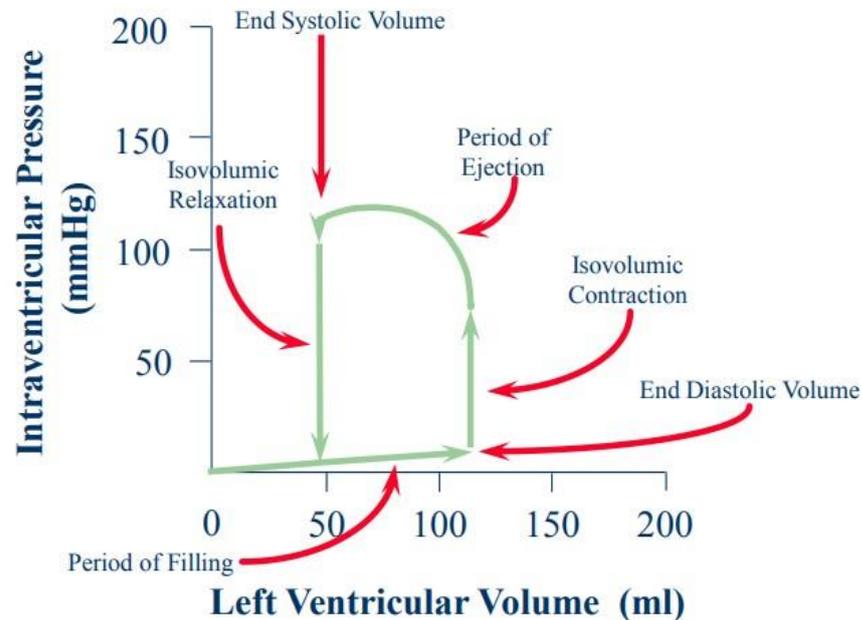
E: Ejection

F: Semi-lunar valves close. (second heart sound)

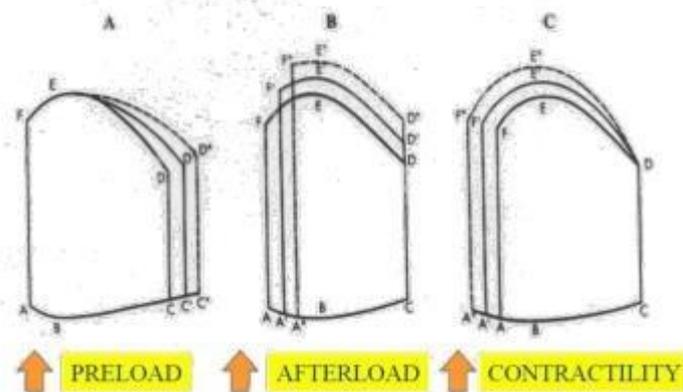
ABC (filling phase) duration is longer than CDEF duration. (why?) because ABC represent diastole while CDEF represent systole..

Valves are there to prevent backflow, while chordae tendineae are there to prevent the prolapse of A-V valves!

## Work Output of the Heart

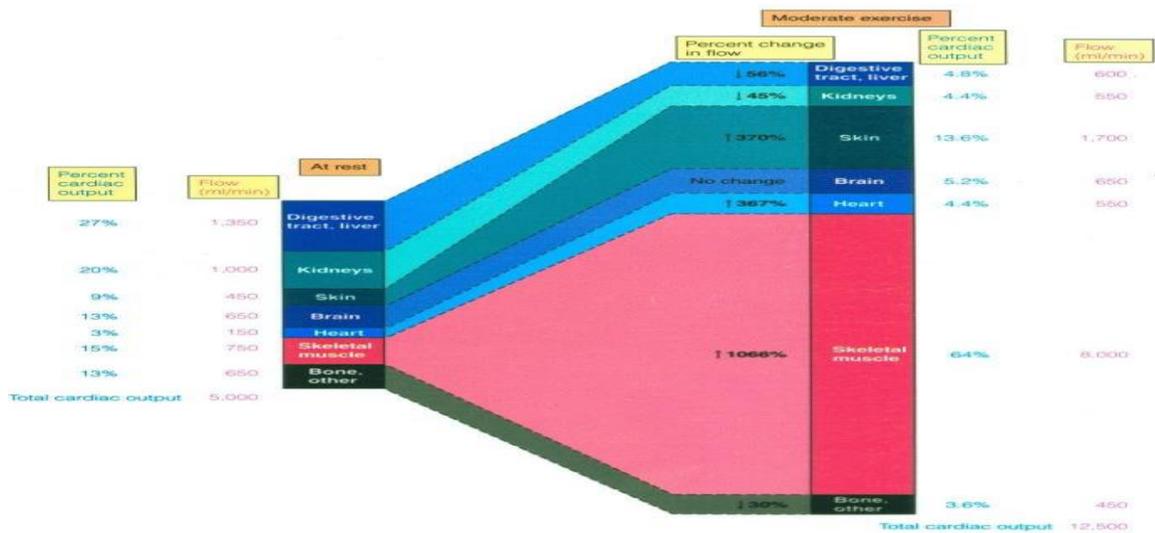


### PRESSURE/VOLUME RELATIONSHIPS UNDER DIFFERENT CONDITIONS

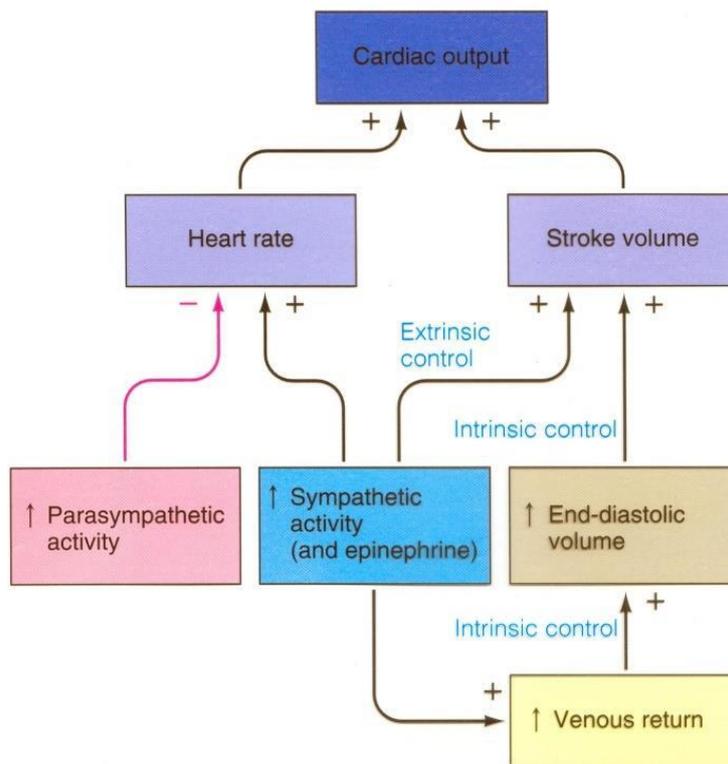


heart work output is affected by pre- and afterload:

- In the first curve from the left, we have an increase in the preload (increase in the EDV), and this means an increase in stroke volume, according to Frank-Starling law (the curve shifted to the right due to the increase in the EDV)
- In the middle one we have an increase in the afterload which leads to a decrease in the stroke volume (shift to the right due to the increase in the ESV) as well as a shift upwards as the ventricles need to generate more pressure to overcome the increase in afterload.
- In the last one, we have an increase in the contractility, which will result in an increase in the stroke volume, by decreasing the ESV (shift to the left due to the decrease in the ESV).



\*\* Magnitude and distribution of CO AT REST and during moderate EXERCISE



\*\* note that stroke volume not affected by parasympathetic