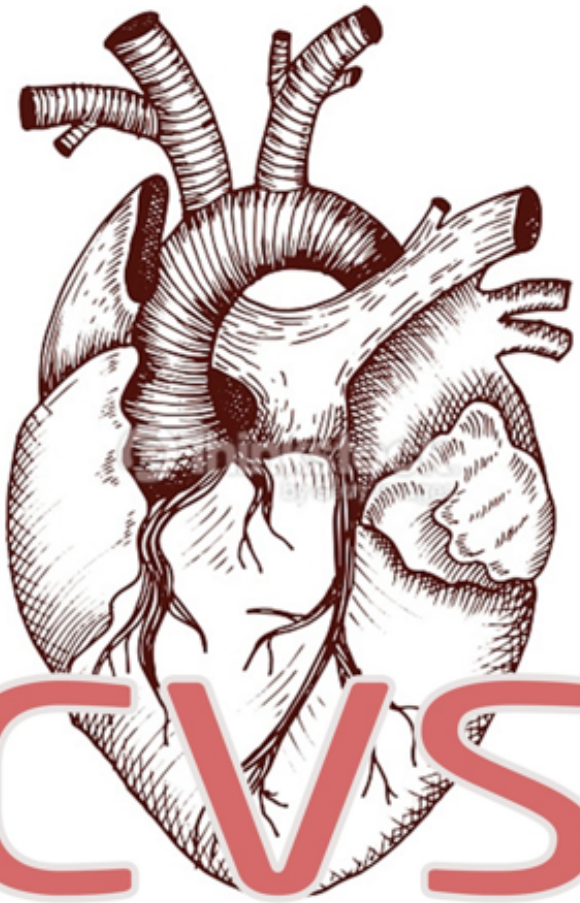


CVS

Physiology

♡ Slide Sheet ♥

Number:	12
Doctor:	Fasial Mohammad
Done by:	Renad Zakaria
Corrected by:	Omayma Hassanin

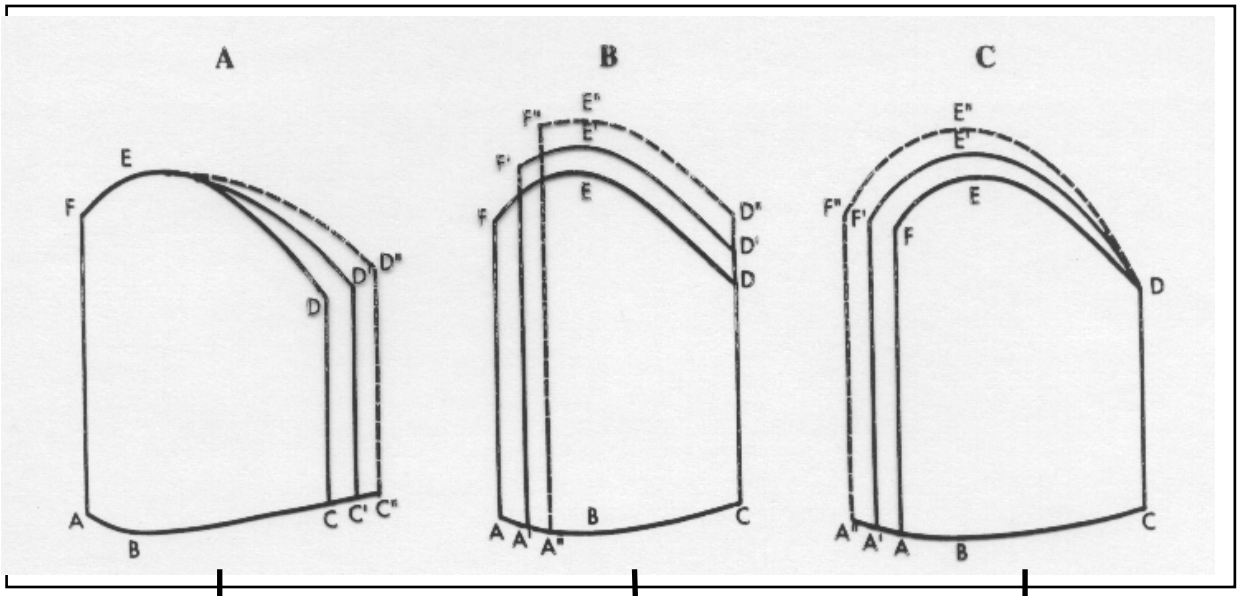
In the previous lecture:

*We talked about the cardiac cycle and its regulation:

-The cardiac cycle's regulation is either intrinsic or extrinsic.

- Intrinsic regulation is represented by the Frank-Starling mechanism, which states that within physiological limits, an increase in diastolic volume will increase the stroke volume. Maximum volume might reach normally around 50 L/minute. (Keep in mind that this maximum value is reached without extrinsic stimulation).

- We talked also about these pictures:



Increase in the preload → an increase in end diastolic volume → an increase in the stroke volume.
-It follows Frank-starling mechanism.

Increase in the afterload→ end systolic volume increases→ stroke volume decreases

Diastolic volume increases→ an increase in diastolic pressure occurs so a decrease in the stroke volume occurs.

The contractility of the heart increases; the stroke volume increases; a decrease in the end systolic volume occurs. - End diastolic volume is not affected.

[A shift of the isovolumic relaxation curve to the left]

- To maintain the stroke volume, you have to increase the work (the area under the curve), so if you increase the area under the curve, you can maintain the stroke volume.

NOTE: Be aware in the afterload, we are talking about diastolic pressure in the aorta or pulmonary artery, not the ventricle!!

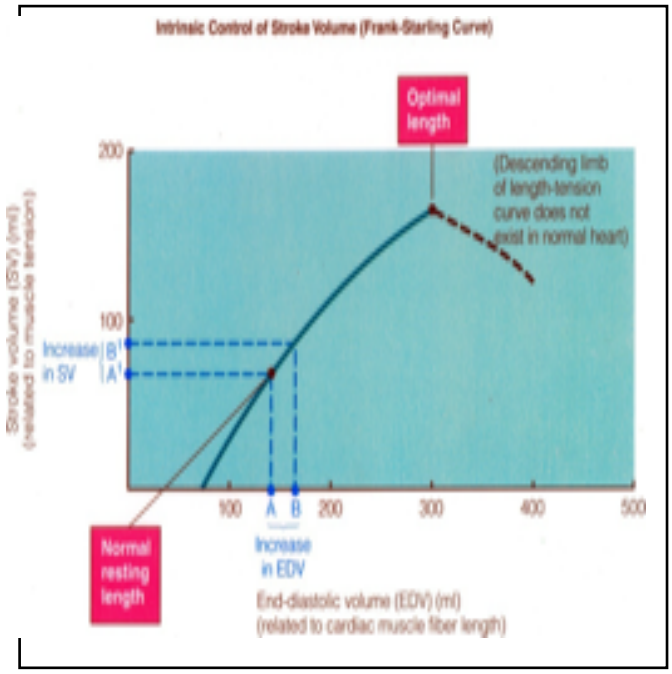
* In this figure you should notice the following:

- EDV presented on the x-axis

- Stroke volume presented on the y-axis

- As we said and according to Frank-starling, an increase in EDV will increase stroke volume until it reaches the optimal length.

- When it reaches the optimal length, the stroke volume will start to decrease, →that means cardiac failure has occurred.



- This figure is the same as that of the Length-Tension Relationship graph, where the length of the cardiac muscle is analogous to EDV, and muscle tension or intraventricular pressure is analogous to stroke volume.

Now, let's start talking about:

Regulation of Heart Rate→

We have: 1- Positive chronotropic factors increase heart rate.

2- Negative chronotropic factors decrease heart rate.

Chronotropic means:

Change of heart rate by a decrease or an increase

Regulation of Heart Rate: Autonomic Nervous System

1- Sympathetic nervous system (SNS) stimulation is activated by stress, anxiety, excitement, or exercise. Its dominant effect is to increase contractility.

2- Parasympathetic nervous system (PNS) stimulation is mediated by acetylcholine and opposes the SNS. PNS dominates the autonomic stimulation, slowing heart rate and causing vagal tone. [Mainly stimulates heart rate.]

* So, if you cut the sympathetic innervations, the contractility will decrease without much change in heart rate.

* If you cut the parasympathetic, the heart rate will increase without much change in contractility.

*If you cut both PNS & SNS, the heart rate will increase, and contractility will decrease.

Atrial (Bainbridge) Reflex

→is a sympathetic reflex initiated by increased blood in the atria.

- Increased blood volume or pressure in the right atrium will stimulate the SA node so permeability of Na in the SA increases, leading to increase in heart rate.

Chemical Regulation of the Heart

- Heart rate increases in response to the hormones epinephrine and norepinephrine.

- Intra- and extracellular ion concentrations must be maintained for normal heart function.

- Contractility increases in response to:

Epinephrine and norepinephrine, sympathetic stimulation and drugs like glucagon.

- Contractility decreases in response to hyperkalemia and acidosis.

Cardiac Output (CO)

We know that the Cardiac Output is the amount of the blood produced by the heart per one minute→ CO= stroke volume * heart rate.

- You should know that there are differences in the basic cardiac output values between individuals, since it is affected by the size and weight so to solve this there is what we call the **cardiac index** which equals to cardiac output divided on surface area (m^2):

Cardiac index = CO /surface area, so if the CO=5 L/min & surface area= 1.6 m^2 then

Cardiac index= 3L/min/ m^2 (surface area= height/weight)

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

- 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.

CO (F)= ΔP/ total peripheral resistance

- Cardiac output is from aorta to the right atrium, so ΔP is difference of pressure between aortic pressure and right atrial pressure. Total peripheral resistance equals all the resistance in all the vessels from aorta until reach the right atrium.

* Let us talk about ΔP, we learned that it is difference of pressure between aortic pressure and right atrial pressure, so what we mean by aortic pressure? Is it diastolic or systolic pressure?

It is neither diastolic nor systolic pressure. Actually, we calculate the mean arterial pressure (MAP); keep in mind we don't calculate the mean like we learned in math !! You can't say mean = diastolic + systolic /2, why?

Because diastole and systole occur at different times and they are in linear relation.

✂✂ We calculate the mean proportional to the time of systole and diastole (calculated by integration), so:

mean arterial pressure (MAP)= 1/3 of systolic pressure + 2/3 of diastolic pressure

*Because the time for the diastole (0.5 sec) is longer than the time for systole (0.3 sec), this means that the diastole contributes more to the MAP than does the systole.

equation become: CO = (MAP - RAP) / TPR

- RAP (right atrial pressure) is equal Zero (it is normally zero), so we can neglect it; thus, CO equals:

CO = MAP/TPR

- So if we want to change MAP, we change the CO or TPR or both of them.

It's worth to know:
- CO is proportional to tissue O2 use.
- CO is proportional to 1/TPR when AP is constant.

- Now we will present what happen in the heart according to frank-starling law:

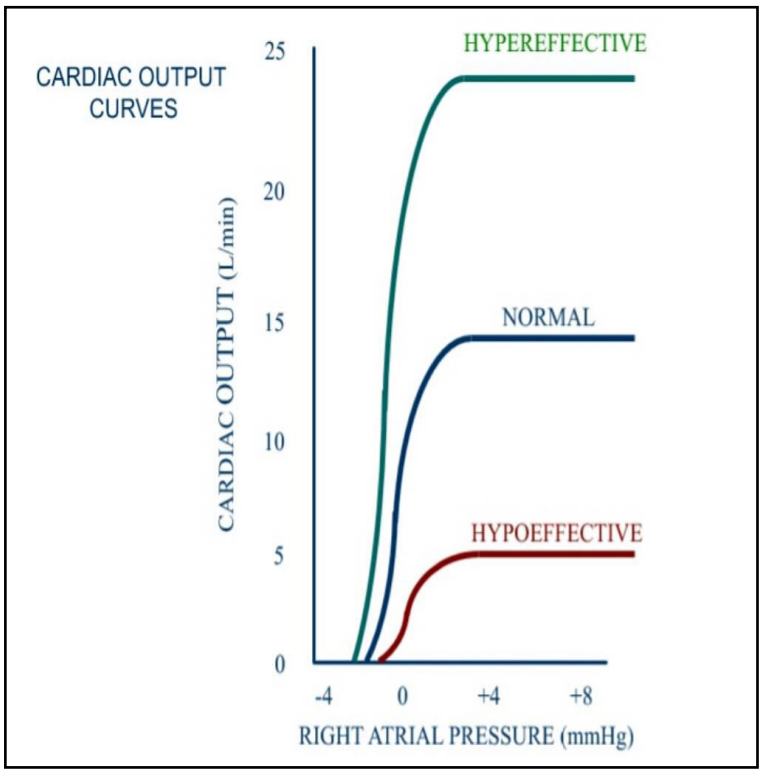
-In the diagram that we will draw, right arterial pressure on the x-axis corresponds to the EDV on frank-starling curve, and cardiac output on the y-axis corresponds to stroke volume on frank-starling curve. (CO and stroke volume are the same since CO= stroke volume * heart rate)

- Now if we increase EDV, the pressure in the ventricle will increase, and accordingly (if we talk about right atrial pressure for example) the pressure in the right atrium will increase because the flow is from right atrium to right ventricle, how come?!

When the pressure in the right ventricle increase, the pressure in the right atrium have to increase to keep the flow from right atrium to right ventricle (if atrial pressure doesn't increase, there won't be blood flow from right atrium to right ventricle!!). For example, if the ventricular pressure becomes 3, the atrial pressure has to become 5 and so on.

- And that's why we can make the right atrial pressure represent EDV on the X axis, since we can measure the right atrial pressure better than the EDV.

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



As you see in this figure:

- when the right atrial pressure equals zero, the CO will be 5 L/min.

- when the right atrial pressure increases due to an increase in EDV (Frank-starling), until it reaches its optimal (Maximum value) which is 15 L/min, we will observe a brief plateau in this curve, as the increase in the EDV won't increase contractility.

- If we increased the right atrial pressure more and more, the cardiac output will decrease, leading to heart failure. (Not seen in the figure)

- If we stimulate the sympathetic, it will increase inotropic effect (contractility):

Let's assume the EDV is constant (fixed) on zero. So, as mentioned before, at normal conditions (when there is no sympathetic stimulation), when the EDV is zero, the CO is 5. However, as illustrated in the graph, under sympathetic stimulation (or a positive inotropic effect), when the EDV -or right arterial pressure- is zero, the cardiac output is 15 L/min. Thus, under positive inotropic effect (or sympathetic stimulation) the curve will shift to the left and upward. The curve shifted to the left and upward represents a hyper-effective heart. → Cardiac Hyperactivity

Remember inotropic means:

Fixed EDV and an increase in stroke volume (thus, an increase in CO.)

** Remember in cardiac hyperactivity, it does not always happen due to sympathetic stimulation, as it can normally occur in athletes.

The optimal (maximum) value of cardiac output in a hyper-effective heart in non-athletic individuals is about 25 L/min. However, in athletes, the max. value for CO may reach 35 L/min.

- In case of cardiac hypoactivity (in MI, sympathetic block (inhibition).. etc), the curve will be lower as we are decreasing stroke volume (the curve will be shifted downward and to the right). The value of the CO when the EDV is zero may reach only 2 L; as a result, the EDV may change and increase in order to reach the 5L/min (according to Frank starling).

** Hypoactivity & hyperactivity (upward and downward) happen due to an increase or decrease in contractility.

** We talked before about Total energy which is:
Total Energy = kinetic energy + external work

You know that the kinetic energy is minimal. It can increase in case of aortic stenosis in which the heart has to develop too much to move the blood through a narrow Orifice, so kinetic energy might constitute 50% of the total energy and that is a serious problem since the total energy will increase so the oxygen consumption will increase, and that's what we called:

Ejection Fraction

- Ejection fraction is the fraction of blood ejected from a ventricle of the heart with each heartbeat and it is an inherent volumetric measure of the pumping efficiency of the heart.

- it's the fraction of the end diastolic volume ejected in each stroke volume, so we can calculate it by:

Ejection fraction = stroke volume /EDV

- It is related to contractility, so it will increase in the case of hyperactivity.

let's take an example:

If the End diastolic volume= 125 ml, End systolic volume = 55 ml, Ejection volume (stroke volume) = 70 ml→

We can calculate: 1- Ejection fraction which will be equal 56% >> (normally 60%)

** stroke volume can be calculated as EDV minus ESV

2- If the heart rate is 70 beats/minute, what is cardiac output?

Cardiac output= HR * stroke volume

=70/min. * 70 ml

= 4900ml/min.

another example:

If HR =100, end diastolic volume = 180 ml, end systolic vol. = 20 ml, what is cardiac output?

CO= 16,000 ml/min and Ejection fraction= 160/180%=~ 90%

-Notice that Ejection fraction is 90% which is very high and indicate positive inotropic effect.

Aortic Pressure Curve

*Aortic pressure starts increasing during systole after the aortic valve opens.

* Aortic pressure decreases toward the end of the ejection phase.

* After the aortic valve closes, an incisura (dicrotic notch) occurs because of sudden cessation of back-flow blood from aorta toward left ventricle. It will stop on the semilunar valve. The aortic wall will stretch a little and the pressure will increase leading to this incisura.

*Aortic pressure decreases slowly during diastole because of the elasticity of the aorta.

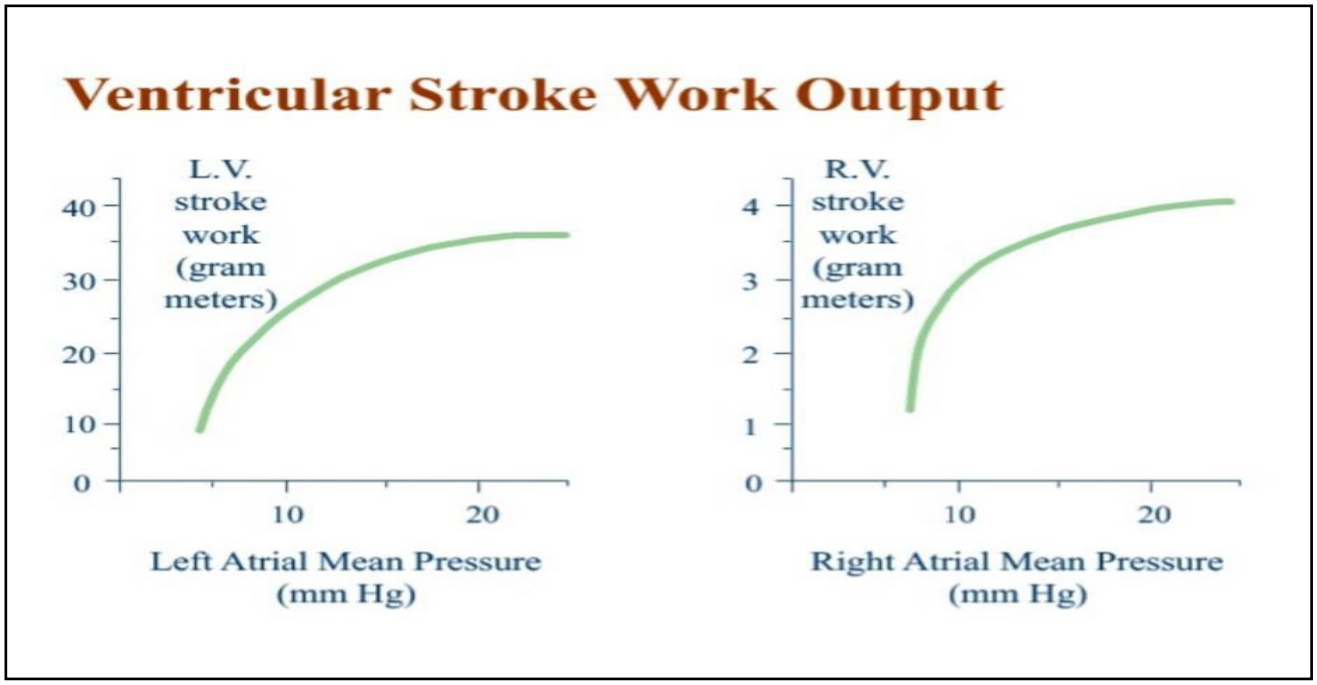
As we said before and according to Frank-Starling Mechanism:

- Within physiological limits, the heart pumps all the blood that comes to it without excessive damming in the veins (if it has 50, it will pump 50 and so on).

- If there is an abnormality like the heart have 70 but it pumps 30, it means we have heart failure. It will make congestive heart failure (stasis)>> (if what comes more than what goes, congestion results).

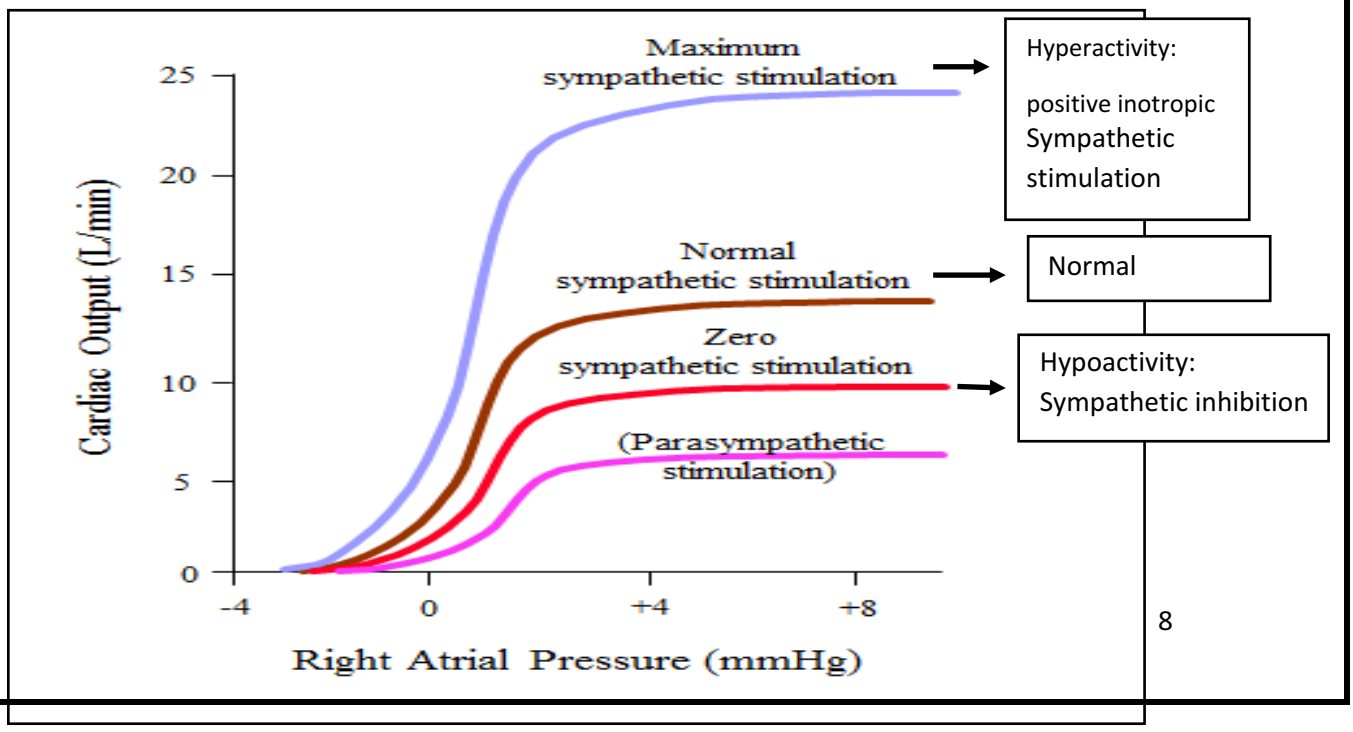
-Extra stretch on cardiac myocytes makes actin and myosin filaments interdigitate to a more optimal degree for force generation.

In the figure below: it shows the difference in work done between the two ventricles. The curves have similar pattern, but the left ventricle does higher work (10 times) as it pumps the blood against higher resistance (notice the differences in the scale).



** The pressure in the left atrium and right is almost the same.

Look at this figure it's the same thing; read the description about it below:



-Sympathetic stimulation causes increased HR and increased contractility with HR = 180-200 and C.O. = 15-20 L/min.

-Parasympathetic stimulation decreases HR markedly and decreases cardiac contractility slightly. Vagal fibers go mainly to atria.

** Sympathetic inhibition: decreases contractility and heart rate, decreases cardiac output→ we say that we have hypo-effective heart. (Shift downward and to the right).

** Forget the parasympathetic effect on the curve; it's neglected (its effect on the CO is because of negative chronotropic effect, not negative inotropic "it doesn't affect the contractility; it only affects the heart rate").

**We have a basal rate for the sympathetic effect on the heart and vessels; this is what gives us the tone of the vessels and heart.

- Because we have this basal tone, we can have positive feed-back (stimulation) and negative-feedback (inhibition).

- If we don't have the negative control, this would be very dangerous, as we only can increase the impulse and never decrease it.

- For example: if the basal rate was 100 impulse/min then we can decrease it down to 20 and increase it up to 200 or 300, but if the basal rate was 0 impulse/min, we can't decrease it.

NOTE: Fast heart rate (tachycardia) can decrease C.O. because there is not enough time for heart to fill during diastole.

Cardiac Contractility

We can measure cardiac contractility as a change in pressure per time→

Maximum dP/dt → we can't measure it; it's a machine that do the job and do the integration.

(dP/dt)/P ventricle is better. P ventricle is instantaneous ventricular pressure.

** dP/dt is not an accurate measure because this increases with increasing preload and afterload.

- But in general, it is fixed EDV with increase in stroke volume.

** Excess K+ decreases contractility.

** Excess Ca++ causes spastic contraction, and low Ca++ causes cardiac dilation.

Let's talk again about……. **Cardiac output**

- Cardiac output: is the volume of blood ejected from either the ventricle per minute.

- It's usually equal the amount of blood that return (venous return) to the heart; this is according to Frank-starling mechanism.

- Cardiac Output is the sum of all tissues' blood flow and is affected by their regulation; if blood flow in the tissue increases, the cardiac output will increase.

** F= ΔP /R (Ohm's law), so accordingly CO = (MAP - RAP) / TPR, and since RAP=0 it becomes:

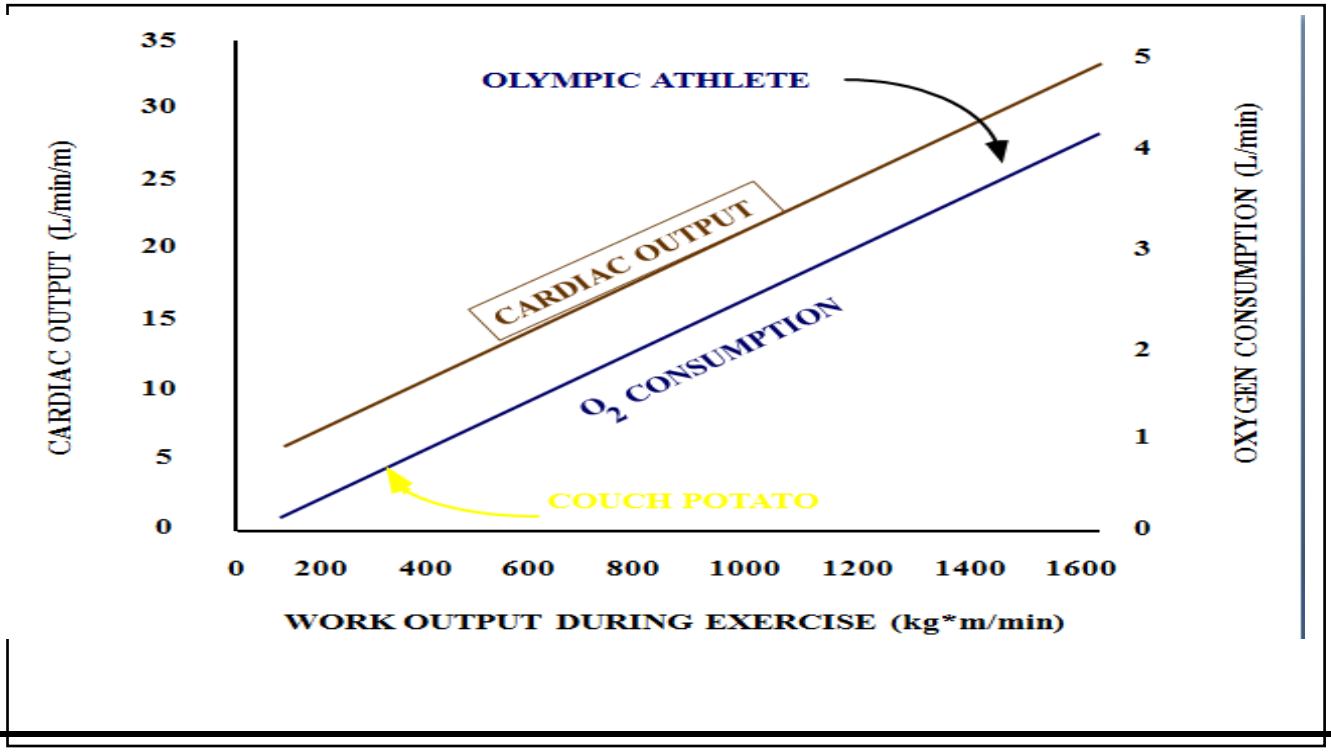
CO=MAP/TPR and so MAP=CO*TPR

** What affects the flow to tissue?

The blood flow to the tissues (CO) is mainly affected by its oxygen requirements and consumption, if the oxygen requirement increases, the blood flow increases.

- So, the cardiac output is thus proportional to the oxygen consumption by the tissues.

** This relation is shown in the figure (in the next page), on the Y axis we have the cardiac output (CO), and on the X axis we have the work output during exercise.



** In the figure above, we notice the following:

1- The line representing the cardiac output goes parallel to the line representing the oxygen consumption.

2- The more oxygen you consume, the more blood flow, so the more will be the cardiac output (more exercise).

3- In athletes the oxygen consumption is very high and that's why the cardiac output is very high, might reach 35 liters per min.

4- The low oxygen consumption is for lazy people.

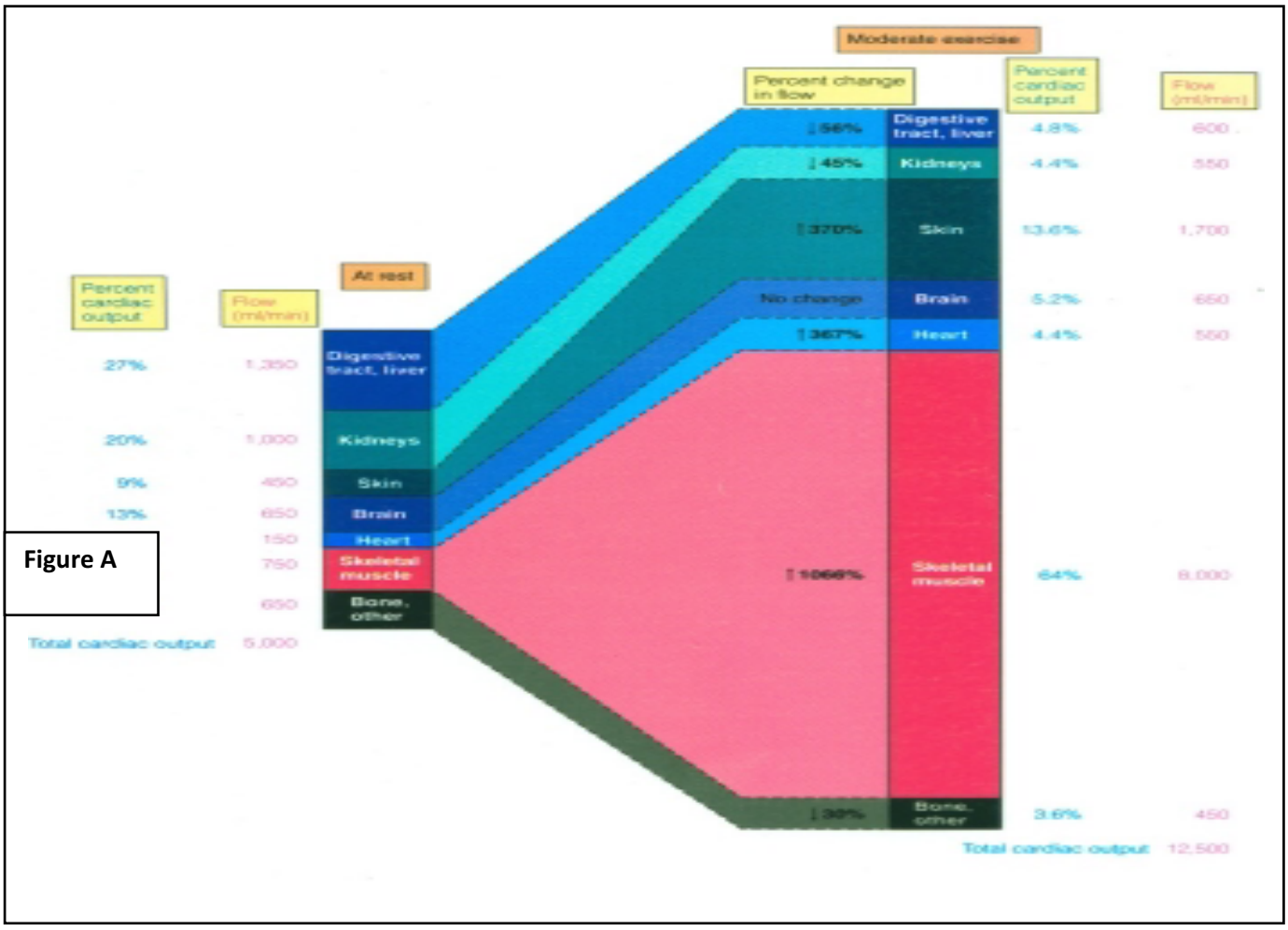


Figure A

** In the previous page, the figure A represents: Magnitude & Distribution of CO at Rest & During Moderate Exercise in different organs and tissues.

- During relaxation, the CO= 5L/min, almost just 1 L goes to the muscles (almost 20% of the CO).

- During exercise, the amount of blood reaching the tissues increases too much, almost 8L/min will reach the body tissues (50% of the CO)→ the CO will become 16L/min.

- In some of the tissues like digestive tract, the blood flow decreases during exercise. That's why it's dangerous to eat and then do exercise, you have to wait for at least 3hrs (depending on the meal components) before exercising.

- How much of the blood goes to the tissues per 100 g of the tissue?

Heart is the organ which receives the most amount of blood per 100 g of the tissue → 70ml/min/100g of tissues.

** When we say per 100g tissue, this is to relate the flow to the size, even though there are certain tissues that have higher blood flow than the heart, when this flow is for the sake of the oxygen need, the heart is on the top, how?

- For example, the kidney, the blood reaches the kidney mainly for filtration and making urine, but the blood flow to the kidney for the sake of oxygen is very minimal.

- As for the adrenal and thyroid gland because they are tiny organs, the blood that flows to them is much higher than they need.

**So, the heart has the highest blood flow "for the sake of oxygen" compared to other tissues.

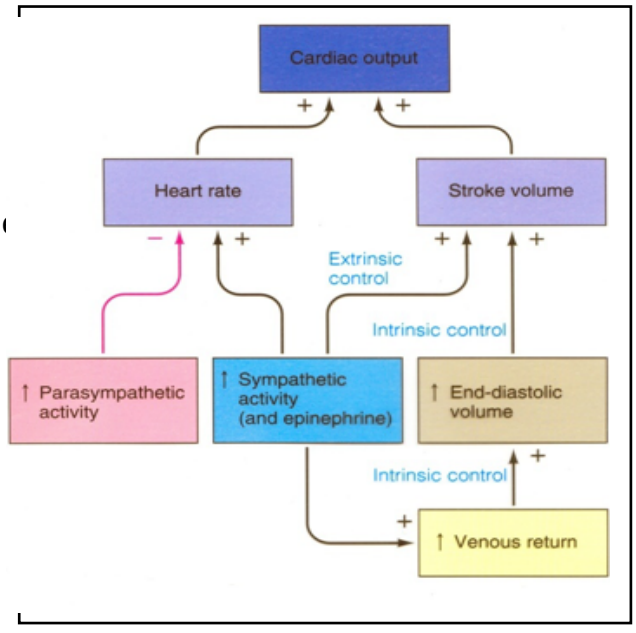
**you can refer to the slides if you want to take a look on the Variations in Tissue Blood Flow.

Cardiac output= heart rate * stroke volume

According to this equation CO is changed by stroke volume & HR.

- This figure summarizes the factors that affect th stroke volume which are:

1- Extrinsic factors: sympathetic stimulation, drugs, and positive inotropic agents.



2- Intrinsic factors (regulation): based on frank-starling law;
an increase in the end diastolic volume, increases
the stroke volume (more passive tension will lead

to more active tension).

- So, increasing the venous return increases the end diastolic volume. End diastolic volume contributes to the preload, and increasing preload increases stroke volume (again frank starling).

- You can also change the stroke volume by changing the contractility, preload, and after load.

- Increasing the contractility increases the force of contraction; thus, the stroke volume would increase (inotropic)→ increased CO.

-A decrease in afterload increases stroke volume (after load is the pressure that the ventricles pump against, "in the aorta and pulmonary arteries". In other words, the afterload of the ventricle is the pressure in the aorta leading from the ventricle.)

Heart rate:

You affect heart rate by:

- Neural stimulation: sympathetic and parasympathetic; this is called chronotropic effect.

- The sympathetic stimulation increases heart rate; has positive chronotropic effect.

- The parasympathetic stimulation decreases heart rate; has negative chronotropic effect.

- Certain hormones:

- Catecholamines "epinephrine, norepinephrine" and thyroid hormones "T3/ T4" increase heart rate.

- Certain chemicals: like calcium.

- Heat: increases heart rate.

_____

The end, sorry for any mistakes