I'd like to begin by defining some terms we already know. (You can skip them if you want)

- **Stroke Volume**: the volume of blood pumped from one ventricle of the heart with **each beat**.
- **Cardiac Output**: is the volume of blood being pumped by the heart by the left or right ventricle in the time interval of **one minute**.
- **Venous Return**: the rate of blood flow back to the heart.
- **Heart Rate**: the speed of the heartbeat measured by the number of heartbeats per unit of time (minutes)
- **End Diastolic Volume (EDV)**: the volume of blood in the right or left ventricle at the end of filling in (diastole) or the amount of blood in the ventricles just before systole.
- **End Systolic Volume (ESV)**: the volume of blood in a ventricle at the end of contraction, or systole, and the beginning of filling, or diastole.
- **Afterload**: It is the aortic pressure the left ventricular muscle must overcome to eject blood. **(Or simply as what the dr. said it's the pressure in the aorta or pulmonary artery during diastole)**
- **Preload**: the stretching of the cardiac myocytes prior to contraction. Preload, therefore, is related to the sarcomere length. Because sarcomere length cannot be determined in the intact heart, other indices of preload are used such as ventricular end-diastolic volume or pressure. **(We use the EDV to express the preload)**

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*A student asked about the difference between ejection fraction and stroke work output:

- Stroke Work Output: it's the energy needed to move the stroke volume.
- Ejection Fraction: it's a proportional value (SV/EDV)

*In this lecture we will be continuing last lecture's topic "Cardiac Output" and we will start with talking about "Venous Return"

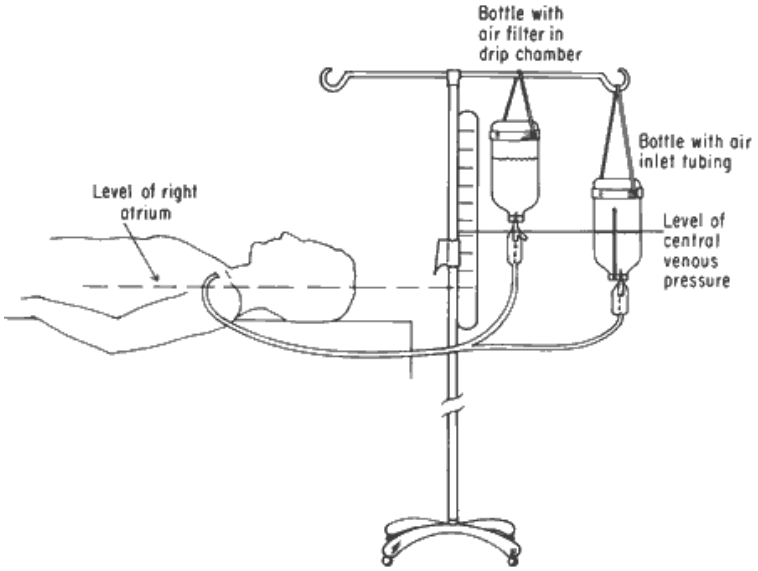
*We talked about the cardiac output curve and related it to the Right atrial pressure.

* Right atrial pressure is proportional to the EDV.

*Measuring the right atrial pressure [also called central venous pressure (CVP)] is easy while measuring the EDV isn't.

*Measuring CVP: (through central venous line):

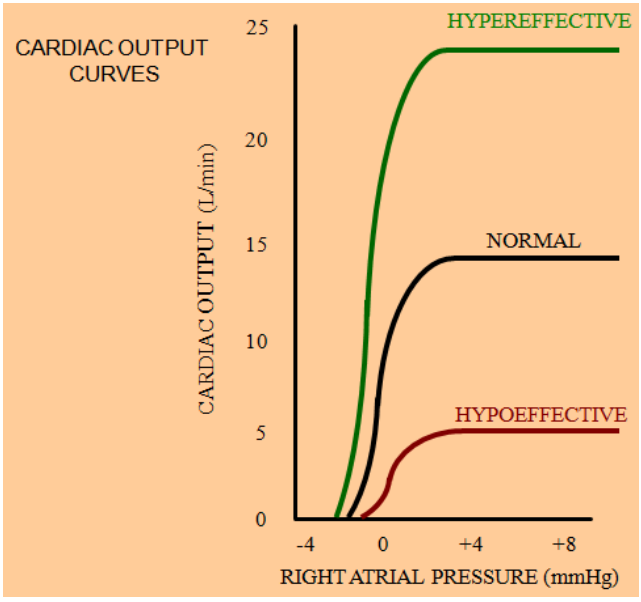
We measure the right atrial pressure (CVP) by inserting a catheter into the jugular vein or SVC until we reach the right atrium. As you can see in the picture the catheter is connected to a manometer (mercurry manometeres used to be used, but now they use digital manometers), and then they measure the central venous pressure (CVP) which is called like this because it's the central part of circulation and it's the part where all veins are drained (RT. Atrium).



*We said that when we want to measure the cardiac output curve we measure it alone, and we measure the venous return curve alone, then we put them together in one graph.

*We talked about factors that shift the caridac curve to the left and others that shift it to the right:

-Here's the cardiac output curve (please refer to it while studying the factors affecting it):



*Remember that the **right atrial pressure (RAP) is proportional to the end diastolic volume (EDV)** in the right ventricle, so eventually every time you increase RAP, the cardiac output (CO) increases.

1)Sympathetic stimulation on the heart will shift the curve upwards and to the left.

2)If the heart is inhibited or damaged (MI for example) the curve is shifted downwards and to the right.

* There are other factors affecting the cardiac output curve, but notice that we are playing with the plateau and pay attention that we're talking about the **cardiac output curve's plateau** and NOT the action potential curve's plateau.

(remember this plateau doesn't continue for a long time as the curve will drop down because according to Frank- Starling if you exceed the optimal value the curve drops down).

*Now we will be talking about the effect of the intrapleural pressure (IPP):

- As we know the heart is located in the chest and is surrounded by the lungs, lungs are surrounded by the pleura (a visceral pleura and a parietal pleura that have in between them the pleural space).

- The intrapleural pressure which is found in the pleural space is slightly less than the atmospheric pressure, in what is known as negative pressure (-5mmHg to -4 mmHg) & that's why it's inflating the lungs, i.e. you don't struggle to take a breath, the air goes in passively according to the pressure gradient.

(atmospheric pressure = 760mmHg but we will consider it our refrence and give it a pressure of zero, that's why the intrapleural pressure is negative being -4mmHg to -5mmHg as it's slightly less than the atmospheric pressure).

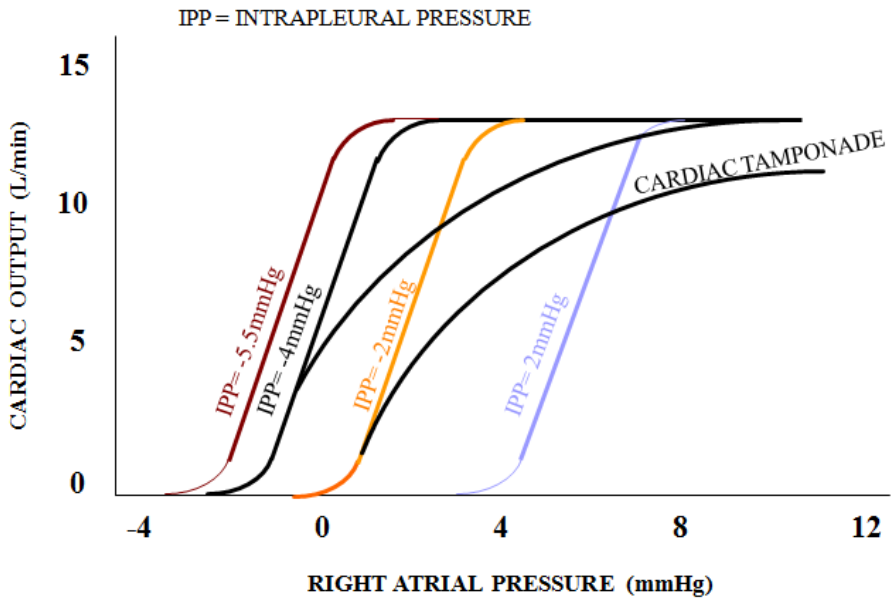
- When the chest is inflated during inspiration due to filling the lungs with oxygen →the volume of the thorax is increased →from the general gas law we know that at a constant temperature the pressure multiplied by volume has a constant value → **P1V1 = P2V2** → that's why when we increase the volume of the thorax –by inflating the lungs- during inspiration → pressure in the intrapleural cavity (IPP) decreases (to keep the value of P x V constant).

-During **inspiration** the **intrapleural pressure** (IPP) **decreases** from **(-4mmHg/-5mmHg) to (-7 mmHg)**, and since the pressure **surrounding** the heart has **decreased,** the pressure in the **right atrium decreases** by the **same value** and **shifts** the cardiac output to the **left**.

- **Decreasing the Rt. atrial pressure shifts the cardaic output curve to the left**

Increasing the Rt. atrial pressure shifts the cardaic output curve to the right (usually the pressure is increased by pleural effusion)

- Check the following graph that shows the relation between the cardiac output and right atrial pressure at certain intrapleural pressures (IPP):



- Notice that the plateau value is NOT AFFECTED by changing the IPP, that's because when we are **changing the IPP** we are acting on the **lungs** which are **around** the heart that's why the heart's right atrial pressure is afffected, BUT we are **NOT acting** on the **heart itself directly** (we are **NOT** playing with the mass of the heart).

- **Pleural effusion**: is excess fluid that accumulates in the pleural cavity increasing its pressure and **as a result** increases the right atrial pressure. **(Affects the heart INDIRECTLY)**

- **Cardiac tamponade**: is **pressure on the heart** muscle which occurs when the **pericardial space** fills up with fluid further than the pericardial sac can stretch. **(Affects the heart DIRECTLY)**

- Pleural effusion does **NOT** affect the plateau value, but this is NOT the case in cardiac tamponade and this can be seen in the graph.

-In the case of **cardiac tamponade** a shift is found but it is **very hard to reach the plateau** (we are talking about something **affecting the heart itself** NOT something around the heart). So to fill the heart with blood a **high pressure is needed** (although the atria and ventricles are elastic and can expand, due to cardiac tamponade there is too much pressure around them that is pressing on them, so the atria and ventricels will need a higher pressure to be able to be filled with blood). That's why the curve is shifted too much and reaching the plateau is really hard.

(So if there is too much fluid in the pericardium the patient may have a cardiac output that is equal to zero because in this case there will be no filling at all).

* **Cardiac output** is determined by the heart's strength (**CONTRACTILITY** and **HEART RATE**)

-**Sympathetic stimulation** will increase contractility and increase the heart rate; this will shift the plateau **upwards and to the left**.

-**Parasympathetic inhibition** affects the heart rate NOT the contractility, and this might shift the plateau **upwards**.

[the dr. said that parasympathetic inhibition does NOT affect the heart's contractiltiy but according to multiple refrences from the internet: the Inotropic state (heart contraction) is only **minimally** affected by vagal influence (parasympathetic nerves), and myocardial contractility is, therefore, **primarily** modulated by the level of the activity in the sympathetic nerves to ventricular muscle].

-**Parasympathetic stimulation** shifts the plateau **downwards**.

- **Hypertrophy** of the heart shifts the plateau **upwards**.

- **Myocardial Infarction (MI)** decreases the heart mass shifting the plateau **downwards**.

- **Valvular disease** (stenosis or regurgitation) shifts the plateau **downwards**.

- **Cardaic tamponade** shifts the plateau **downwards**.

-**Metablolic damages** shift the plateau **downwards**.

-**Myocarditis** ,which decreases the mass of the heart, shifts the plateau **downwards**

* So in general **anything that increases the function of the heart shifts the the cardiac output curve's plateau upwards while anything that decreases the heart's function shifts the plateau downwards.**

***** Cardiac Output (Q) (CO) = Stroke Volume (SV) x Heart Rate (HR). This means that CO is affected by SV and HR, so now we will be talking about factors affecting the heart rate and factors affecting the stroke volume.

- **Factors affecting the heart rate are**:

1)Autonomic nervous system (ANS):
Sympathetic stimulation increases the HR while parasympathetic stimulations decrease the HR.

2) Hormones: Epinephrine, NE & Thyroid hormones all increase the HR.

3) Atrial reflex: also called Bainbridge reflex:

Increasing the volume coming to the right atrium (venous return) will press on the SA node, increasing the pressure on the SA node will in return increase the heart rate and increase the cardiac output.

- **Factors affecting the Stroke Volume:**

1)E**D**V: an increase in the E**D**V inceases the SV. (**D**irectly proportional)
2)ESV: an increase in the ESV decreases the SV. (Inversely proportional)

Now we will be talking about how different factors affect the SV by affecting the EDV and ESV

- An increase in venous return increases the EDV that in return -& according to Frank-Starling law- increases the stroke volume and vice versa.

- The blood filling time is affected by the maximum heart rate **{220-age}, HR** should not reach more than the the allowed heart rate which is **(90% x [220 – age(yrs)])**. So if a person is 20 years old his/her maximum heart rate is 220-20=200, but it shouldn't exceed more than (**90% x 200 = 180)** (which is the allowed HR) or the person will suffer from heart problems. (Notice that the maxHR varies according to age and generally decreases with age).

- Increasing the heart rate decreases the time for diastole decreasing the EDV which in return decreases the SV.

- If the **HR = 75 → Cardiac cycle = 0.8 seconds**, while if **the HR = 100 → Cardiac cycle <0.8 seconds (0.6 seconds)**

Remember that a normal cardiac cycle (1 diastole and 1 systole for the ventricles & same for atria) takes 0.8 seconds (which for ventricles takes 0.3 seconds for systole while diastole takes 0.5 seconds).

When increasing the heart rate there's a decrease in the cardiac cycle time, and the **major decrease is in the diastole time** (systole is decreased but not a lot, instead of being 0.3 seconds it becomes 0.29 seconds for example, while diastole becomes 0.31 seconds instead of being 0.5 seconds).

- **A decrease in diastole time decreases the blood filling time decreasing the EDV that in return decreases the SV and vice versa.**

- The ESV is affected by the contractility; **increasing the contractility decreases the ESV that in return increases the stroke volume and vice versa**. (remember the ESV is the volume left in the ventricle after its contraction and the ejection of blood, so if the ventricle increases in its contractility, more blood will be ejected and as a result the blood volume left in the ventricle after systole (ESV) decreases).

- Contractility is affected by: sympathetic stimulation/ hormones (NE/ epinephrine/ glucagon/ T3&T4) … all are positive inotropic agents.

(Remember we said that **parasympathetic nerves** do NOT really affect the heart's contractility but affect the heart rate)

- Glucagon is a hormone that increases the blood sugar level, but sometimes it's a magical drug that is a great positive inotropic agent (increases contractility).

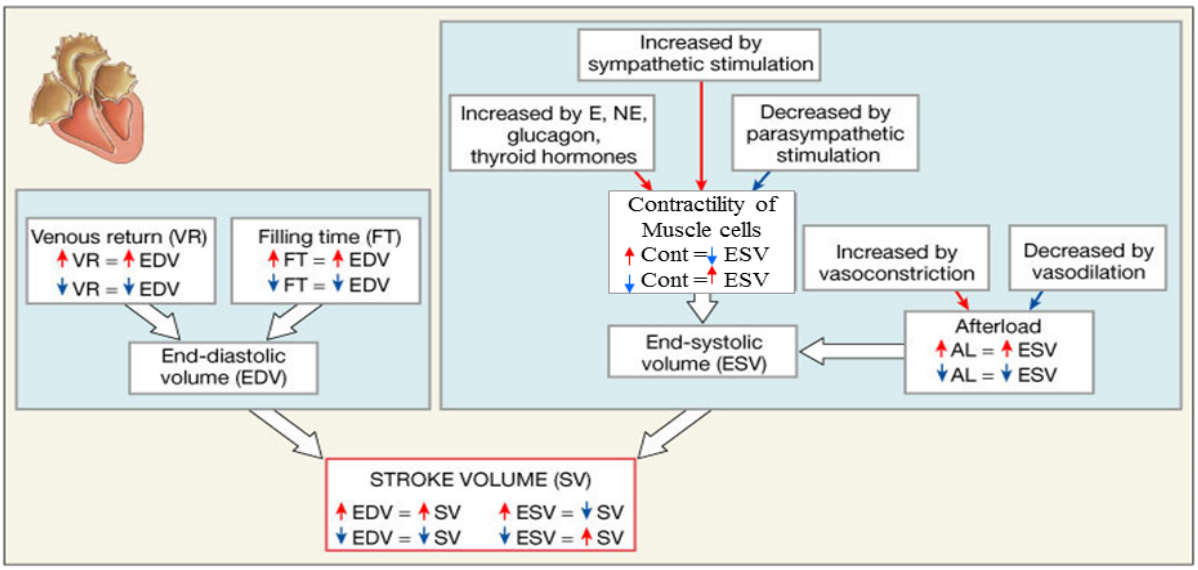
- Afterload (pressure in the aorta on the left side or pulmonary trunk on the right side during diastole that the ventricles must overcome to eject blood) is affected by vasodilation and vasoconstriction that affect the resistance and as a result affect the pressure.

- **Increasing the afterload increases the ESV and decreases the SV and vice versa.**

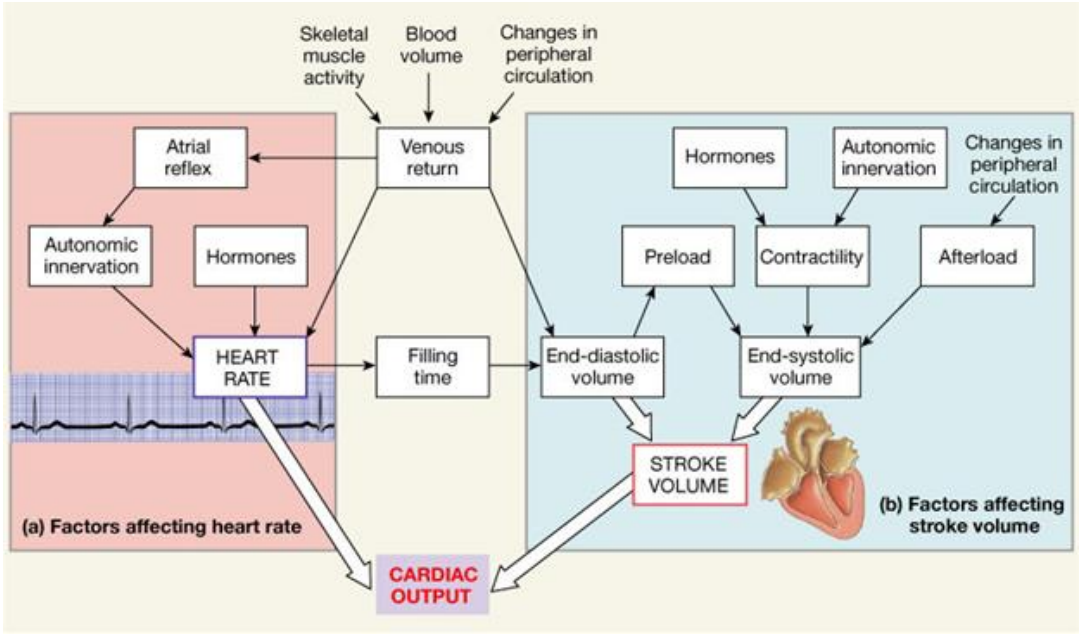
(an increase in afterload means that there's an increase in the pressure in the aorta or pulmonary trunk that the ventricles must exceed in order to eject blood, so the amount of blood ejected somehow decreases (a decrease in the SV) and this will increase the amount of blood left in the ventricle after systole (ESV)).

*Remember that SV is directly proportional to the EDV and inversely proportional to the ESV.

*The following figure summerises how different factors affect the SV by affecting the EDV and ESV



- The following diagram summerises the factors that affect the cardiac output by affecting the SV & HR:



*venous return can increase cardiac output by either increasing the heart rate or by increasing the EDV which in turn increases the stoke volume.

*heart rate plays a role in the filling time.

*EDV and ESV are affected by 3 factors:
1) Preload = EDP (End Diastolic Pressure), corresponds to EDV.
2) Afterload: the pressure in the aorta or pulmonary trunk during diastole.
3) Contractility: affected by hormones and the ANS.

* Flow (F)= ∆P/R (∆P: difference in pressure / R: resistance)

*When there is an **increase in the difference** between the **pressure in veins** and **pressure in the right atrium**, there is an **increase in the pressure gradient**, and in return the **flow increases towards the right atrium, i.e. increase in venous return.**

*Increasing the venous pressure → increases venous return (due to increase in the gradient between veins and the right atrium) → increases the filling → increases the preload (EDV) → increases the cardiac output (according to Frank-Starling law).

* decreasing the HR → increases the filling time → increases the EDV → increases the SV → increases the CO.

*Don't get confused by the relation between the HR and SV and their effect on the cardiac output; I'll explain it now.

Remember that the amount of blood pumped to the body **each minute** is called cardiac output. Cardiac output is the product of HR and SV [CO = HR x SV].

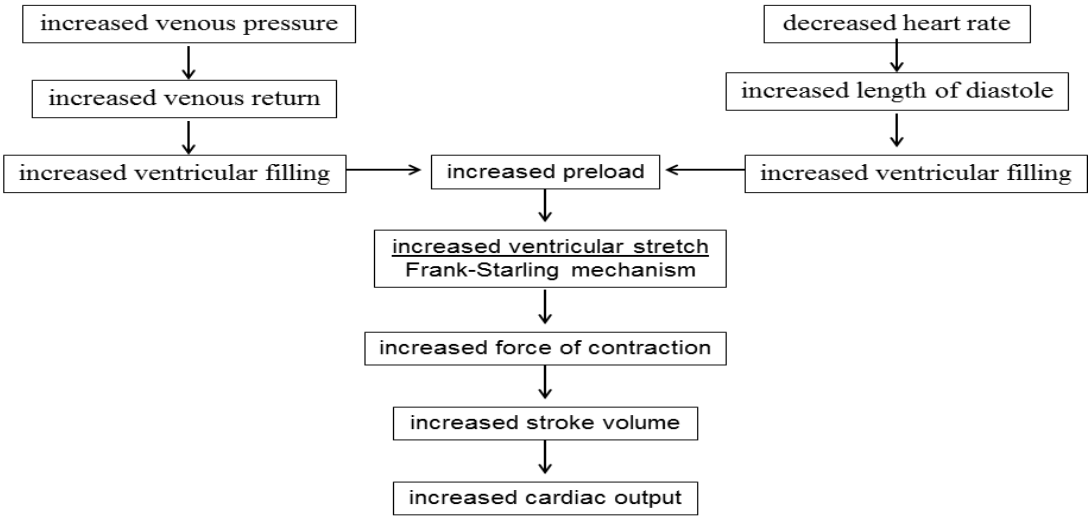
An increase in heart rate can be acceptable or unacceptable; if we take a 20 year old person as an example the acceptable increase in heart rate for this person is **90% x (220-20) =180 bpm (beat per minute)** exceeding 180 bpm will be unacceptable, in a certain situation (excessive exercise for example) this person's HR increases more than the normal HR level but still **does NOT exceed 180**, this person will still have **adequate filling time**, therfore, **adequate EDV**, and the **stroke volume decreases <u>ONLY A LITTLE BIT</u>**, so the SV will still be acceptable, that's why this person will have **more heart beats per minute** with **NORMAL amounts of SV** so the result here will be an **increase in HR** associated with an **increase in cardiac output** (the **increase in HR is much much much more than the insignificant decrease in SV** → cardiac output increases).

But if this 20 year old's **HR exceeded the 180 bpm,** the heart is pumping blood too quickly and the **filling time is decreased** (the increase in HR is too much that the heart is not having enough

time to fill the ventricles with blood) , so the **EDV decreases to a large extent** resulting in **a LARGE decrease in the stroke volume**, in this case the amount of **blood ejected in each beat is inadequate** and as a result the total amount of blood being pumped from the heart each minute **(cardiac output) is decreased**.

- Usually heart failure patients have low ejection fractions (EF = SV/EDV), meaning that they have decreased SV, that's why usually they are tachycardiac (increased heart rates) to compensate for the large reduction in SV in order to have adequate cardiac output.

*The following table explains how the SV is regulated by the preload:



- So an **increased Preload increases SV** (Increased preload increases the length of the cardiac sarcomere towards the optimal length. This will increase the force of contraction. Increasing preload is associated with increased EDV and as result SV will increase).

* (increased sympathetic activity/increased epinephrine/other factors) → increased contractility → increased force of contraction → increased SV (by decreasing ESV) → increased cardiac output.

***Cardiac contractility**

-Ventricular pressure starts in zero → then a sharp increase in the ventricular pressure during isovolumetric contraction → measuring the slope of this change over time provides us with dP/dt (dP is the change in pressure and dt is the change in time).

- However, dP/dt is not an accurate measure because it increases with increasing preload and afterload.

-The best way to measure contractility is by calculating the **maximum** change of pressure in the ventricle per unit time, i.e (dP/dt max).

-There are other measures for contractility but they are NOT the best, for example:measuring the ejection fraction (an increase in ejection fraction reveals an increase in contactility and vice versa).

-Excess K^+ decreases contractility.

-Excess Ca^{++} causes spastic contraction, and low Ca^{++} causes cardiac dilation.

- An increase in arterial pressure (aorta or pulmonary trunk) → increases afterload → decreases the blood volume ejected into the artery → increases the ESV → decreases the SV → decreases cardiac output.

The dr. said that he will be explaining the measurment of cardiac output in another lecture and started discussing venous return

VENOUS RETURN

- Arteries and veins have the same wall structure except that the veins are thinner (less smooth muscles) since they work with less pressure.

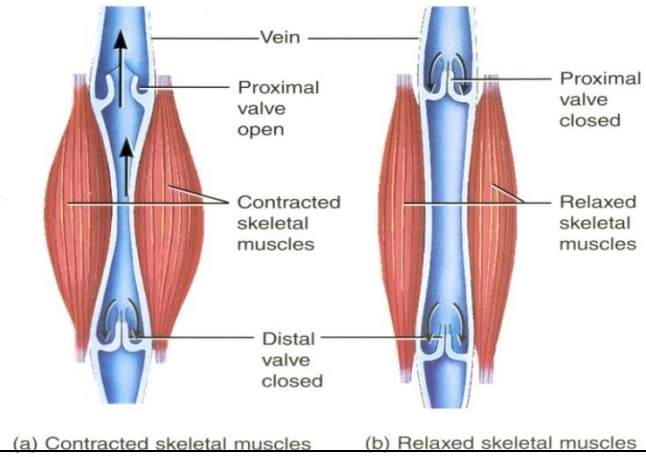
- Capillaries are made of a single epithelial layer covered by adventia. They lack smooth muscles that's why there's nothing as capillary vasoconstriction or vasodilation. (Can be a trick in the exam)

-In contrast to arteries, veins have valves. Functions of valves:

1) Assure a unidirectional flow of blood (towards the heart).

2) They decrease the pressure in veins.

Veins are found in between skeletal muscles, and when these muscles contract they squeeze the blood found within two adjacent valves in upward and downward directions. The valves,



however, are one-way valves. So, the closure of the lower valve prevents the squeezed blood (due to skeletal muscle contraction) from moving downwards. The upper valve opens allowing the blood to pass through. As a consequence, blood always moves towards the heart. (Remember: there is always a degree of skeletal muscle contraction (tone)). As a result only a small amount of blood is left between 2 adjacent valves; this means that there is no continuation of blood flow/blood coloumn (it is interrupted via valves as valves work as "Blockers" to **partition** long veins with high venous pressure **into** shorter, gated segments (gated by valves) with much lower venous pressure (that is because valves have decreased the height of the long water column to multiple short columns).

- Although there is always a pressure gradient between distal parts of the heart (like veins) and the right atrium, that is supposed to direct the blood flow from veins to the right atrium, the presence of venous valves is really important, because the effect of gravity on venous blood is much higher than the effect of pressure gradient.

- If a person stands still for a while, after about 1 hour, the column of blood from the heart to the leg becomes continuous due to gravity and as a result the pressure in the person's leg which is the column of water increases.

If we suppose the Rt. atrial pressure is zero, and the hight from this person's heart to this person's leg is 136cm, how much is the pressure down in this person's leg?

The distance from the heart to the leg is 136 cm, so 136 cm is the column of water = pressure, but we must divide it by mercury's density which is 13.6 → 136\13.6= 10 **cm** of mercury =100 **ml**. of mercury = 100 mmHg – the pressure on this person's leg-.

The pressure downward equals 136 cm of water which is 100mmHg, 100mmHg is a really high pressure –not normal- and with time the valves will become incompetent → veins will appear dilated , tortuous and bluish because they contain deoxygenated blood and this is called **varicose veins**.

* Varicose veins → less venous return→ slow movement of blood in veins/ stagnation of blood →may lead to DVT →may lead to a pulmonary embolism.

-Varicose veins may be also a result of (Pressure on veins: normally by pregnancy, pathologically by abdominal tumors … Generally anything that increases the pressure on the iliac veins whether the 2 aforementioned causes or any other cause.)

* Venous valves are compressed by physical exercise, I.e. by skeletel muscle contractions, that's why, having some exercise like walking aids in protection from varicose vein development, since the valves are compressed and so, there is blood flow towards the heart rather that stagnation & by that, there'll be protection from DVT too.

*Competent valves (aid in/facilitate/increase) venous return.

* Skeletal muscle contraction facilitates venous return.

* Venous Return: the volume of blood returning to either the left side or right side of the heart **per minute**.

-**Venous Return must equal the Cardiac output**.

VR = $\triangle P/R$ = CO
VR = (Venous pressure –Rt. Atrial pressure)/ resistance to venous return

*Rt. atrial pressure (CVP) = 0 means that it is equal to the atmospheric pressure = 760 mmHg and if we say the pressure = +2, this means +2 against the atmospheric pressure which is equal to 760 +2 = 762 mmHg, while -2 means -2 against the atmospheric pressure which is equal to 760 -2 = 758mmHg.

*if we consider CVP to be zero, then the pressure in the veins down should have a positive value, i.e. higher than CVP to create a pressure gradient.

- CVP is normally zero but might reach 20-30 mmHg →heart failure patients must keep monitoring their CVP (they already have HF and their heart doesn't pump the normal amount of blood) →if these patients need IV fluid we must be careful to the amount of IV fluid given → extra fluids in the circulation kills the patient →because an increase in the intravenous fluid, increases the venous return, and due to HF, the heart is NOT able to pump blood normally → fluid accumulates in the lungs and venous system.

- Rt. atrial pressure (CVP) is determined by **balancing** the **amount of blood being realeased/ pumped by the heart** out of the right atrium and **flow of blood from the large veins into the right atrium**. (A balance between blood entering and leaving the Rt. atrium).

The amount of blood leaving the heart is determined by **contractility** of the heart.

-(Remember **Venous Return = (Venous pressure –Rt. Atrial pressure)/Resistance**)

- Increasing the heart contractility→increases the SV→decreases the ESV→decreases the Rt. atrial pressure→the difference in pressure between veins and the Rt. atrium increases→the pressure gradient increases→venous return increases (more suction towards the Rt. atrium)

This is called "**Cardiac Suction**" as if the heart sucks blood due to the increase in the pressure gradient caused by the increase in heart contractility.

- Under steady-state conditions, Venous Return = Cardiac Output → so increasing the heart's contractility increases both the venous return and cardiac output.

* Factors that **increase** the Right atiral pressure **(RAP) (CVP)**:

1- **increased blood volume**

2- **increased venous tone → means** increased pressure in veins → increased blood being pushed into the Rt. atrium → increased RAP

3- **dilation of arterioles →** decreased resistance → increased blood flow to the Rt. atrium → increased venous return

4- **decreased cardiac function** = decreased contractility → increased ESV → increased Rt. atrial pressure

*Factors that facilitate venous return

(VR= ΔP(Venous pressure –Rt. Atrial pressure)/Resistance)

1) Increased Blood volume:

- Increased BV → increased venous pressure → the difference between the venous pressure and Rt. Atrial pressure is increased → increased pressure gradient → increased venous return → increased EDV → increased SV → increased CO.

(We have mentioned that an **increase in blood volume** leads to an **increase in the right atrial pressure**, and we've just mentioned that an increase in BV **increases the venous pressure** as well and as a result the **pressure gradient increases**. But pay attention to that in this case **the increase in venous pressure is much higher than the increase in the right atrial pressure**, and this is why the difference in pressure between the veins and the Rt. atrium is increased leading to an increase in the pressure gradient → venous return increases).

- How is blood volume increased?

- ADH → water and salt retention
- Shifting fluid from the interstitial fluid into plasma
- Polycythemia Vera (increased RBCs count) whether idiopathic or secondary as in SMOKERS that have more RBC count as to compensate for their increased demand for oxygen.

2) Skeletal Muscle Pump:

- Contraction of the muscle → presses on veins → in 2 adjacent valves the upper valve (closer to the heart) will open while the lower one (distal from the heart) closes → blood is pushed upwards towards the heart → the venous return is increased.

3) Respiratory Pump:

- During inspiration → the chest volume increases → P1V1=P2V2 → the intrapleural pressure (IPP) decreases → the **right atrial pressure decreases** by the same amount of decrease in the IPP → pressure gradient increases → venous return increases.

- **Taking more inspiration increases the venous return.**

- In inspiration the chest dilates decreasing the IPP, as a result the pressure in alveoli decreases allowing air to enter from outside into the alveoli.

4) Cardiac Suction (Increase in heart contractility):

Increased contractility → decreased pressure in the heart → increased pressure gradient → increased venous return → increased cardiac output.

5) Competent Venous Valves:

- They will prevent back flow of blood away from the heart → they direct blood flow towards the heart → venous return is increasd → EDV is increased → increased CO.

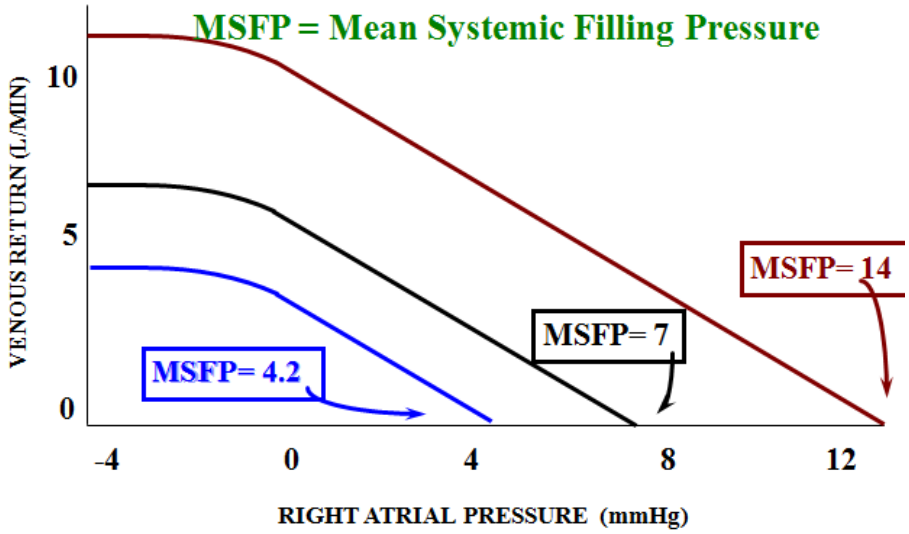
6) Sympathetic Stimulation:

- Results in vasoconstriction and **venoconstriction → venous pressure is increased** →pressure gradient between venous pressure and right atrial pressure is increased → venous return is increased.

* Someone asked about the realtion between **Polycythemia Vera (PCV) (increased RBC count) and venous return**, the answer was that this depends on 2 factors (Blood volume and viscosity). **Usually at initial stages/ mild form** it will **increase the blood volume** and as a result **increase venous return**, but in case of **severe PCV** the **viscosity is largely increased** resulting in an **increase in the resistance** that might **decrease the venous return**. (So it depends on the **severity of PCV).**

*** VENOUS RETURN CURVE:**

-



- In order to relate the cardiac otput curve with the venous return curve, the X-axis must be the rt. atrial pressure in both curves, while the Y-axis represents either the cardiac output or the venous return.

- Imagine the heart pump stops → blood level will be equilibrated in the whole circulation → All parts of the body will have the same pressure value –including the right atrium- → **NO PRESSURE GRADIENT** → no blood flow (both venous return and cardiac output will be absent).

Guyton has measured this pressure on dogs and he extrapolated it on humans to find it to be **7mmHg** (which is the mean pressure that exists in the **vascular system** when the cardiac output stops and the pressure within the vascular system redistributes to be equal in all body parts).

Since pressure has been equilibrated in the whole **systemic circulation**, pressure anywhere will be **7mmHg** and this is called the **Mean Systemic Pressure.** If we include the pulomnary circulation with it we call it **Mean Circulatory Pressure.**

So if the heart pump stops, the **systemic pressure** will be 7mmHg, this means the pressure in the Rt. atrium will be 7mmHg instead of being zero → no pressure gradient and no flow (Flow=ΔP/R, ΔP=zero, Flow=zero)

If the Rt. atrial pressure (RAP) decreases from 7mmHg to 6mmHg, there will be a difference in the pressure gradient and as a result there will be some venous return. As the **RAP decreases even more** (for example 5mmHg or 4mmHg, etc.) the **pressure gradient** between veins and the Rt. atrial pressure **increases**, and as a result **venous return is increased**.

- The venous return increases linearly with decresing right atrial pressure below the mean systemic pressure (MSFP) until the curve reaches a plateau.

(Decreasing the RAP increases the ΔP and as a result VR increases)

(The 7mmHg mentioned earlier is the Mean Systemic Pressure. Because the **mean systemic pressure** is the **pressure <u>responsible</u> for <u>filling</u> of the Rt atrium**, we call it "**Mean Systemic Filling Pressure (MSFP)**".

MSFP: mean pressure inside the systemic circulation when the heart is stopped.

Conclusion: When the Rt. atrial pressure is equal to MSFP, venous return is zero, and when the Rt. atrial pressure is less than MSFP, venous return increases.

- What happens if the **Rt. atrial pressure (RAP) goes below zero (becomes negative)**?

(You will need to **refer to the venous return curve**)

We said that as the RAP decreases we will have more venous return, this is correct until the Rt. atrial pressure reaches zero, but when it decreases beyond zero becoming negative there's only a slight increase in venous return, and by the time the **RAP is -2mmHg** the venous return curve will have reached a **plateau** where there is **no more increase in venous return and the amount of venous return will remain constant** even if RAP decreases more, and this can be noticed by referring to the curve.

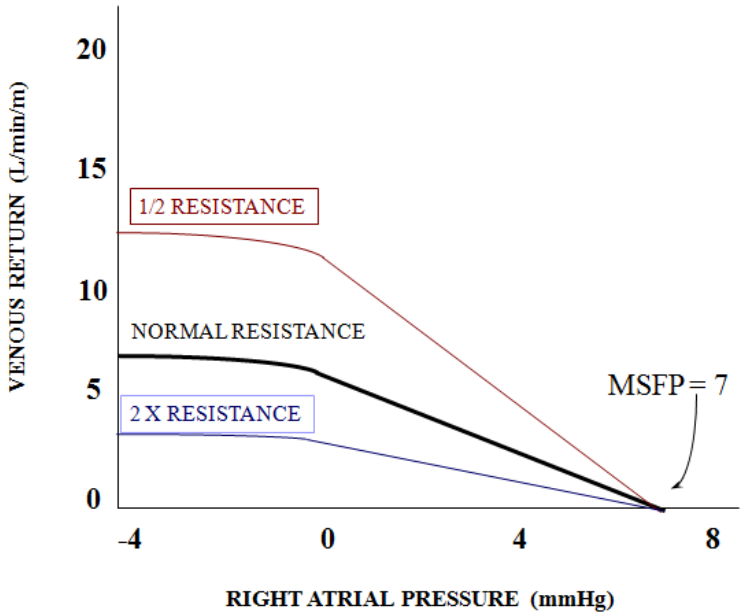
This plateau is caused by the collapse of the large veins (SVC & IVC) entering the chest due to the negative RAP, because this negative pressure in the Rt. atrium will suck the walls of the veins together at the area where they enter the chest preventing any additional flow from the peripheral veins. (Imagine the large veins as balloons with negative pressure inside them, they'll collapse).

So essentially, all veins in the chest remain partially collapsed until the buildup of **upstream** blood increases their intraluminal pressure allowing them to open, but then they become collapsed again & open later & so on.
(The collapse was a limiting factor for further increase in venous return).

* How can we **increase MSFP** after equilibrating the pressure in the body?
Mainly by **increasing the blood volume**, this can be done by giving IV fluid or blood transfusion.
This shifts the **venous return curve** to the **right.**

* How is **MSFP decreased**?
By decreasing the blood volume; hemorrhage (This shifts the **venous return curve** to the **left).**

***The effect of Resistance on venous return curve**



- Remember: **VR=ΔP/R** or could be written as **VR = (MSFP - RAP) /RVR**
  RVR= resistance to venous return
- So venous return is affected by MSFP, RAP, and RVR.
- The one single most important factor MSFP depends on is the blood volume.
- **Veins** contain **2/3** of our total blood volume, while **arteries** contain **15%**.
- The **main resistance** in the circulation is in **arteries** NOT veins, while **MSFP** is affected mainly by **veins** and NOT arteries.
- A **change in resistance** is due to **arteries** and this is achieved by **vasoconstriction (**increased resistance**) or vasodilatation (**decreased resistance**).**

Arteries contain 15% of our blood volume, you constrict or dilate 15% of BV, yet this will not affect the MSFP (changing the resistance doesn't affect the MSFP and this is shown in the graph)

- So how does resistance affect the venous return? **Increasing the resistance** decreases the flow (flow=ΔP/R) → the **venous return decreases** & vice versa. (**MSFP remains constant**).
(**VR = (MSFP-RAP)/RVR** → MSFP remained constant so the pressure gradient was not affected, while the RVR increased and was responsible for the decrease in venous return)

- MSFP is more affected by veins not arteries
Venoconstriction (constriction of veins) can occur due to sympathetic stimulation.
As we said veins contain 2/3 of our BV, so **constricting** 2/3 of our BV → **increases MSFP** (Rt. atrial pressure remains the same) → (ΔP= MSFP – RAP) → **gradient increases** → **venous return increases**.

- Anything that causes **arteriolar dilation** (Beriberi - thiamine deficiency for example) **decreases the resistance for venous return** (RVR) and as a result **venous return is increased**.

-What is **A-V fistula**? A connection between arteries and veins that can either occur naturally or as in hemodialysis applied on kidney failure patients.

In hemodialysis blood is taken from **arteries**, filtered by the machine, drained back through the patient's **veins** (so there's a connection between arteries and veins), sometimes patients need it 3 times a week, so doctors make a permanent connection between arteries and veins called **A-V shunt**, here, a **shortcut** has been formed for blood flow **between arteries and veins**, so the **resistance decreases and venous return increases**. (Note: that this increase in venous return is acute; after a while adaptation will take place & venous return will be back to its previous values).

-**Hyperthyroidism: increases metabolic rate** and as a result **oxygen consumption is increased**, tissues will **require more blood**, total (summation of) blood flow to the tissues increases (**cardiac output increases**), and the **venous return is increased**. (So, in hyperthyroidism the **resistance to venous return decreases**, and **VR increases**).

-**Anemia:** decrease in RBC count → decreases viscosity →decreases the resistance to venous return →increases the cardiac output and venous return.
(An increase in HR can be noticed in anemic patients as to compensate for the decrease in the oxygen carrying capacity).

-**sympathetic stimulation** → increases MSFP due to **venoconstriction** →increases the pressure gradient →increases venous return.

- **Blood volume**: an increase in BV → increases the MSFP and RAP but the increase in MSFP is much more than the increase in RAP → the gradient increases → venous return increases.

- **Venous Compliance** (how much veins can accommodate blood for change in pressure)

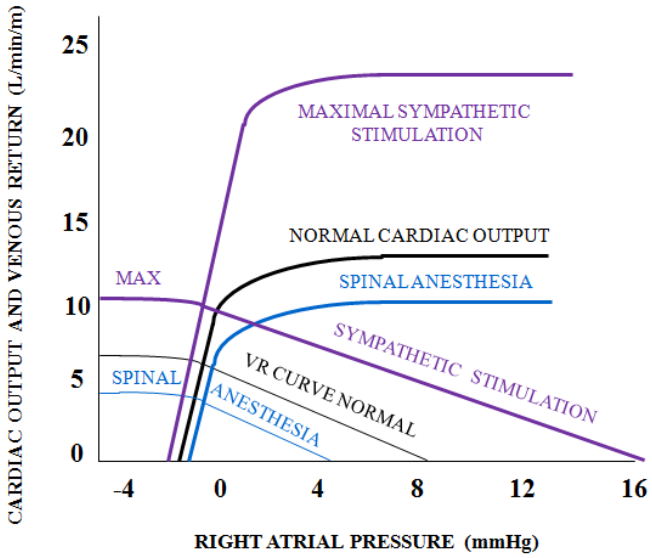
If venous compliance decreases this means that any small increase in volume will increase the pressure too much. While if venous compliance increases, veins will accommodate more blood for less pressure increase.

A decrease in compliance (muscular contraction or venous constriction)→ increases the MSFP → increases venous return.

-**Obstruction of Veins:**

Venous pressure increases → venous resistance increases → venous return is decreased.

* **CARDIAC OUTPUT AND VENOUS RETURN CURVE**



- The curves on the right represent cardiac output and those on the left represent venous return.

- Remember CO and VR represent the amount of blood being pumped from the heart or brought back into the heart per minute respectively.

-We look at the intersection points between both curves to determine the CO & to describe how certain factors affect them both together, look at the intersection points and notice the following:

- When **RAP is zero**, both **venous return and CO** are **5 L/mints**. This is **normal**.
- Sympathetic stimulation increases both CO and VR. (The CO curve is shifted upwards & to the left and the VR curve is shifted to the right & upwards).

- In spinal anesthesia there is an inhibition in the sympathetic stimulation which decreases both CO and VR (CO goes below 5L/mints and RAP is less than 7 mmHg).

Good Luck ☺

Done By: Zaina Obeidat