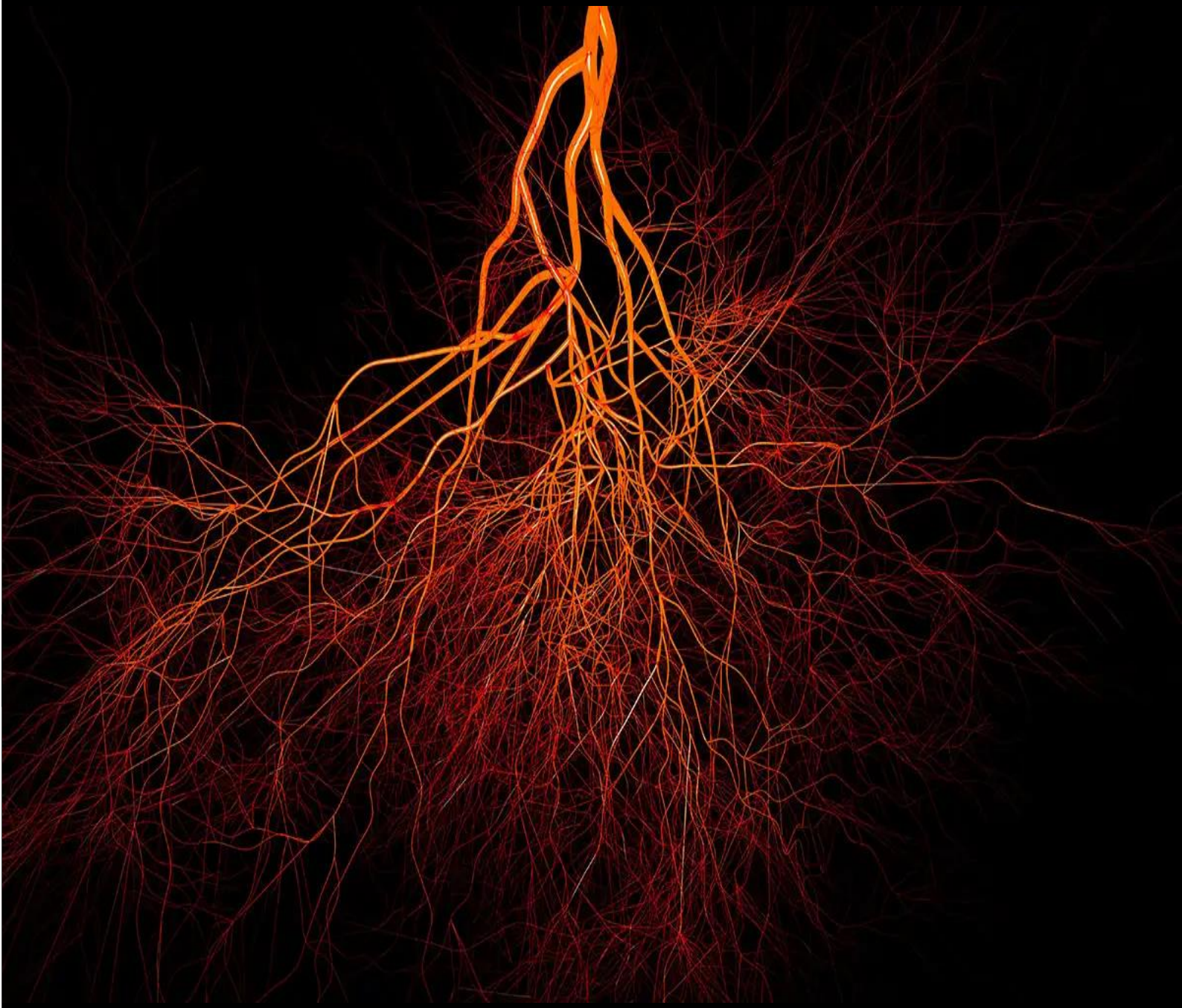
Microcirculation



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Note: any piece of info with a * preceding it, is for reading only.

Microcirculation: is the blood flow through the smallest vessels of the circulatory system (i.e. capillaries, venules, arterioles and shunts) . The most basic and important function of microcirculation is the transport of nutrients to the tissues and different organs and removal of their excreta. *(except for the cornea)

Capillaries have walls that are thin and constructed of a single layer of endothelial cells (simple squamous) that are highly permeable, therefore water, cell nutrients and excretion can easily and quickly be interchanged between the tissues and the circulating system.

Over 10 billion capillaries in the body with surface area of 500-700 square meters perform function of solute and fluid exchange.

Now Let's remember **the heart is composed of four champers:**

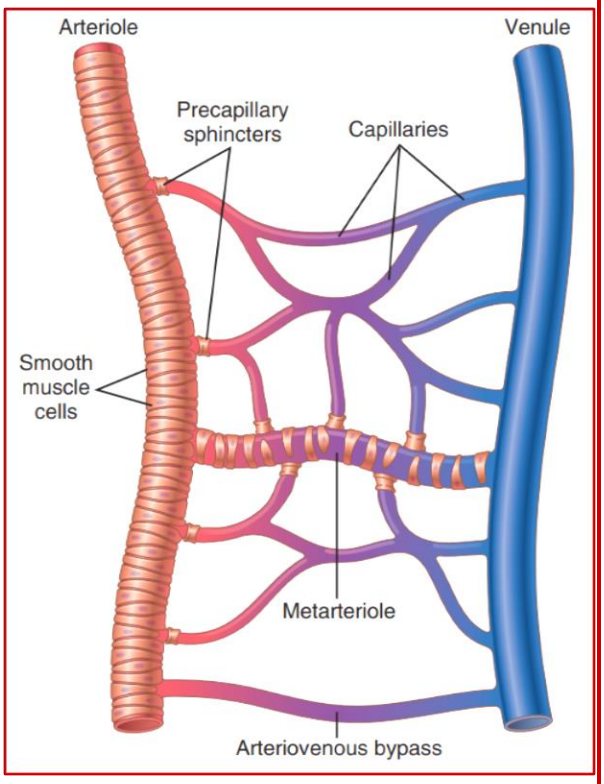
1-right ventricle/2-left ventricle/3-right atrium/4- left atrium.

- the left ventricle gives off the systemic arteries (the so called "aorta")

Structure of the microcirculation and capillary system:

The microcirculation of each organ is organized to serve that organ's specific needs. In general, each nutrient artery entering an organ branches several times before the arteries become small enough to be called arterioles. Then the arterioles themselves branch many times, reaching very small diameters where they become metarteriols. (terminal branches of arterioles) then these give branches to supply blood to capillaries. then blood moves from capillaries to veins, reaching the heart again (specifically: the atrium).

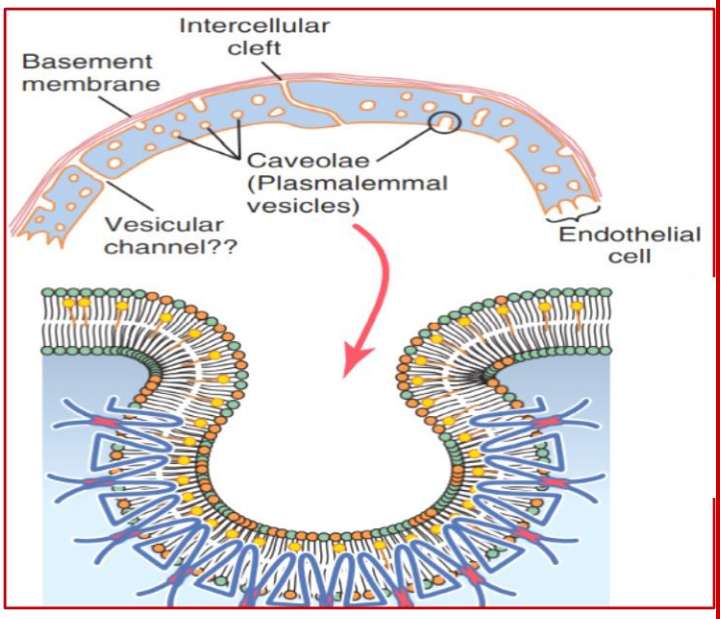
The arterioles are highly muscular, and this is important because blood pressure inside them is relatively high compared to venules, this makes arterioles able to change their diameters. The metarterioles do not have a continuous muscular coat, but smooth muscle fibers encircle the vessel at certain points. (ponder the figure to understand the whole idea)



At the point where each true capillary originates from a metarteriole, a smooth muscle fiber usually encircles the capillary. This structure is called the precapillary sphincter. This sphincter can open and close the entrance to the capillary.

Structure of the Capillary Wall:

the wall is composed of a unicellular layer of endothelial cells and is surrounded by a thin basement membrane on the outside of the capillary. The total thickness of the capillary wall is only about 0.5 micrometer. The internal diameter of the capillary is 4 to 9 micrometers, barely large enough for red blood cells and other blood cells to squeeze through.



Passages in the capillary wall:

There are two small passageways connecting the interior of the capillary with the exterior. One of these passageways is an ***intercellular cleft***, which is the thin-slit(شق) between adjacent endothelial cells.

Because the intercellular clefts are located only at the edges of the endothelial cells, they usually represent no more than 1/1000 of the total surface area of the capillary wall, however, the rate of motion of water molecules, as well as most water-soluble ions and small solutes, is so rapid that all of these substances diffuse with ease between the interior and exterior of the capillaries through them.

Now is the explanation of the other passage, ***Plasmalemmal vesicles*** (Caveolae= small caves):

Present in the endothelial cells are many minute plasmalemmal vesicles, also called ***caveolae*** (small caves). *** These plasmalemmal vesicles form of proteins called caveolins that are associated with molecules of cholesterol and sphingolipids.

They are believed to play a role in endocytosis (the process by which the cell engulfs material from outside the cell), and Transcytosis.

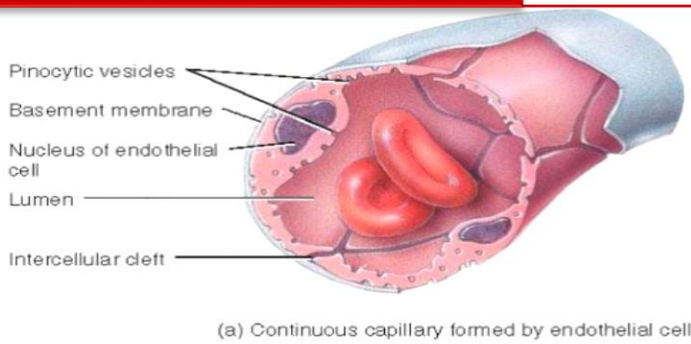
Solutes and water move across capillary wall via intercellular cleft (space between cells) or by plasmalemma vesicles.

This description of these passages (pores) is general, special types of pores occur in the capillaries of certain organs. The "pores" in the capillaries of some organs have special characteristics to meet the special needs of the organs. Some of these characteristics are:

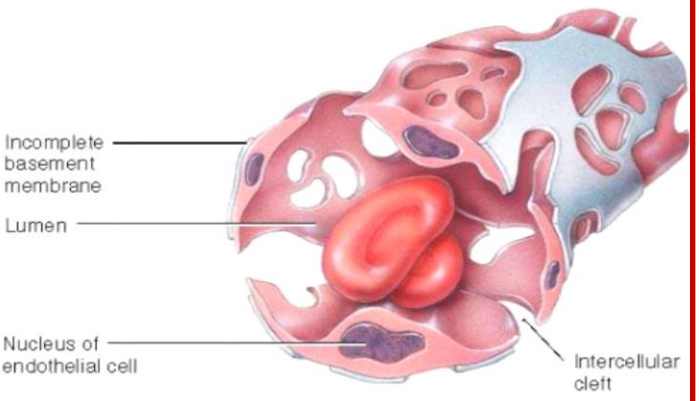
In the brain, the junctions between the capillary endothelial cells are mainly tight junctions that allow only extremely small molecules such as water, oxygen, and carbon dioxide to pass into or out of the brain tissues.

In the liver, the opposite is true. The clefts between the capillary endothelial cells are wide open so that almost all dissolved substances of the plasma, including the plasma proteins and even blood cells, can pass from the blood into the liver tissues. Such capillaries are called ***"SINUSOIDS".***

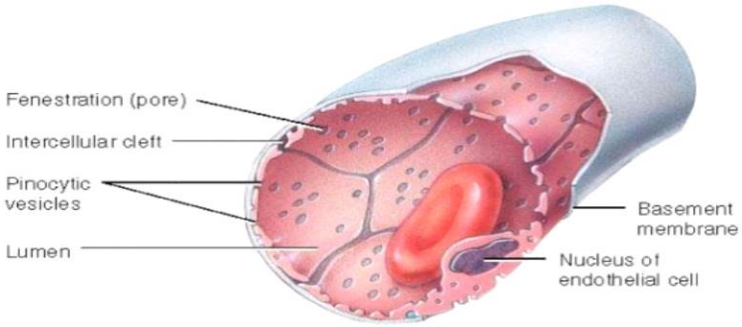
Capillary types:



(a) Continuous capillary formed by endothelial cells



(c) Sinusoid



(b) Fenestrated capillary

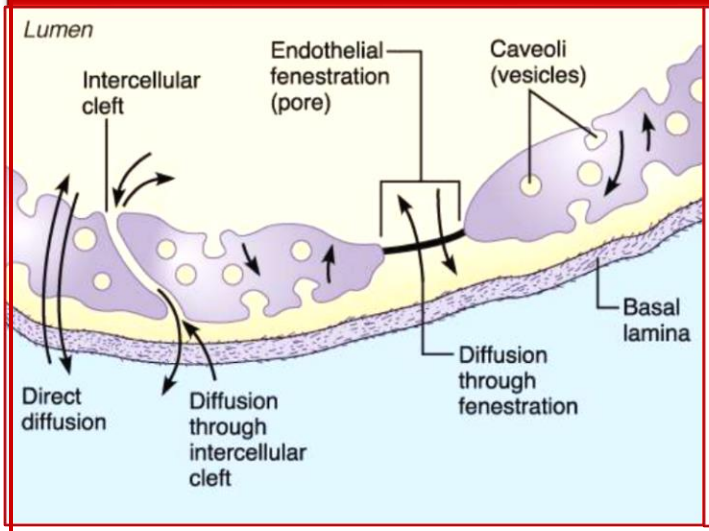
A-is a normal capillary with intracellular clefts.

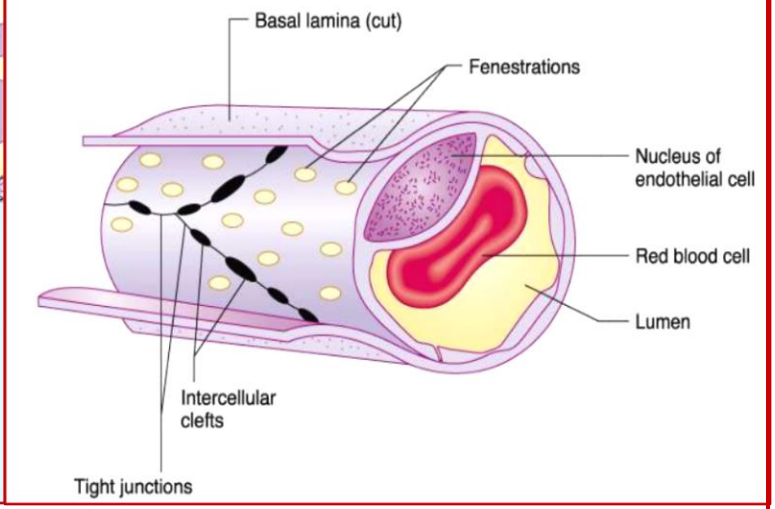
B-Fenestrated capillary that has a lot of Fenestrations (pores or windows) these pores increase the flow of nutrients, waste, and other substances.

C- "Sinusoid" discussed above.

Capillary Exchange of Respiratory Gases and Nutrients:

as you see in the figures bellow nutrients can pass either throw the clefts or through fenestrations or they can simply diffuse through the endothelial cells.(depending on the type).





قالت لي النفس: أنت كالنائم، له أن يرى وليس له أن يأخذ شيئًا مما يرى إلا وصفه، وحكمته، والسرور بما التذَّ منه، والألم بما توجَّع له.

DIFFUSION THROUGH THE CAPILLARY MEMBRANE:

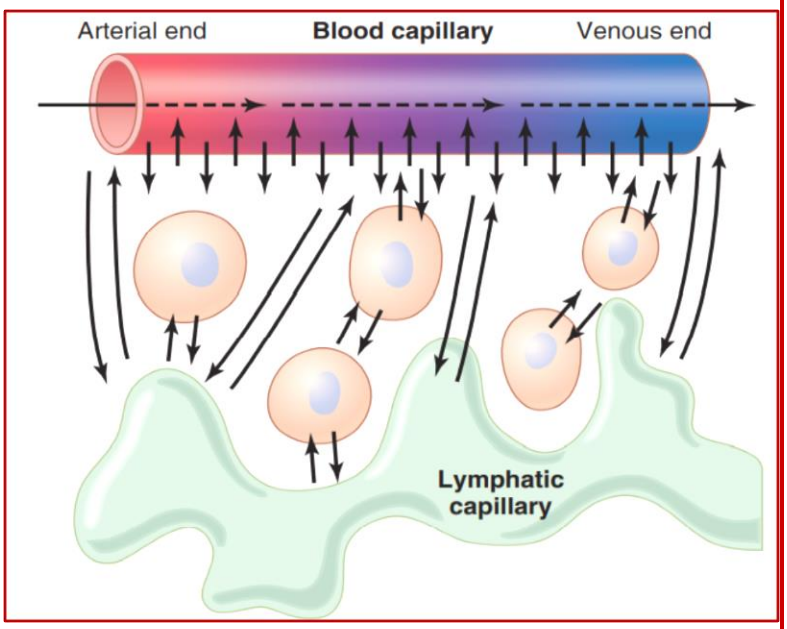
By far the most important means by which substances are transferred between the plasma and the interstitial fluid is diffusion, as the blood flows along the lumen of the capillary, tremendous numbers of water molecules and dissolved particles diffuse back and forth through the capillary wall, providing continual mixing between the interstitial fluid and the plasma, however something extremely important must be appreciated, we'll proceed through it now.

*So simply as the blood is moving through the capillaries, water and dissolved substances diffuse out of the capillary to the interstitial fluid and they diffuse back to the capillary. (look at the figure bellow to understand).

Effect of Molecular Size on Passage Through the Pores: The width of the capillary intercellular cleft-pores, (6 to 7 nanometers), is about 20 times the diameter of the water molecule, which is the smallest molecule that normally passes through the capillary pores.

The diameters of plasma proteins, however, are slightly greater than the width of the pores (so they don't pass through these pores), for this reason, the plasma protein concentration in the plasma is not equal or close to that in the interstitial fluid.

Other substances, such as sodium ions, chloride ions, glucose, and urea, have intermediate diameters. Therefore, the permeability of the capillary pores for different substances varies according to their molecular diameters.



NOTE: The capillaries in different tissues have extreme differences in their permeabilities, such as the previously mentioned example of the liver's sinusoids

SOLUBILITY (in lipid or water):

Lipid soluble substances diffuse directly through cell membranes of endothelial cells of capillaries (I.E.CO2, O2). Lipid insoluble substances such as H2O, Na, Cl, glucose cross capillary walls via intercellular clefts and pores.

Note: oxygen can cross any membrane as if the membrane doesn't exist.

-Co2 is more soluble than oxygen, so its Easier for it to cross the membrane.

-the more soluble the gas, the easier it diffuses across the membrane.

Hence if the thickness of the interstitial space increases, or the surface area decreases (any abnormality in the lung) oxygen will be firstly affected. If the 2 gases are affected, then the damage is severe.

Substance	Molecular Weight	Permeability
Water	18	1.00
NaCl	58.5	0.96
Urea	60	0.8
Glucose	180	0.6
Sucrose	342	0.4
Inulin	5000	0.2
Myoglobin	17,600	0.03
Hemoglobin	68,000	0.01
Albumin	69,000	0.001

Note: These values are for skeletal muscle capillaries, in other capillaries (such as the sinusoids) differences are present.

Note from 3dwi: the doctor didn't mention 90 percent of this in the lectures. but they are in the slides.

I think he assumed that this is general info but fortunately, I know that your knowledge barley exceeds what you have learned in school.☺☺☺

- The doctor mentioned some pressure values, which are demonstrated in the figure:

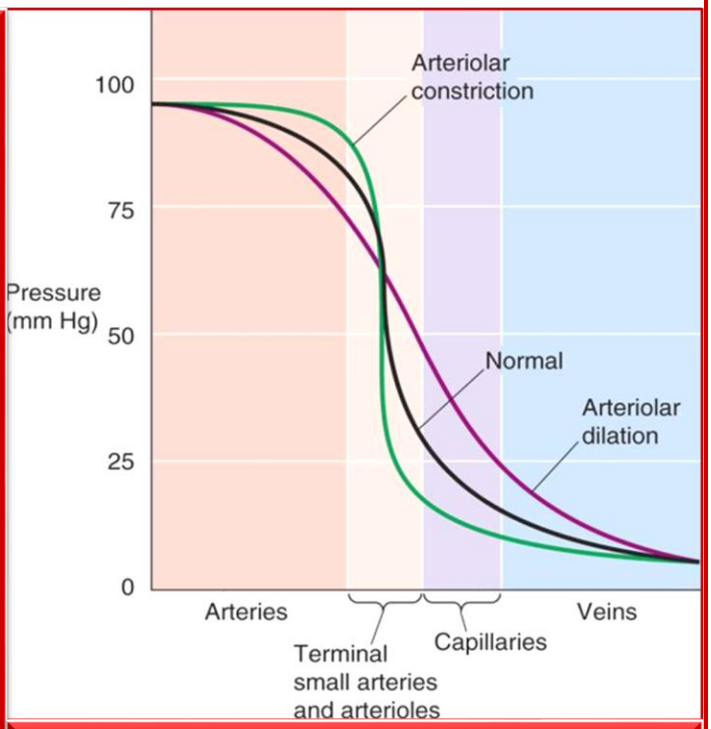
A- Arteries at the beginning:
(100 mmHg above atm.)

B- Arteries at the end, or arterioles at the beginning:
(85 mmHg above atm.)

C- Arterioles at the end, or capillaries at the beginning:
(40 mmHg above atm.)

D- Capillaries at the end, or veins at the beginning:
(20 mmHg above atm.)

E- Veins at the end, or the right atrium:
(0 mmHg above atm.)



Notice how the pressure falls as we move from the artery to the vein.

These numbers are estimated.

Flow is a product of a driving force, and just like that, blood flow is a product of the pressure difference (so for a blood flow to occur there must be a pressure difference), and obviously any flow is proportionally related to the driving force, and inversely related to resistance.

*Our doctor asked and requested the answer in a philosophical aspect:

- what do we mean by resistance? **It's a vague expression about how difficult certain process will occur.**

When we talk about uncharged molecules, then we can describe it with the term: Permeability which is the opposite of resistance, on the other hand, when we talk about ions (charged molecules), then we can describe it with the term: conductance.

Now consider the following formula:

Q = DF*K (Q: Flow, DF: driving force, K: permeability)

Take this example for better understanding:

If there was more filtration from a capillary, this will lead to an accumulation of a fluid in the interstitial space, or what we can call

Edema, the too much filtration which has caused edema, is due to either: too much driving force, or too much permeability, or too much of both, (keep that in mind).

***Plasma is divided into: 92% water, and 8% others.**

- the exchange occurs between the interstitial fluid and plasma.

*blood volume represents 7% of total male body weight, let's say for example we have a 5000 mL blood, this blood is distributed in the cardiovascular system as follows:

1- Systemic veins: 3000 mL
2- Systemic arteries: 750 mL
3- Pulmonary circulation (arteries+ capillaries+ veins): 450 mL
4- Heart: 400 mL
5- Systemic capillaries: 400 mL

The most important is the systemic capillaries, because that's where blood truly communicate with cells.

-We mean by the communication between blood in capillaries and cells in tissues, the diffusion or what we can better call ***"filtration and reabsorption".***

To distinguish between diffusion and filtration, you can say diffusion is a molecule to molecule transport, on the other hand, filtration is bulk flow, the doctor gave a very good visualizing example which is: الجمل بما حمل, and the driving force for diffusion is concentration gradient or sometime electrochemical gradient, whereas the driving force for filtration is the hydrostatic pressure.

The driving force of the filtration is a summation of **four forces (pressures),** two inside (intravascular), and two outside (extravascular: interstitial), we call these four forces: ***"starling forces".***

Now consider the following formula:

NFP = (BHP + IFOP) – (BCOP + IFHP):

Net filtration pressure (NFP) balance of 2 pressures:

***Two pressures promote filtration:**

1. Blood hydrostatic pressure ***(BHP)*** generated by pumping action of heart Falls over capillary bed from 35 to 16 mmHg. (the capillary has two ends arterial end which is connected to the artery and a venous end which is connected to the vein the pressure starts in the capillary high=35 near the arterial end and keeps falling until it reaches the venous end=16) *the numbers are estimated*.
2. Interstitial fluid osmotic pressure ***(IFOP)*** 1 mmHg.

***Two pressures promote reabsorption:**

1. Blood colloid osmotic pressure ***(BCOP)*** promotes reabsorption Averages 28 mmHg, due to presence of blood plasma proteins too large to cross walls.

2.Interstitial fluid hydrostatic pressure***(IFHP),*** close to zero mmHg.

**********Don’t memorize the numbers☺

Take a deep breath and Get ready for too many calculations: -

There are two types of plasma proteins, which are: albumin and globulin, but we do care about albumin not about globulin, albumin concentration is 3.5-5.5 g/dl, whereas concentration of globulin is 2-3.5 g/dl, also albumin’s molecular weight is smaller than globulin, and it’s equal to 70000 Dalton , whereas globulin’s molecular weight is equal to 140000 Dalton, that means if we have 1gm of globulin, and 1gm of albumin, then 1gm of albumin contains twice the number of molecules in 1gm of globulin.(don’t memorize the numbers).

To conclude: because albumin has a smaller molecular weight than globulin, then it’s more important than globulin.

*number of molecules is more important than the size of the molecules in our studying aspect, because different molecules with different sizes attract water at the same rate when the number of molecules is fixed for each molecule

For example: a certain blood vessel with a Pc equals to 30 mmHg, let’s say that the oncotic pressure is equal to 28 mmHg, then 22 mmHg due to the albumin, and6 mmHg due to the globulin.

Now we want to calculate the pressure which is made by the albumin, in general, if we have a concentration of albumin equals to 70000g/L, let’s say this will make a solution of an osmolarity equals to 1000 mOsmol, then an albumin concentration of 45g/L will make a solution of an osmolarity equals to 0.6 mOsmol, (keep in mind that 1 mOsmol of albumin makes a pressure equals to 19.3 mmHg)

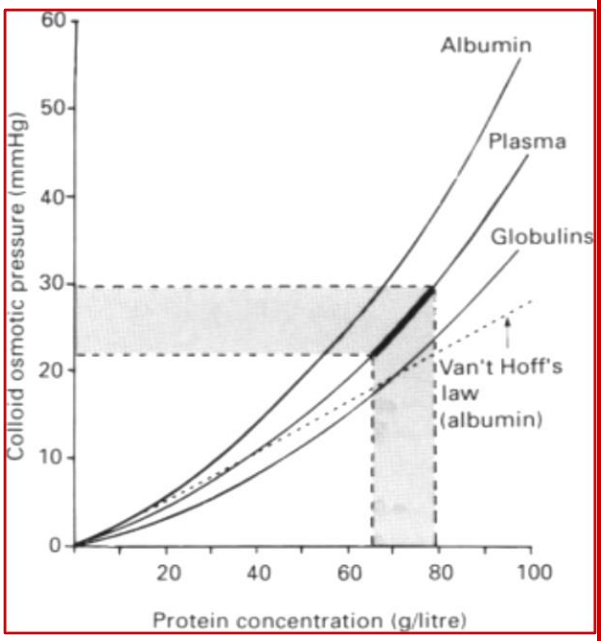
*this number 19.5 mmHg is very important to memorize.

so 0.6 mOsmol will make a pressure equals to 12 mmHg, (this is the supposed value)

note: the doctor will give us the numbers we need in the exam don’t memorize

any of it just memorize the 19.3 mmHg.

Ponder the following slope, which represents the relation between the albumin concentration and the oncotic pressure.



And here is the question: why the relation Isn't linear and is more than expected?

- that's because albumin attracts ions such as chloride, and chloride attracts sodium, and ions attracts water with it.

It is ***Donnan effect******that is, extra osmotic pressure caused by sodium, potassium, and the other cations held in the plasma by the proteins.

And that's why at 0.6 mOsmol we will Have a pressure value of 22 mmHg, (the real value), instead of 12 mmHg, (the supposed value).

Ok, let's talk more about albumin: -

- it's a protein, (لا يا شيخ), and like all proteins, you provide your body with it by nutrition, and it's digested in the GI tract to small amino acids, in human plasma, albumin concentration is approximately 3.5 g/dl, (gram per deciliter), if this value decreases in the plasma of the blood, (we call this case: ***hypoalbuminemia***)

>3.5 g/dl.

Hypoalbuminemia is a condition where your body doesn't produce enough albumin protein that's responsible for keeping fluid in your blood vessels.

- there are several causes of hypoalbuminemia such as:

1- ***Malproduction*** of the albumin in the liver because of some abnormalities like: liver cirrhosis (fibrosis) تشمّع الكبد, or maybe due to a liver damage (hepatitis)

malproduction: decrease in production

2- Malabsorption

3- Malnutrition

4- Some kidney diseases, lead to a loss of albumin in the urine, (in the normal conditions: Albumin is not filtered by the kidney, you can't find albumin in the urine)

*they all will lead to a generalized edema, (edema everywhere).

Interstitial fluid hydrostatic varies among different tissues, it's value sometimes is positive, sometimes is negative, and sometimes is zero, for example:

- in lung it's = -5 (negative sign means it is less than the atmospheric pressure) it is negative because there are a lot of lymphatics in the lung.

- in subcutaneous in the skin it's = -2

- in capsuled tissues it's = + (because the capsule exerts pressure on the tissue thus increasing the hydrostatic pressure in the tissue).

الزمن يمحو الزمن، والعمل يُغيّر العمل، ودقيقة باقية في العمر هي أمل كبير في رحمة الله.

Keep in mind that, whenever there is a dilatation, that means more blood in the vessel, and whenever there is a constriction, that means less blood in the vessel.

However, there is a difference between venous constriction and dilatation, and arterial constriction and dilatation, for example: venous constriction will affect the capillary pressure more than the arterial constriction, if you raise the arteriole pressure from 50 mmHg to 60 mmHg, at the same time, you raise the venules pressure from 15 mmHg to 25 mmHg, (which are the same change of 10 mmHg), the result will be that the arterial pressure will be affected by just 15% of the total arterial pressure, and the venous pressure will be affected by 85% of the total venous pressure.

To conclude: a change in the caliber (the internal diameter) of the venous system is reflected more in the capillary Pc (capillary pressure) than the same change in the arterial. *side note this is because: (because the veins are more numerous and more permeable thus a change in the venous capillary pressure would have more impact on the movement of the fluid compared to the impact of the same change in arterial pressure.)

There are three types of capillaries in the human body: -

1- **Only filtration** (from inside to outside), and this is the glomerular capillaries which is found in the kidney. - the filtration in the glomerular capillaries alone is 180L per day.
2- **Only reabsorption** (from outside to inside) and this is found in the GI tract.
3- **Both**, (filtration at the arterial end, and reabsorption at the venous end), and this represents the majority of capillaries among the body, for example: skeletal muscles.

Filtration in our bodies across the systemic capillaries equals to 20 L per day, and reabsorption equals to 17 L per day, the question is**: where are the 3 liters??**, they must return back by lymphatic vessels to the systemic veins, the lymphatic system is our body's **"sewerage system"**, it maintains fluid levels in our body tissues constant by removing all fluids that leak out of our blood vessels.

However, lymphatics have a limited capacity, if the limits are exceeded, this will lead to accumulation of the fluid forming edema called: ***"lymph edema".***

There are two types of edema:

1-Localized edema by a local factor
2-Generalized edema by a systemic factor, such as: heart failure.
Edema of two types can be life-threatening edema: edema here can kill you in two hours, or it can be a non-life-threatening edema.

- edema in lungs is called: ***Pulmonary edema.*** pulmonary edema safety factor, is the high presence of lymphatics in lungs to protect it from edema.

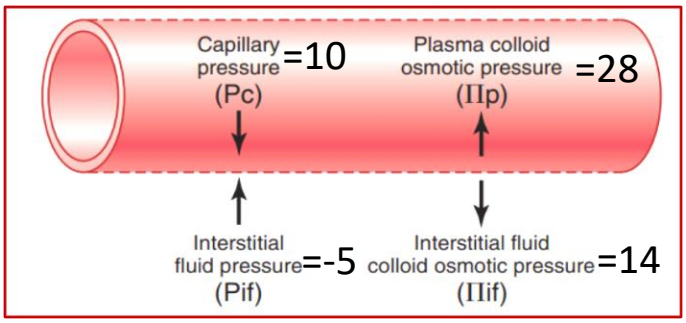
- edema in brain is called: ***brain edema.***

- edema in heart is called: ***pericardial effusion.***

- edema in larynx is called: ***laryngeal edema.*** (happens among children).

- colloid osmotic pressure is not the same among the different tissues, for example: in the liver sinusoids, it's very easy for protein to move from blood toward the interstitial fluid, so it's concentration in the interstitial fluid may be around 6 g/dl.

take this example to understand how can fluid moves between capillaries and the interstitial:



1- Pi= -5
2- πi= 14
3- Pc= 10
4- πc = 28
(π=colloid osmotic pressure.)
Way1---NFP= (Pc-Pi)- (πc- πi), (from the book)

Way2---NFP= (Pc+ πi)- (Pi+ πc), (from the doctor)

With either way the answer is +1, in other words the net filtration is 1 mmHg toward the interstitial fluid.

At the end of the lecture the doctor asked a question:

What are the similarities of the pressure values of starling forces between different tissues?

Answer: the colloid osmotic pressure in all capillaries is the same, due to the nearly constant amount of proteins in the different capillaries.

يا كَبِيرَ الهِمَّة : لا يضُرُّك التَّفرُّد ، فإنَّ طُرقَ العَلاءِ قَلِيلةُ الإيناس.

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