Basic Biomedical Sciences 1

Lecture 2: Hemodynamics of Circulation

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BLOCK 03 | MODULE 02

HEMODYNAMICS OF CIRCULATION

Dynamics

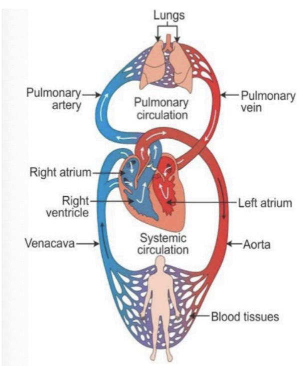
- Refers to the movement of bodies and the action of force.

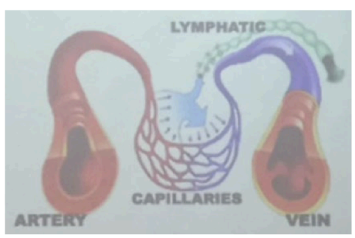
Hemodynamics

- Is the movement of blood. It is the process by which the blood goes around the circulation, including the forces that affect its movement.

THE HEART, ARTERIES, CAPILLARIES, VEINS, AND LYMPHATICS

- The **circulatory system** observes the needs of the tissues in the body.
- That is to transport nutrients, hormones or transmitters to the metabolizing tissue and to remove the waste products for disposal.
- All this is to maintain the most favorable environment for tissues.
  - That means that the removal of waste and delivery of oxygen and nutrients is so that the tissues can work in the most favorable way possible.
  - So that means that each and every single cell of the body is connected to the circulatory system.





- To do this circulatory system requires **conduits,** the blood vessels to the body and to the lungs. That means that there are two circulations in the body — **pulmonary and systemic** — and from the lungs and the body back to the heart itself.
- And we also need the interface for the actual exchange of nutrients and waste takes place, and that is the **capillaries**.
- And of course, we need the pump that will keep the whole thing going. That's the **heart**.
- Then there is the **lymphatic system**.
  - In simplest terms, there are a series of blind-ended tubes that wrap around each and every living tissue of the body each and every step, and their purpose is to assist in the removal of excess fluid, transport fats, and support immune function.
  - They're just an **accessory**.
- This means that all the components of the circulatory system, from the afferent vessels, to the pump, to the efferent vessels, are programmed for one purpose and one purpose only, to deliver the oxygen rich blood towards the organs while extracting waste and carbon dioxide for excretion.
- The circulatory system is as its name implies a circuit.
  - That means it's a closed loop.
  - It is composed of the conduits to and from the central pump, and the conduits are arteries, veins, and the veins to the accessory — the lymphatics — and the capillaries between artery and vein that handle the exchange in nutrients and waste.
  - So that means that, since it's a closed loop at any given time, the amount of blood in one part of the loop is the same as the amount of blood in any other part of the loop.
  - That's how it is if it's normal.

COMMON STRUCTURE OF THE CONDUITS OF THE VASCULAR TREE

- The conduits are arteries, veins, and lymphatics.
  - The lymphatics and capillaries are **unilayered** (only have one layer), otherwise the veins and arteries have a common structure composed of 3 layers.

(1) Connective Tissue | Tunica Adventitia

- The outermost connective tissue layer for support and protection of the blood vessel.
- In large blood vessels, they also have their own blood vessels supplying that big blood vessel, which are called **vasa vasorum**, and they also have nerves which are called **vasa nervorum**.

(2) Smooth Muscle | Tunica Media

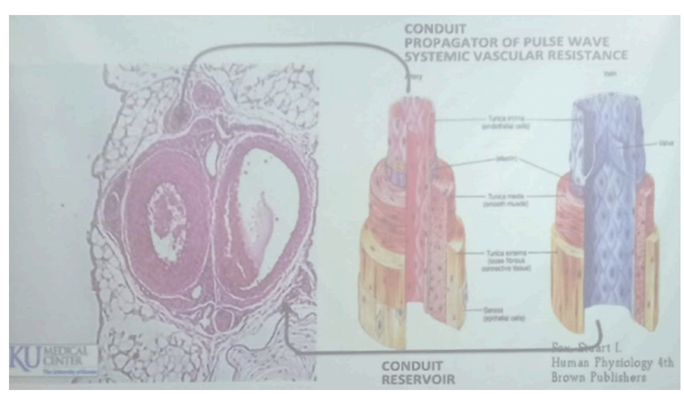
- The second layer that is responsible for constriction (the ability of the blood vessel to recoil).

(3) Endothelium | Tunica Intima

- The innermost layer
- It has 2 important structures, the **internal** and **external elastic membrane**.
  - These are important because they are found in large blood vessels for the purpose of elasticity or recoil.

ENDOTHELIUM

- Consisting of endothelial cells, it is the thinnest type of membrane.
- It is also the most genetically stable, that means that it does not change and mutate but it renews itself every 100 days.
- The endothelium is the largest organ (in the old days we thought it was the liver or the skin) spread in one layer thick.
  - It has approximately 6 tennis courts.
- It is composed of a single layer of **endothelial cells**, followed by **basement membrane**, then **smooth muscle cells**, and then the supporting tissue, usually the **pericytes**, and then the **connective tissue**, and these comprise the **blood vessels**.
- It is the single most important structure of the body.
- It is not just a barrier between the blood and the extravascular space but is a hormonal organ which releases the hormones.
  - The most potent vasoconstrictor, **endothelin**, and the most potent relaxant (dilator), **nitric oxide**, is also produced by endothelium.
  - **Platelet-activating factors** and **anticoagulants** also come from the endothelium



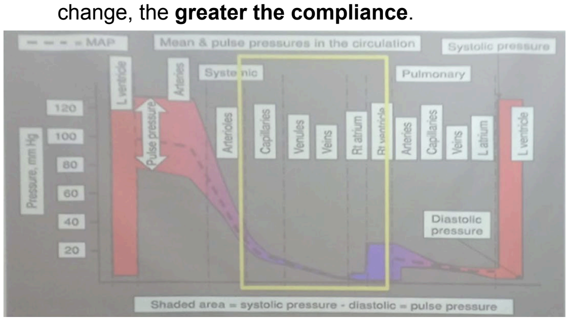
ARTERIES VS. VEINS

Thickness of Tunica Media

- The **vein** has a thinner tunica media, which allows it to become distensible and allows it to become compressible because it does not offer much resistance.
    - Therefore, it is not only a conduit, but it also is a reservoir.
    - The vein is capable of accommodating huge amounts of blood, that is why in the anatomy specimen, the vein is invariably larger than the artery.
- The **artery** has a very thick tunica media, and this allows less distensibility and it allows a blood artery to keep its shape.
    - Therefore, it is not only a conduit. It is a propagator of pulse waves and the source of systemic vascular resistance.
    - It is responsible for the blood to keep going forward.

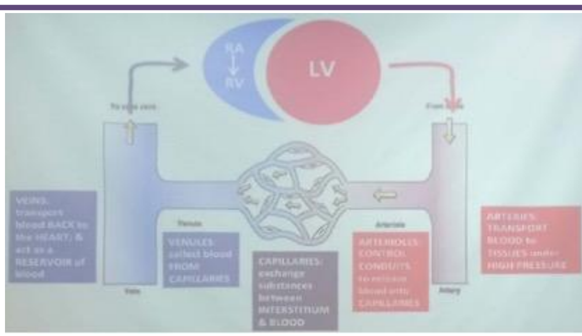
Compliance

- Directly related to volume change and inversely related to pressure change.
- Compliance is the ability of the blood vessel to accommodate volume.
    - The **greater the change in volume** for a given pressure change, the **greater the compliance**.



- The **veins** receive blood from the capillaries (capillary→ venule→ vein), and because it receives from the capillaries and the capillaries are millions, then that means there is a larger volume of blood going into the veins and therefore there is a greater volume change from the little capillaries to the vein.
- The **arteries** come from the heart, and the amount of blood coming from the heart is ejected at such a great force that the body is able to get all of the vessels filled and all of the tissue perfused with just that one pump, so therefore the artery has a great pressure change but the volume is not significantly changed.
    - The arteries are **not distensible** (the higher pressure), it is only one vessel from the heart.
    - The veins have a larger volume and no pressure to deal with because the capillary does not have pressure.

Circulation



- The blood that exits the heart comes from the **left** side. It is driven by the driving force of the heart as it contracts, so it requires the thicker-walled artery to transport blood under a pressure that is big and strong enough to reach all the way from the head to the foot.
- **Arteries:** Transport blood to tissues under high pressure
    - The **arteries** get progressively smaller until they reach the smallest unit, which is the **arterioles**.
- **Arterioles:** Control conduits to release blood into capillaries
    - The arteriole is the main constricting force that regulates the flow into the capillary.
- **Capillaries:** Exchange substances between interstitium and blood
    - The **capillaries** are where the actual exchange of material occurs. It is only in the capillary where there is exchange from the interstitial fluid into the blood vessel.
    - In the conduits in the arteries, there is no exchange and they just serve as conduit and for pressure forward, but the exchange occurs in the capillary.
- **Venules:** Collect blood from capillaries
    - The capillaries carrying their waste product go down into **venules**
- **Veins:** Transport blood back to the heart and act as reservoir of blood
    - The venules coalesce to become larger veins and finally return to the right side of the heart.
- There is no exchange in the artery and vein, only in the capillary. This means that when the blood moves out of the heart, it does so at a speed that is able for all the tissues to get their fair share.

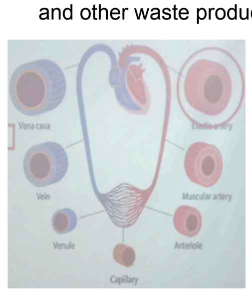
CROSS-SECTIONAL AREAS AND VELOCITIES OF BLOOD FLOW

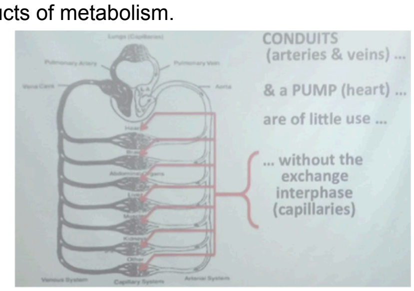
Vessel	Cross-Sectional Area (cm^2)
Aorta	2.5
Small arteries	20
Arterioles	40
Capillaries	2500
Venules	250
Small veins	80
Venae cavae	8

- The velocity of flow is inversely proportional to the cross-section of the passage.
- The **aorta** is the biggest vessel (has an average cross-section area of 2.5 cm^2), but the relationship is flow velocity is inversely proportional to cross-section, but it is fastest in aorta.
- Putting all the **capillaries** together, the cross-sectional is 2,500 cm^2.
- Therefore, since the relationship is:

$$\textbf{Flow velocity} = \frac{Q\ (Total\ flow)}{Cross-sectional\ area}$$

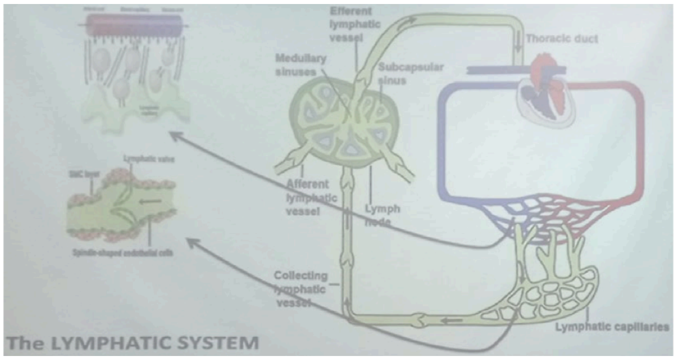
- It means that the flow velocity is inversely proportional to the cross-sectional area, then therefore it is slowest in the capillary because the cross-sectional area of the capillary is huge even if the aorta is the biggest.
- This is necessary because the most important thing is the exchange of life-giving oxygen and nutrients with carbon dioxide and other waste products of metabolism.





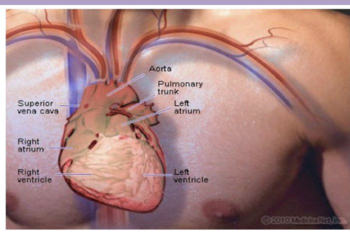
THE LYMPHATIC SYSTEM

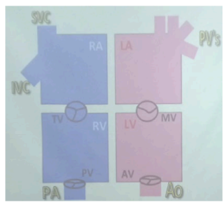
- Blind-ended channels that help to absorb proteins from the interstitial space for transport to the veins
- The lymphatics serve as an accessory drainage for the interstitium, and then once they get all the excess that is in the interstitium, they just bring it back to the vein



NORMAL HEMODYNAMICS

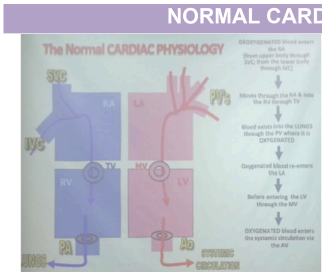
THE NORMAL CARDIAC STRUCTURES

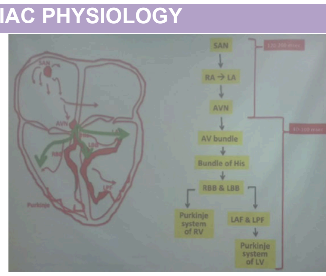




- In the landmarks of the chest, contrary to popular belief when putting the heart in the context of the chest, the heart is not the left side but is in the center and the apex points to the left, but it is in the center.
  - From the front, 2 large veins can be identified, from the upper body, the **superior vena cava** and **inferior vena cava**.
  - 2 large arteries can be identified, the main **pulmonary artery** and the **aorta**.
  - The **heart** itself, the **coronary arteries** (left and right coronary artery), and finally the whole thing is enclosed in the **pericardial sac**.
- The heart begins to twist around the **15 to 20th week of gestation** so that instead of a single tube, it becomes a complex tube.
- The normal cardiac structure consists of 4 chambers, 2 in the upper which are the **atria** (**right and left atrium**) separated by **interatrial septum**.
- There are also 2 in the lower part which are the **ventricles (right and left ventricle)** separated by **interventricular septum.**
  - The entrance to the right ventricle is guarded by the **tricuspid valve** and the entrance to the **left ventricle** is guarded by the mitral valve.
  - The exit from the right ventricle is through the **pulmonic valve** into the **pulmonary artery** to the **pulmonary circulation**, and from the left through the **aortic valve** into the **aorta**, that is to the **systemic circulation**.
  - Entering into the heart are the **superior vena cava** and **inferior vena cava** on the right side carrying **deoxygenated blood** and the **pulmonic veins** on the left side which carry **oxygenated blood**.

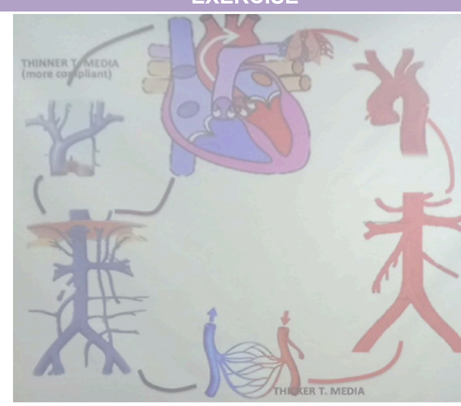
NORMAL CARDIAC PHYSIOLOGY





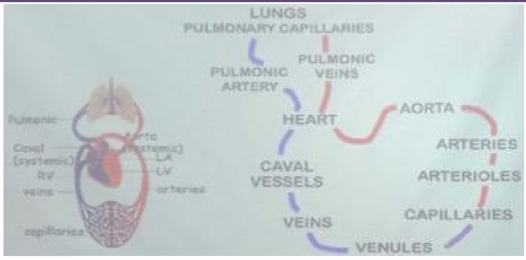
- The deoxygenated blood enters the right atrium from the upper body (**superior vena cava**) and from the lower body (**inferior vena cava**)→ into the **right atrium** and then through the **tricuspid valve** into the **right ventricle**→ blood then exits into the lungs through the **pulmonic artery**.
- In the lungs, the blood is oxygenated. The oxygenated blood returns to the **left atrium**→ through the **mitral valve** into the **left ventricle**→ and then out through the **aortic valve** into the **systemic circulation**.
- These 2 occurs in parallel (not in sequence), which means they are all continuing at the same time so that as the blood enters the right atrium, blood is also entering the left atrium, and as the blood is exiting the right ventricle, blood is also exiting the aorta.
- This kind of system can only be made possible because of the pause and that is why there is the normal conducting system.
  - From the **SA node**, located in the sulcus terminalis between the orifice of the superior vena cava and coronary sinus, when the impulse moves in, it activates the right atrium and the left atrium before going to the **AV node**, and that will cost approximately 120-200 milliseconds, which is enough to get all the blood to get in.
  - Then there is a pause, and the blood enters into the ventricles and then it will take another 40-100 milliseconds from the **AV bundle** all the way to the **Purkinje system** so that the heart will contract and exit all the blood.
- When the electrical phenomenon begins, it is not the contraction (the electrical phenomenon precedes the contraction).
  - It starts in the **SA node**, activates the atria (**right and left atrium**) and causes the **P wave**, then the atria contract.
  - After the depolarization comes the contraction.
  - Activation of the bundle branches, and then the Purkinje, and then the ventricular depolarization and then the ventricles contract.
  - Contraction of the atria→ blood enters
  - Contraction of the ventricle→ blood exits

EXERCISE



- The entry from the body is through the **superior** and **inferior vena cava**, and the heart also has its own venous system through the **coronary sinus**.
- It then goes to the **right atrium** then **right ventricle**, then comes out through the **pulmonary artery** (the only artery in the adult that carries deoxygenated blood).
- It then carries the blood to the lungs where it is oxygenated.
- It enters back into the **left atrium** through the pulmonic veins and then **left ventricle** and then exits through the **aorta**.
- The aorta has 2 parts, the **upper aorta** (ascending, transverse, descending) that is supplying the upper body and the **abdominal aorta** supplying the lower body. These are just conduits (corridors).
- It then goes to the **capillary system**, then it goes to the **venules**, from the lower body (**inferior vena cava**) or upper body (**superior vena cava**), and then back into the **right atrium**.
- The thicker tunica media in the aorta allows the blood to be propagated all the way down and then the thinner media in the veins allows the blood to be accommodated all the way back.

What do blood vessels do?



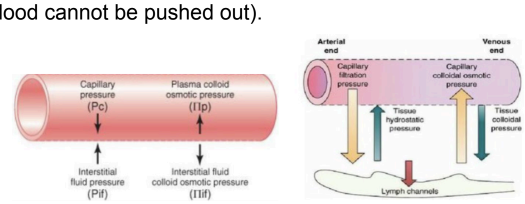
- Hemodynamics ensures that the oxygenated blood cell travels from the heart going to the destination and then back again.
- From the heart to the **aorta** to the **arteries** and then to the **arterioles**, which are the smallest, and create **systemic vascular resistance**. Then it goes to the **capillaries** for exchange, then to the **venules** to the **veins**, and then to the **caval vessels** (inferior and superior vena cava) to the **heart** to the **pulmonic artery** to the **lungs** to the **capillaries** to the **pulmonic veins**.
- The volume of blood that exits from the heart and into the systemic circulation is essentially the same volume that goes into the pulmonic.
    - Despite the pulmonic being a very small circulation, it is still able and necessary to get all the blood into the pulmonic circulation equal to the systemic and this is because blood has to be oxygenated.
    - Therefore, the circulatory system is regulated by many things not just the demand because the demand of the lungs is small since the lungs are nothing but air spaces and it does not need lot of blood and yet the whole blood enters into the pulmonary system because the lungs are necessary to oxygenate, and therefore they need to have that circulation there.

How does the circulatory system manage to do what it does?

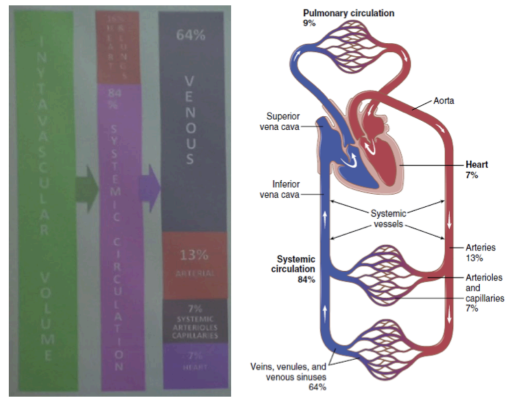
- **The intra- and extravascular fluid volumes**
    - We are about **60-70% water**, the majority of that is **intracellular (6065%)** and only 1/3 is in the **extracellular space (35-40%)**.
    - The extracellular space is also divided into the **interstitial space (65-70%)** and the **intravascular space (30-35%)**.
    - The blood is a very small minority, only about **10-14%** of the total body water and the majority of the water is found inside the cell.

How are the intravascular and interstitial fluid kept separated?

- **Starling's forces** is represented by the force that keeps the blood within the blood vessel and the force that pushes the blood outside of the blood vessel (plasma, because the solid part of blood cannot be pushed out).



- 2 forces of Starling are the **colloidal osmotic pressure (COP)** and the **hydrostatic pressure**.
    - The **colloidal osmotic pressure** which is primarily determined by protein (specifically albumin) is a force that keeps the blood within the blood vessel.
    - The **hydrostatic force** is dependent on blood pressure and is what pushes the blood away (negated by the colloidal osmotic pressure).
- In the **conduits** (**arteries and veins**), when the blood vessel moves through the interstitial space, the interstitial space is equal to the hydrostatic pressure of the blood vessel, and the colloidal osmotic pressure is also equal.
    - Since they are equal, the forces do not move against each other and they are able to stay within their own chamber and that is what makes a conduit (no exchange happens, the pressure within and the pressure without are the same)
- In the **capillaries**, the arterial end still has a significant amount of pressure which causes the capillary pressure to rise. The hydrostatic pressure is now greater than the interstitial fluid tissue hydrostatic pressure, and as a result the movement will be from the capillary into the interstitial space.
    - The artery carries oxygenated blood, so it comes out carrying oxygen, nutrients, hormones, neurotransmitters, at the arterial end. The exchange takes place in the tissue and the waste products of the tissue are drawn back into the capillary.
    - At the venous end, the capillary oncotic pressure is now higher than the colloidal osmotic pressure of the tissue. Since the force that keeps blood in is higher in the venous end, it pulls in the waste products (CO2 and other waste products).

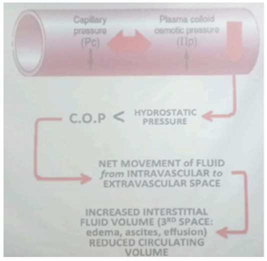


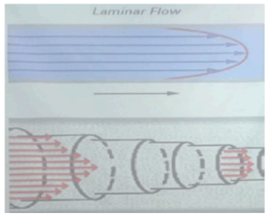
- In the intravascular space, at any one time, the majority is in the **systemic circulation (84%)** and only a little bit left in the **heart and lungs (16%)**.
- In the systemic circulation, a large proportion is in the **vein (64%)**, **13% in the arteries**, **7% in the systemic arterioles and capillaries**, and only **7% in the heart**.
    - 64% of the circulating blood is in the vein because of their property of being very distensible, and that is also why the veins are called **capacitance vessels because** they are a reservoir for blood in case any extras are needed.
    - There is only 7% in the capillaries, that means that the exchange takes place there at any one time, the 7% immediately moves out so that is why at any one time there is only a small amount of blood within the capillary in order that all of that blood will be exchanged in the proper time within the certain cardiac cycle.
    - After the capillaries, all of the blood that goes back to the heart is a huge volume coming into the vein, and compliance is directly related to the volume change and that is why the veins are compliant and much bigger.

APPLICATION

- A man has **liver cirrhosis** (advanced liver disease).
    - Since the liver is for synthesis of all proteins and the main component of colloidal osmotic pressure is albumin, therefore if the liver is malfunctioning and diseased, the synthetic function is affected and the colloidal osmotic pressure will fall because it is dependent on albumin.
    - Nothing happens to the hydrostatic pressure but the colloidal osmotic pressure is less than the hydrostatic pressure so therefore there will be net movement of fluid from intravascular to extravascular space because the intravascular space cannot hold on since it does not have

enough protein, but the hydrostatic pressure is still there and is quite strong and therefore is going to push it out.
    - Clinically, the patient will have an increased interstitial space and that is the current space that means the patient will have edema, ascites, and effusion. As a result, the circulating volume is contracted because it is at the expense of intravascular space. The interstitial space is going to increase so the circulating volume is going to become less.





PHYSICS OF FLUID MOVEMENT IN A CYLINDER

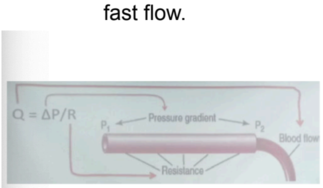
- At any one minute, the volume of blood in any part of the circulation is the same. It means that in any one minute, when the blood exits from the heart, it flows immediately all around and it is only possible because of the inverse relationship between cross-sectional area and velocity of fluids in the cylinder.
- The formula is:

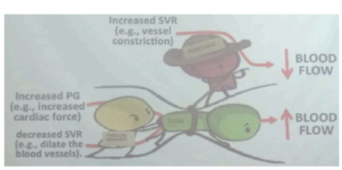
$$\boldsymbol{Velocity}\ (\boldsymbol{V}) = \frac{Flow\ (F)}{Cross - sectional\ Area\ (A)}$$

- The cross-sectional area of the capillaries is the largest, therefore it is going to become the area where the flow is lowest, and this is necessary because that is where exchange takes place.
- In the aorta, since it is just a conduit and it needs to take the pressure from the heart so therefore the velocity there is way fast and that is necessary because there is no exchange that is necessary, it just needs to get to its destination as quickly as possible.

Laminar Flow

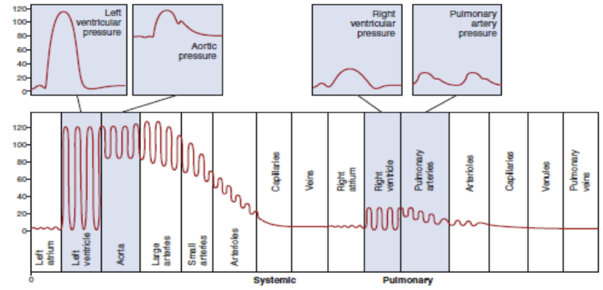
- It is not only the diameter of the vessel that determines forward flow.
    - The behavior of fluids in a cylinder is subject to laminar flow.
- When making a fluid move in a cylinder, the flow in the periphery is going to be much slower because of the effect of friction and because the friction causes a drag, the flow is going to be fastest in the center.
- In a large blood vessel like the aorta, then there is a really fast velocity because it is in the center and the periphery is going to be quite far from the center.
    - But as the artery gets smaller and smaller, there is going to be much contact between the periphery and the blood so there is not much laminar flow in the smallest of blood vessels because the friction is very near to the center and therefore the flow will become slower and does not allow fast flow.





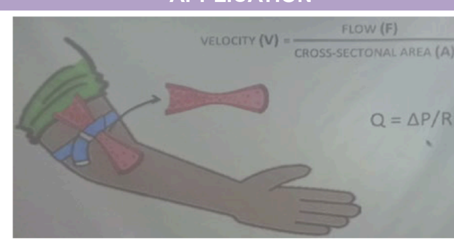
- Laminar flow is the most efficient method of getting from one point to the other, but in the smallest vessels (capillary, arteriole), it is not needed, it is needed to stay a while in order to get exchange.

Pressure Gradient lets the CVS keep the blood moving



- The only way that the blood will flow in a system like this is that there is a **pressure gradient**, that means there must be a pressure change from the aorta and then to the smaller artery to the lesser and lesser so that flow is directly related to the change in pressure. That means if there is a greater change in pressure from the aorta to the blood vessel, then it is going to flow much faster.
- That can be shown in the **AV fistula** of a hemodialysis patient in which there is an artery that is flowing very fast (average velocity: 60 to 120 cm/sec) which will go to a vein which is flowing very slowly (average velocity: 10 cm/sec). If there is a fistula (abnormal communication between artery and vein), then the flow is going to increase (explode) because the gradient is now great and that is why dialysis patients have big blood vessels in their arm.
    - The greater the pressure gradient, there must be a greater flow but then the flow is also inversely related to resistance, that means the greater the resistance (or the smaller the blood vessel), then there will also be initially an increased flow but when the blood vessel is also constricted peripherally, then there will be a decreased blood flow.
    - Therefore, if the resistance is initial (only at that area), the flow will increase, but if the resistance is uniform (distal), then it is going to have a slower blood flow. This is the reason why the pressure gradient will be able to keep the blood moving forward so the pulmonary circulation will have as much blood as a systemic circulation.
- In the pulmonic circulation, there is not much need for a greater velocity because the distance from right ventricle all the way to the left atrium is short so therefore there is not much difference there and the pressure is relatively low, but that low pressure still results in a greater flow (equal to the higher pressure in the systemic circulation).

APPLICATION



- During a medical procedure, a tourniquet was applied to the arm.
- Decrease in **cross-sectional area** slows down the velocity.
    - Since according to the formula, the smaller cross-sectional area, the higher the velocity so therefore when applying a tourniquet, there will be a faster flow, but is inversely proportional to the flow.
- But **flow volume** may not be significantly reduced because the **pressure gradient increases** even if there is **increased resistance**.
    - The flow will be faster but the volume will be less.
- **ANALOGY**: When only one leaflet of the door is open and then everybody goes out, you will get there faster but few will be able

to get out, but if the door is opened all the way, you will be able to get there much slower but there will be more people getting out at the same time.

- The flow is also inversely related to the resistance (tourniquet) but it is directly related to the pressure gradient.
  - Therefore, when there is a constriction, the gradient will be reduced so the pressure change will be reduced because there will be the same pressure. Therefore, the cross-sectional area decrease will slow down the velocity
  - The velocity is inversely proportional to the cross-section. When placing a tourniquet, the narrow cross-section means the velocity decreases, but the flow will not be significantly reduced because the pressure gradient will be able to compensate.

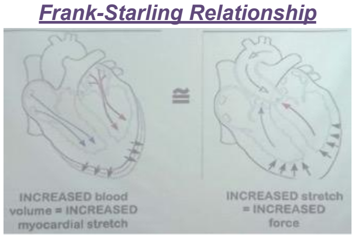
CARDIAC PUMP

- A major determinant of hemodynamics. It ensures that adequate volume will be transmitted to the systemic circulation as well as the pulmonic circulation

Definition of Terms:

- **Stroke volume**: volume of blood that exits the ventricle during each pump.
  - The cardiac pump produces the stroke volume.
  - May be less if dehydrated and may be more if well hydrated.
  - It is compensated by the cardiac output
- **Cardiac output**: stroke volume times number of heart beats per minute (***CO*** = SV x HR)
  - When you are dehydrated, the heart rate will increase.
  - If the stroke volume is reduced by dehydration, but the heart rate increases in compensation, at the end of 1 minute, the cardiac output is unchanged. That is why **heart rate** is an important determinant of the cardiac output.
- **Mean arterial pressure**: force exerted to ensure circulation and tissue perfusion (hydrostatic pressure). It is directly related to the cardiac output and also to systemic vascular resistance (**MAP**=CO x SVR)
  - The greater the cardiac output, the greater the hydrostatic pressure, and it is also directly related to the pressure within the constriction (systemic vascular resistance).
- Stroke volume is affected by **preload**, **afterload**, and **cardiac contractility** (determines the volume of the heart exiting)
- **Preload**: refers to (the volume of blood causing) ventricular stretch at the end of diastole (EDD)
  - It is the volume causing ventricular stretch at the end of the diastole.
  - It is how much blood remains in the heart after the heart has fully relaxed (end-diastolic), so that means it refers to **venous flow** (because that is the amount of blood that enters the heart in the right ventricle from the inferior and superior vena cava and on the left ventricle from the pulmonic veins).
  - Venous flow is the determinant of preload.

<u>Frank-Starling Relationship</u>

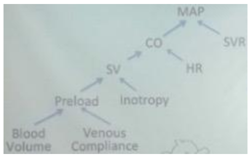


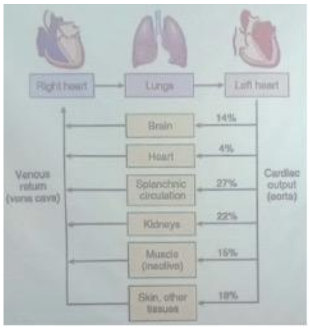
- When stretching the muscle in the heart, the amount of stretch is directly proportional to the amount of contraction. That means the more you stretch, the more force it will be.
- If the heart is filled very much, it will respond to the bigger force.
- The heart fills during **diastole**, and the **heart rate** is the vital sign that is important for the maintenance of diastole. If the heart rate is slow, it allows more time for the heart to fill. If the heart rate is fast, there is less time for the heart to fill.
- Therefore, when the heart rate is slow, the heart fills very much, and then when it contracts, it can be felt.
- In **premature ventricular depolarization**, when there is a regular rhythm and then a premature beat, and then after there is a pause during which the heart fills, and then it contracts and is felt, that is why the people who have PVCs, PVDs, or PADs feel the palpitation because it is the force that was felt.
- The **Starling's law** of the heart means that the greater the stretch, the greater the force of contraction, but this is only up to a limit because eventually if stretched beyond its limit, it will eventually lose its function (like a piece of rubber).
- The **Frank-Starling's law** of the heart is that if in a normal structure heart without excessive volume changes, the greater the stretch the greater, the return contraction.

- **Afterload**: refers to the resistance the ventricle needs to overcome to eject blood with every beat (SVR)
  - When the blood is exiting from the heart, the pressure that it generates together must be enough to overcome the constriction of the main component of systemic vascular resistance (SVR), which is the **arterioles** (the smallest unit of the artery)
  - It is able to do that because the arteriole controls how much blood goes into the capillary, so in times of need (e.g., running), then the arterioles will allow more blood to enter, and then during the time of sleep, the arterioles will not allow more blood to enter. The capillary filling is not continuous, it comes and goes.
  - When there is an afterload, this is the systemic vascular resistance, the resistance to forward flow. If the blood pressure is not enough to overcome the systemic vascular resistance, the blood will go nowhere and that is why it is important in the vital signs to get blood pressure
  - Afterload is the second workload of the heart and it refers to the amount of force/work the heart has to do in order to overcome systemic vascular resistance.
- **Contractility**: refers to the heart's ability to squeeze blood out with every beat (inotropic)

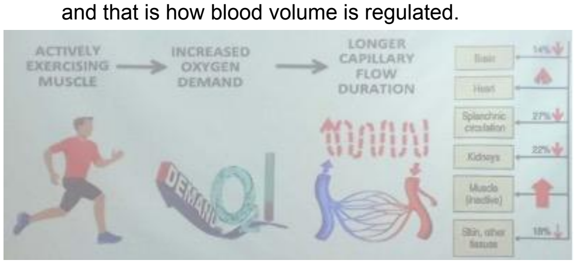
CARDIAC OUTPUT

- The blood filling the ventricles at the end-diastole is determined by circulating **blood volume** and **venous compliance**. It is totally dependent on venous return, and this creates the **preload**.
  - The preload determines stroke volume, which is the amount of blood that exits the heart with every stroke, and it is dependent on how strong the heart contracts.
  - If the heart is not a good contractor, stroke volume reduces
  - If the heart is strong, then the stroke volume is adequate.
  - *<u>Stroke volume x Heart Rate = **Cardiac Output**</u>*
- The **cardiac output** determines **mean arterial pressure**, that means that it is directly related to blood pressure.
  - The greater the volume, the greater the blood pressure but it is also subject to systemic vascular resistance.
  - *<u>Effect of resistance to forward flow + Cardiac Output = **Blood Pressure**</u>*
  - Blood pressure is not just the cardiac output. It is also dependent on **systemic vascular resistance.**





- **Cardiac output** is the sum of all the local tissue flow
  - *Cardiac Output = Total Tissue Blood Flow*
  - The circulatory system works to maintain optimum environment for metabolic tissue and it does so by regulating the rate of blood, so blood flow is commensurate to the needs of tissue.
  - The greater the metabolic rate, then also the more blood there is, but there are exceptions:
    - The lung is very small and does not do much, it just exchanges air and yet the volume of blood going to the lungs is large because it needs to oxygenate.
  - In the same way, the volume of blood going to the kidneys is inordinately high and that is because although the kidneys do not themselves use a lot of blood, what they are is excretory so a large volume of blood needs to get to the kidney in order that the body gets rid of its waste products, and that is how blood volume is regulated.

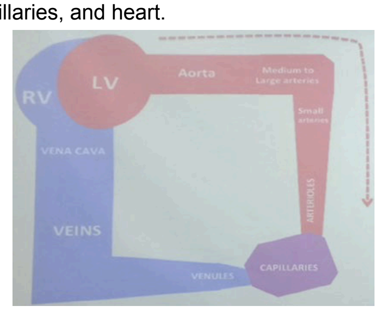


BLOOD FLOW

- **Blood flow** is controlled according to the needs of the metabolizing tissue
  - During the inactive state, the muscles only get about 15% of the blood flow.
  - If one starts exercising, that means the muscles are going to have increased oxygen demand, and due to the increased oxygen demand, a longer time in the capillary is needed to get increased oxygen.
  - The longer capillary flow duration means that the oxygen will get there, but you can only get longer capillary flow if there is more blood going there, and therefore during the time of exercise of the muscle, there is a massive increase in the muscle blood flow and some increase in the heart blood flow (heart is a muscle) and decrease in the blood flow to the other areas.
  - The body is a very primitive organ and it does not know the difference between physical and emotional/mental stress.
    - If there is a fire and you get stressed because you need to get out of the way of danger, then the body will respond by increasing blood flow to the muscles, heart, and reducing blood flow to the other parts of the body, that is why you can lift a whole piano when there is a fire, but after the fire, you are not able to.
    - If you are upset, that upset is also emotional stress and since the body does not know the difference, it responds in the same way. The blood pressure and heart rate goes up and blood is siphoned away from organs the body thinks it does not need. The body responds by fight or flight so all the blood goes to the muscles and are ready to fight or to run away. All the other organs have a lesser blood flow and that is why you get pale because the blood is siphoned in the skin, and that is also why when you are upset, you feel like going to the bathroom all the time because the splanchnic circulation is considered not important in the fight or flight response so the blood withdraws from the GI tract.

APPLICATION

- There is a fire and you need to remove a 32-inch tv down to the garage. You are sweating and you have not had breakfast yet. Which organs will require more blood and which will be able to be put on hibernation?
  - Muscle, heart, and to some extent the skin. Since you are sweating, the skin should have more blood in order to cool you off. There is a decreased demand from the GI tract, brain, since you have not had any food yet.
  - Blood kept in the “reservoir” (veins) released back into active circulation via venous contraction→ vein collapse→ increased circulating volume
  - As a result, the blood kept in the reservoir (veins) are going to be squeezed out because of the increased demand needed, and since you have not had any food yet and are dehydrated, what happens is that the veins will collapse and they will send the blood to the circulation to augment the blood flow to where it is needed and there will be an increase in the blood flow in the artery, systemic arterioles, capillaries, and heart.



- The pump pushes the circulating blood through the arteries, and they are called the **afferent vessels**, towards the tissue and that is going to the interface which is the capillaries.

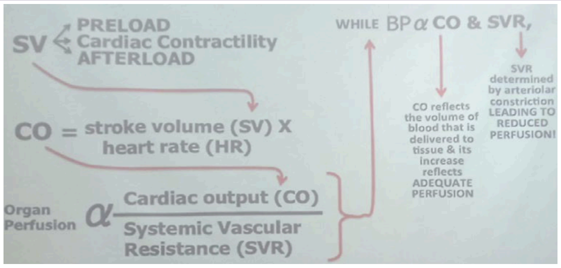
Why do we need an aorta?

- The aorta is not just the biggest blood vessel in the body. It is the conduit through which the blood is ejected from the left ventricle into the systemic circulation.
- It is an organ which is capable of storing pressure
- **Systole:** Aorta expands and absorbs the pressure wave from the contraction of the ventricle (stores energy from pressure wave)
- **Diastole:** Aorta releases the pressure wave via elastic recoil in order that the blood will go forward.
- In the tunica intima of the aorta, there is an **internal** and **external elastic membrane** in order that the elastic recoil of the aorta is very large and this is responsible for the **continuous capillary filling** throughout the diastole.
- **Windkessel Effect:** When the heart pumps, the aorta will dilate and then when the heart relaxes, the aorta continues and is never stopping because it is able to save that pressure.
  - Among all the blood vessels in the body, only the aorta is a Windkessel. It is like a capacitor because it is a form of air, when the capacitor hits, the air will push the fluid forward.
  - The exchange of nutrients occurs in the capillary level.

HOMEOSTASIS | BALANCE

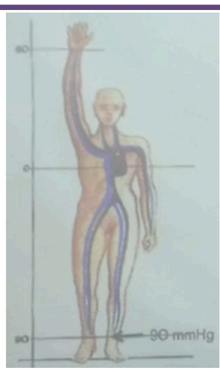
- There is a balance between oxygen requirement and oxygen delivery and the cardiopulmonary system ensures that there is an adequate oxygen delivery to commensurate with the oxygen requirement.

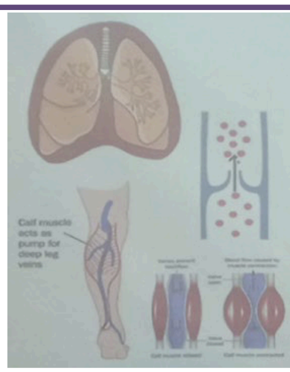
Is a "normal" BP a reflection of adequate perfusion?



- Stroke volume is dependent upon **preload**, **contractility**, and **afterload**, and *Cardiac Output = Heart Rate.*
- The **organ perfusion** is dependent directly on **cardiac output (CO)**, but is inversely proportional to **systemic vascular resistance (SVR)**.
  - **Cardiac output (CO)** reflects the volume of blood that is delivered to tissue and its increase reflects **adequate perfusion**.
  - **Systemic vascular resistance (SVR)** is determined by arteriolar constriction leading to **reduced perfusion**.
  - The more cardiac output, the more perfusion because of the hydrostatic pressure.
  - If there is an increased systemic vascular resistance, there is a resistance to forward flow and therefore, the more the systemic resistance, the less the organ perfusion.
  - The **blood pressure** is directly related to **cardiac output**, but it is also directly related to **systemic vascular resistance** so that therefore, if the blood pressure is maintained because all the blood vessels are constricted, then the perfusion of the organs is compromised, and the **cardiac output** is needed since it is the most important determinant of tissue perfusion.
    - Just because the blood pressure is normal, it does not mean that it is adequately perusing all of the tissues of the body.
- Therefore, organ perfusion, blood pressure, and good circulation are not the same.

How does blood return to the heart?





- The blood in the **artery** is driven by the driving force of the contraction of the heart.
- The **veins** have a pressure of about 0.
  - When lying flat, the pressure is around **0 mmHg** in the feet all the way to the heart. The terminal of all the veins of the body is the right atrium and the pressure there is 0.
  - When standing, the effect of gravity raises the pressure to about **90 mmHg,** and the blood has to fight that pressure to get back to the heart, and it is 0 in there.
- There are 3 mechanisms as to how does it get back
  - The proper inhalation is **full expansion of the chest**, and this creates a vacuum because the chest is a closed cavity and then the lungs, when the lungs expand, there is no way for the chest to get out of the way, therefore creating negative pressure intrathoracic, and that creates a **vacuum effect** and the vacuum effect causes the blood to be sucked upward.
    - Many people have varicose veins because the veins need the proper expansion of the lung to be able to be sucked up and we do not get much effect due to sedentary lifestyle.
  - The **integrity of the valves**. The valves of the vein are different from the other kinds of valves in the heart. They are not active valves so they do not open and close and they are a parachute.
  - When inhaling, the parachute opens and then blood goes through. When exhaling, the parachute closes and the blood is prevented from backing up.
  - Unfortunately, laminar flow allows the blood to flow fast, but in addition to the friction of the blood vessel wall, there are valves which have a tendency to pull the area and create little clots.
  - When there is no movement of the legs, the blood flow becomes static and the blood tends to pull the area and causes a little clot (not enough to cause DVT) that will organize and then pull up the valves since it is stuck to the wall.
  - Prolonged immobilization increases the risk for varicose veins and venous insufficiency.
- The **calf pump**. The most important aspect of the return flow because when the gastrocnemius muscle is constricted, it is able to push 20% of the lower body blood volume back into the heart.
  - When wearing high heels, you are constantly dorsiflexed, and that means that there is no flexion at the back and therefore the blood is going to cool.

NEURO-ENDOCRINE CONTROLS

Oxygen Delivery

- It is dependent primarily on **cardiac output (CO)**.
- It is hindered by **systemic vascular resistance (SVR)**.
- **BP:** *Blood Pressure = CO x SVR*
- **CO:** *Cardiac Output= Heart Rate x Stroke Volume*
- The **cardiac output** is directly affected by an increased **heart rate**, an increased **stroke volume**, but it is not going to be affected by **blood pressure**.

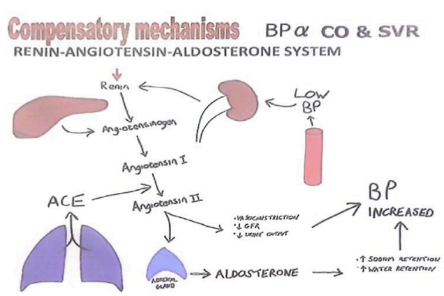
Compensatory Mechanism

- **↓BP:** ↑ HR, SV, and SVR in order to maintain CO
- **↓CO:** ↑ HR and SVR
  - The main organ responsive to decreased flow is the **kidney** because it is the main organ for controlling blood pressure.
  - When there is a decreased flow in the kidney, the glomerulus receives less blood, and it stimulates the glomerular tuft, and the glomerular tuft is stimulated to produce **renin**, and renin stimulates the liver to produce **angiotensinogen**.
  - In the blood, the angiotensinogen is converted to **angiotensin I**, which is still inactive and needs to be converted to **angiotensin II,** which is the second most potent vasoconstrictor of the body.
    - The most potent vasoconstrictor in the body is **endothelin**, which is produced by the endothelium.
    - Angiotensin I is converted to angiotensin II by the action of **ACE (angiotensin-converting enzyme), which is produced by the lungs.**

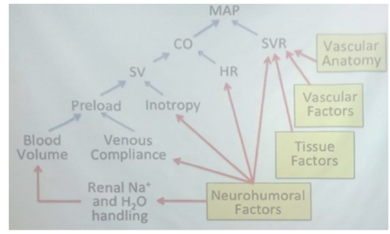
- Angiotensin II also causes adrenergic stimulation, which causes **increased heart rate**, and because it is a vasoconstrictor, it causes **increased systemic vascular resistance**.
    - It also stimulates the adrenal gland to produce the mineralocorticoid (**aldosterone**) that produces sodium, therefore water, which **increases preload.**
- When there is decreased perfusion, the **sympathetic nervous system** causes the release of **catecholamines.**

Cardiovascular Adrenergic Receptors

- The adrenergic receptors are the parts of the different working tissues, especially muscle and skin, that receive the adrenergic stimulant.
- **α1**: **Post-synaptic neurons of the vascular smooth muscle, and their effect is vasoconstriction.**
    - (+) inotropic, (-) chronotropic effects on the myocardium
- **α2**: **Pre-synaptic modulation of large vessel vascular tone**
    - Counter-regulatory to α1
    - It **inhibits norepinephrine**, the most important neurotransmitter
    - Reduces adrenergic activity
    - In CNS, it causes peripheral **vasodilation**.
    - Alpha-adrenergic drugs generally cause vasoconstriction. If there is someone who is resuscitated because of vasoconstriction, it reduces flow to the brain. Since α2 is present in adrenaline, it has a protective effect on the coronary and cerebral, making **adrenaline (epinephrine)** the most important resuscitation drug.
    - Post-synaptic receptors can mediate **arteriolar** and **venous vasoconstriction** (stimulated later on).
- **β1: Increases heart rate** and **myocardial contractility**
- **β2: Vasodilation** and relaxation of bronchial, uterine, GI smooth muscle
    - It relaxes the smooth muscles of the bronchi, that is why β2 agonists are good for asthma, they relax the uterus that is why they are also used in premature contractions.
    - **Drives K+ intracellularly** so that they may cause **hypokalemia** and contribute to development of arrhythmias
- **Dopaminergic**: **Pre-synaptic and post-synaptic receptors** found in the renal, cerebral, and mesenteric vascular beds
    - When stimulated, they cause **vasodilatation**.



- Therefore, the neurohormonal factors affect the renal by causing sodium and water retention, and thus **increasing blood volume and increasing preload.**
    - They also **increase venous compliance** because they will also have an effect on the constricting ability of the artery and the vein. They will also affect inotropy because they are inotropic agents.
    - They will **increase heart rate** by the release of adrenergic stimulation and **increase systemic vascular resistance.**
    - Other factors that affect SVR are the anatomy (vasoconstriction due to tourniquet application), vascular factors (endothelin, nitric oxide, endothelium), and other tissue factors.
- All of the things that happen are interrelated and they will all have an effect somewhere else.

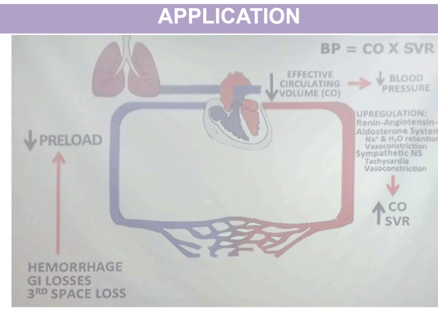


INTRODUCTION TO ABNORMAL HEMODYNAMICS

SUMMARY OF NORMAL HEMODYNAMICS

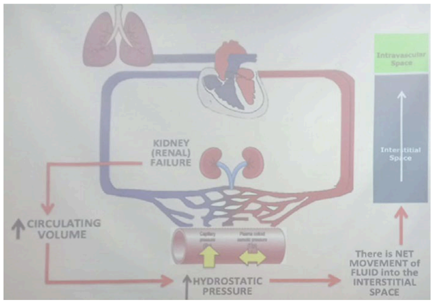
- The **intravascular fluid volume (30-35%)** is the smallest part of the components of the fluids of the body, and the **interstitial space (65-70%)** is more than twice in size.
- The forces that keep the blood within the circulatory system are kept in balance. The **colloidal osmotic pressure** keeps the fluid within the blood vessel while **hydrostatic pressure** pushes the fluid out of the blood vessel.
    - The colloidal osmotic pressure equals the colloidal osmotic pressure in the interstitial fluid and in the conduit blood vessels.
    - The interstitial hydrostatic pressure equals vessel hydrostatic pressure in the conduit vessels. Therefore, there is no net movement.
- In the capillaries, at the arterial end, the **capillary hydrostatic pressure** is greater than **tissue hydrostatic pressure** pushing the plasma and everything out into the tissue.
    - At the venous end, the **colloidal osmotic pressure** is greater than the one in the tissue causing the blood to move back in carrying all its waste products for excretion.
- The **efficiency of the cardiac pump** is that it is automatic because it is continuously depolarizing and repolarizing in the cardiac action potential. The efficiency of the cardiac pump is subject to the demands of workload: Preload, Afterload, and Inotropy
    - The **preload** is the amount of venous return and it is approximately the end-diastolic diameter (how much the heart dilates).
    - The **afterload** is the resistance to forward flow that has to be overcome by the **cardiac contraction** and finally the **inotropy**.
    - They are affected by neurohormonal factors primarily, but other factors affect systemic vascular resistance including **vascular anatomy, vascular factors, and tissue factors**.

APPLICATION



- You have diarrhea or blood loss. What are the consequences of hemorrhage, diarrhea, or 3rd space loss? Which part of the circulation is affected?
    - If there are losses, the **circulatory volume** is affected. If there is a reduction in circulatory volume, the **preload** will be affected because it is the distention of the ventricle with the return, and is dependent on venous return.
    - The preload will decrease, as a result, there is a reduction in the amount of blood excreted (**decreased stroke volume**), which **decreases blood pressure** and will activate the neurohormonal system and causes upregulation of the RAAS, sympathetic nervous system,

contraction of the venous system in order to compensate for the loss. As a result, there is an **increase in cardiac output and systemic vascular resistance.**
  - If you have hemorrhage, GI losses (diarrhea), or edema, you will not just be going to collapse and die. Your body will try to compensate by these mechanisms.



- A patient has renal failure. What does the kidney do?
  - The primary role of the kidney is water and electrolyte balance and is an excretory organ. When the kidney fails, there is an imbalance. If the kidney is unable to produce its function, which is water and electrolyte balance, it will retain water because it cannot leave anymore, therefore there is an **increased circulating volume.**
- It will increase cardiac output and i**ncrease hydrostatic pressure**, and the volume of the blood is increased, but it does not mean that the protein will increase. There will be a dilution of the protein, therefore **colloidal osmotic pressure may decrease** and there will be an increased hydrostatic pressure. There will be a net movement of fluid from the intravascular space into the interstitial space, causing an **increase in interstitial or 3rd space,** and it will be clinically manifested as edema.

SUMMARY

- Hemodynamics refers to the **process** by which **blood** makes its way through conduits (**blood vessels**) as driven by a pump (**heart**).
- Hemodynamics allows the provision of the **optimal environment** for tissue metabolism according to the needs of that tissue.
- This continuous process of **circulation** is made possible by the action of the **pump** and the physics of the movement of fluids within a cylinder; and modified by the **neuroendocrine system** in accordance with the needs of metabolizing tissue.