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Physiology

Doctor 2019 | Medicine | JU

◉ Sheet ○ Slides

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Contributed in the Scientific Correction

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Microcirculation and Edema

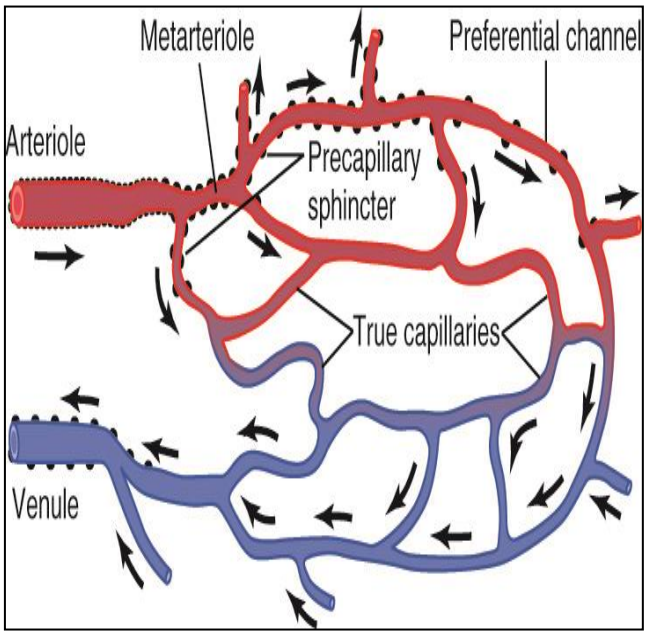
The most important point in the capillary circulation is the area of exchange between interstitial fluid and plasma

If there is a concentration of O2 this concentration will be almost the same in all parts of the arterial system

The only place where nutrients move between the interstitium and plasma is the capillary so after they pass to the venous side then the concentration of certain nutrients changes, this tells you that this capillary is the only side where exchange occurs

So the microcirculation is important in the transport of nutrients to tissues and site of waste product removal from interstitium to the plasma (then for example to the kidney if they are to be excreted into the urine).

Over 10 billion capillaries with surface area of 500-700 square meters perform function of solute and fluid exchange. (we have capillaries more than the population of the whole world) ++ surface area of the capillary is very large that's why it is a good area to exchange substances.



This is a capillary structure

The arterial side starts from the large big artery from the aorta which divides into three main big arteries which are the left subclavian and the common carotid and the brachiocephalic.

Brachiocephalic will divide into right subclavian and common carotid

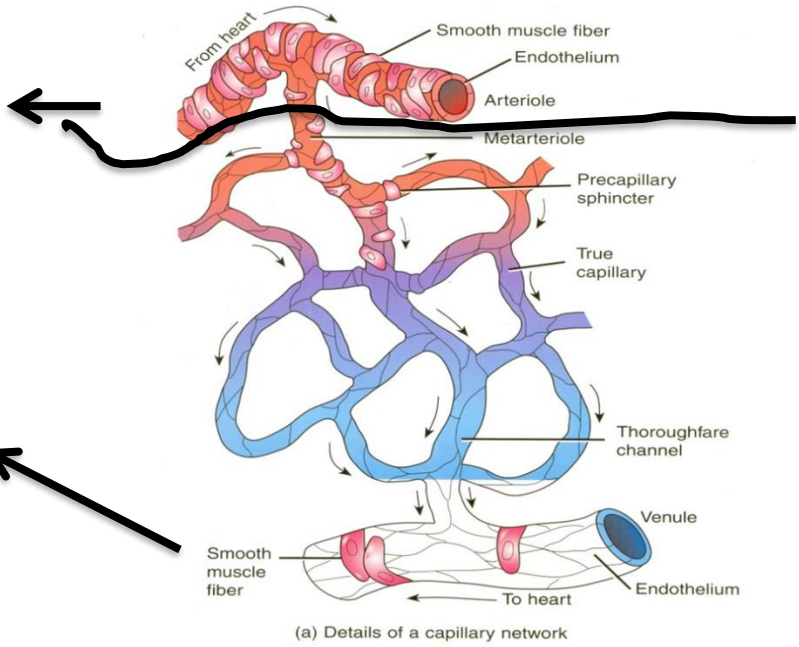
And from these arteries we have medium size arteries and small arteries then arterioles.

Now the precapillary sphincter works like a valve like structure that constriction of this sphincter decreases the blood flow to the capillary while relaxation increases it.

And then the capillary after they exchange substances they collect again to form the venural side of the capillary of venules and then small veins then medium size veins then the two major veins that go to the right atrium superior and inferior vena cava (ما غيرهم اللي شرحتهم دوك مها

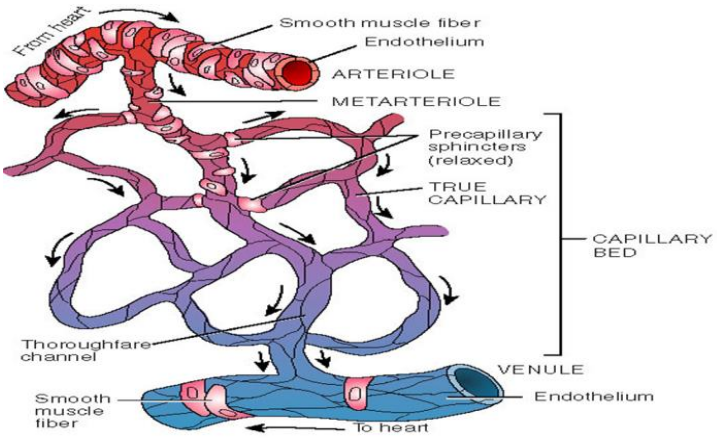
The arterial side of the capillary

When u say a vein the direction of blood inside vessels is into the heart

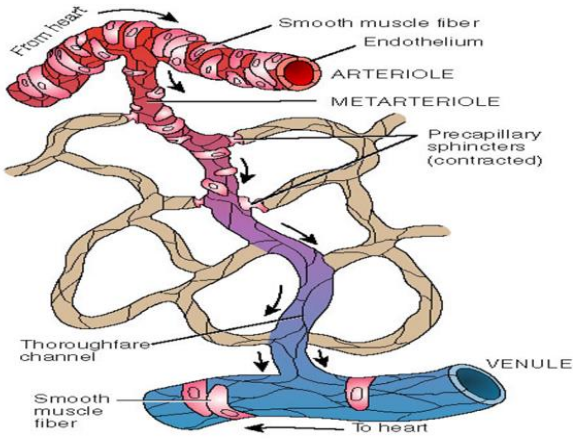


(a) Details of a capillary network

This area of exchange is very important. when u say disease in the heart u may replace the heart but disease in the capillary is very bad because u cannot replace capillaries and if u want to treat them it's not that easy like treating the heart.



(a) Sphincters relaxed: blood flowing through capillary bed



(b) Sphincters contracted: blood flowing through thoroughfare channel

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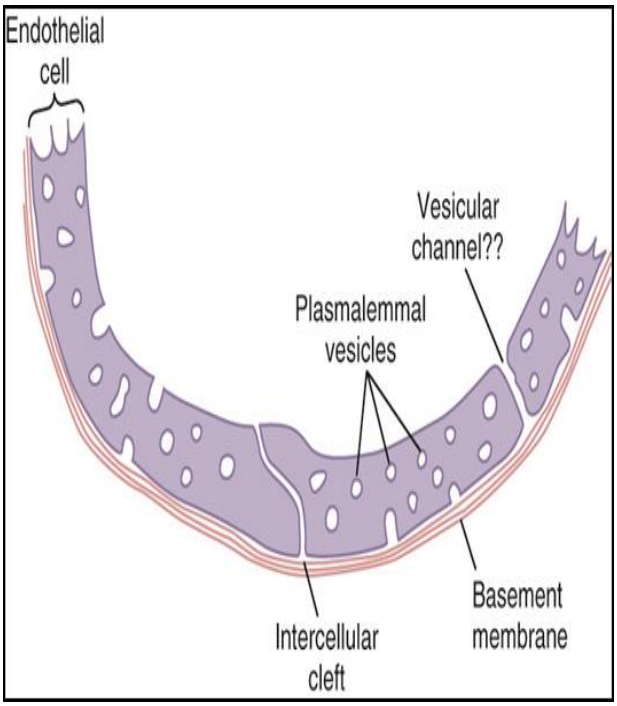
Increase of the blood flow in the capillaries

decrease of the blood flow in the capillaries

The contraction and relaxation of capillaries is called vasomotion or vasoactivity, this motion regulates the amount of blood that goes to the capillary.



A capillary is composed of unicellular layer of endothelial cells surrounded by a basement membrane. and these are unique cells coz they secrete hormone like the endocardium which is important for the blood flow.

The endothelium secretes nitric oxide which is vasodilator (relaxation) and endothelin (for contraction) and this balance between hormones is the cause of vasomotion of precapillary sphincters

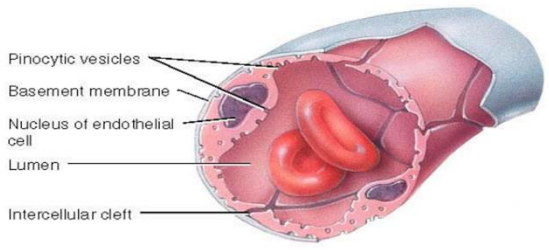
Diameter of capillaries is 4 to 9 microns.

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

Note that capillaries consist of endothelium and they don't have smooth muscles so vasomotion actually happens in the precapillary sphincters or the arterioles.

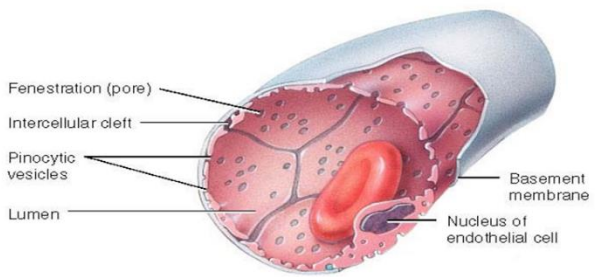
So the major resistance of the vessels of cardiovascular system occurs at the level of arterioles not vessels coz they don't have smooth muscle.

Capillary types



(a) Continuous capillary formed by endothelial cells

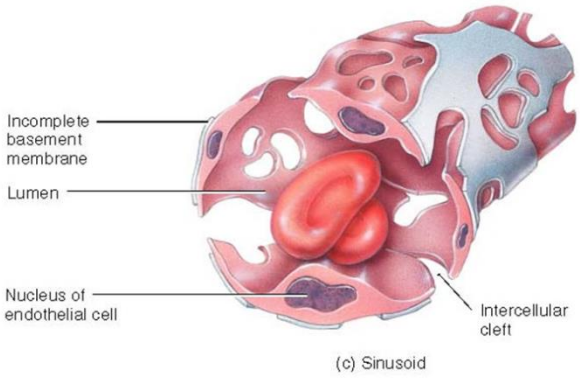
A) continuous capillary: endothelial cells are very connected to each other and no much spaces or intercellular clefts between them … capillaries are not that permeable to fluid or charged substances (found in brain and form blood brain barrier).



(b) Fenestrated capillary

B) fenestrated capillary:

Has fenestrations (pores) that can permeate large substances but not as large as cells or plasma proteins like albumin or globulin found in the kidney for the plasma filtration through the glomeruli (الكبيبات)… that's called glomerular filtration.



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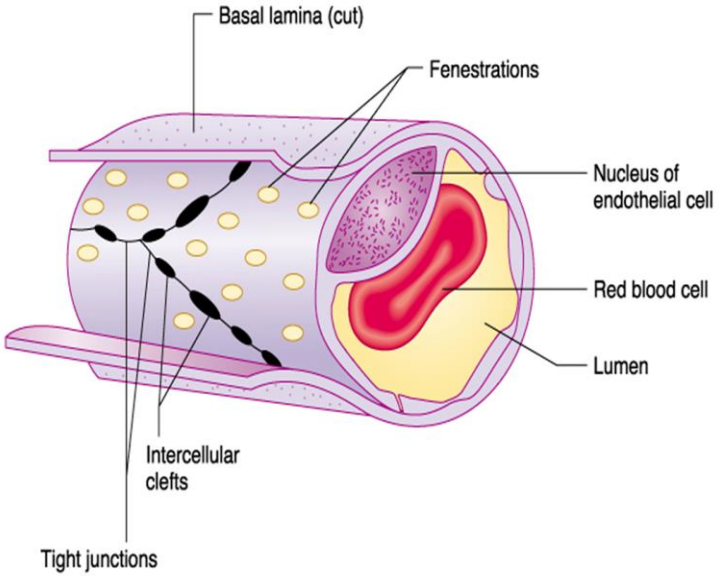
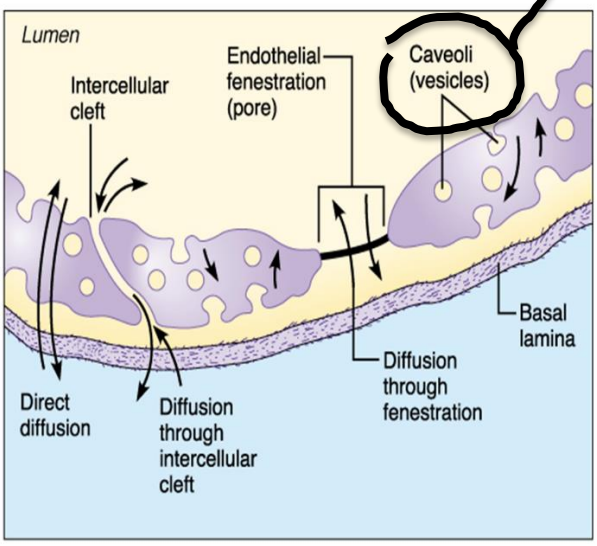
C) sinusoidal capillary: has very large opening intercellular spaces between them (found in the portal veins in the liver … where the absorptive proteins pass through the signal sources and they go to the liver for formation or metabolism of proteins

Capillary Exchange of Respiratory Gases and Nutrients



Now this is a capillary – unicellular – so a row of cells (one layer of cells) covers the lumen of the capillary – does not have smooth muscle so no vasomotion

Proteins can pass through the capillary by exocytosis or endocytosis



Movement of substances between blood and interstitial fluid by 3 basic methods:

Diffusion (simple/ facilitated)

Transcytosis(endocytosis/exocytosis)

Bulk flow (like in the intercellular space fluid pass according to pressure from higher to lower through intracellular clefts) ---> the major way by which fluid passes from interstitium to the capillary and vice versa where all plasma contents pass through except cells or proteins)

NO let us talk about diffusion:

- Most important method
- **Substances move down their concentration gradient**
    - **O_2** and nutrients from blood to interstitial fluid to body cells (by simple diffusion).
    - **CO_2** and wastes move from body cells to interstitial fluid to blood (by simple diffusion).

- Diffusion: to move substances from high (force, concentration...) to low (force, concentration,).
- Can cross capillary wall **through intracellular clefts, fenestrations or through endothelial cells.**
-
    - **Most plasma proteins cannot cross the membrane by**

    They can across the membranes or move from by vesicles (three main big arteries which are the left subclavian and the common carotid and the brachiocephalic transport or endocytosis and exocytosis), Except in 2 places:

    - **Except in sinusoids** – proteins and even blood cells leave and across the membranes without need of vesicles they move by diffusion.
    - **Blood-brain barrier** – continuous capillaries in brain have tight junctions and limit diffusion which forms blood brain barrier.

AND now transcytosis: when a small quantities of material enter one cell by endocytosis and leave the same cell by exocytosis to move to specific cell.

(متل طيران ترانزيت)

SO;

- Small quantity of material
    - Substances in blood plasma become enclosed within **pinocytosis vesicles** that enter endothelial cells by endocytosis and leave by exocytosis
    - Important mainly for large, lipid-insoluble molecules that cannot cross capillary walls any other way.

BULK FLOW:

- Passive process in which large numbers of ions, molecules, or particles in a fluid move together in the same direction (bulk flow)

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So bulk flow is the movement of fluid from one side to another (plasma to outside or outside to plasma)

- Based on pressure gradient
- **Diffusion** is more important for solute exchange
- **Bulk flow** more important in capillaries for regulation of relative volumes of blood and interstitial fluid as an example: if we have dehydration then the pressure inside the plasma is low then the fluid moves from interstitial to the plasma to control the blood volume and pressure on the other hand if the fluid concentration in interstitial is lower than plasma then the fluid will move to the interstitial and the patient will have edema.
  Note: edema is a collection of fluid in interstitial space.

2 ways that fluids can move by;

1-Filtration: movement of fluids from capillaries into interstitial fluid (رشح)

2-Reabsorption: movement of fluids from interstitial fluid into capillaries (إعادة امتصاص)

Before we start here are some information that we need to know;

***Osmotic pressure, colloid or oncotic pressure: pressure cause by the difference in protein concentration between the plasma and interstitial fluid, we call it colloid because if you but the proteins in solution and shake them they will form a colloid (سائل غروي)**

***The only difference between the plasma and interstitial is proteins.**

***We have other osmatic pressure causes by ions but we will talk about colloid osmotic pressure.**

***Now the colloid pressure is due the proteins and proteins cannot across the membrane so to equilibrate the pressure /osmosis they withdraw the fluid/water toward them (they cause reabsorption) so the two forces that are found in the capillaries are hydrostatic pressure that push the fluid away from the capillaries to interstitial and the other is colloid which is due to the protein and moves the fluid from interstitial to the capillary.**

***So the other 2 forces that found in interstitial fluid are hydrostatic pressure in interstitium and that pressure pushes the fluid away to capillaries which cause reabsorption and the other force found in capillaries is colloid pressure.**

***And capillaries wall not permeable to protein so you found very little amount of protein in interstitial so the colloid pressure for interstitial is very low.**

***In interstitial there are vacuoles or cavities and they usually form negative pressure so usually the colloid pressure in interstitial is negative.**

*** Jayton is the first person how measures the hydrostatic pressure and found it negative.**

SO Remember

Reabsorption: the movement of fluid from the interstitium to the capillaries (from out to in).

Filtration: The movement of fluid from the capillary to the interstitum (from inside to outside).

And since the proteins are stuck in the capillaries they cause a colloid pressure to reabsorb the fluid.

Colloid=something relates to proteins.

So now let us talk about 4 forces:

2 in the capillaries, hydrostatic and colloid pressure.

2 in the interstitium, hydrostatic and oncotic pressure of interstitium.

And now what are the forces that lead to reabsorption and filtration:

We have 4 forces and they are:

1. **Blood hydrostatic pressure** (BHP) generated by pumping action of heart, causing filtration (pushing the blood outside the capillary/movement of blood from the capillaries to interstitium).

Falls over capillary bed from 35(in arteriole side) to 16 (In venous side) mmHg

2. Interstitial fluid osmotic pressure (IFOP): 1mmHg, causes also filtration.

(proteins cause blood flow toward it)

In liver the most IFOP amount (because it is so permeable to proteins), In brain 0 (no permeable to protein)

2. **Blood colloid osmotic pressure** (BCOP) promotes reabsorption.

- Averages 36 mmHg

- Due to the presence of blood plasma proteins too large to cross walls.

*Plasma proteins are 3 kinds (albumin, globulin, fibrinogen)

4. Interstitial fluid hydrostatic pressure (IFHP)

- Close to zero mmHg
- From interstitial to plasma, it low sometimes it is negative due the fluid in cavities and this cavity cause negative pressure.

Note: the numbers not for memorize.

*We can calculate net filtration pressure:

NET FILTERARTION FORCES=Forces causes filtration –forces cause reabsorption

NFP = (BHP + IFOP) – (BCOP + IFHP)

So these forces are called starling forces.

*Usually what is filtered is reabsorbed (if not we may have edema), but in some causes what is filtered more than what is reabsorbed.

*The extra filtered is reabsorbed through the lymphatic system, so the lymphatic system reabsorbed the extra filtered but the lymphatic system has a capacity about 3L/day.

*If what is filtered is more than this (the capacity of lymphatic) it will be collected in interstitial space, in that because we have what we call it edema.

*So edema is collection of fluid in interstitial space.

*Remember what is filtered is reabsorbed.

Starling's Law…

Starling's forces ----> in reference to the person who first described them…

1)blood hydrostatic pressure (BHP)

2)interstitial fluid hydrostatic pressure (IFHP)

3)blood colloid osmotic pressure (BCOP)

4)interstitial fluid osmotic pressure (IFOP)

Nearly as much reabsorbed as filtered (but normally what is filtered is a little bit more than what is reabsorbed so what is extra filtered (excess: on average about 25% of fluid) is absorbed by lymphatic system to be eventually returned to blood (lymphatic capillaries' capacity is about 3L/day))

If excess fluid is more than this, it would be collected in the interstitial space causing edema ---> so edema is collection of fluid in the interstitial space

At the arterial end, net outward pressure of 10 mmHg and fluid leaves capillary (filtration)

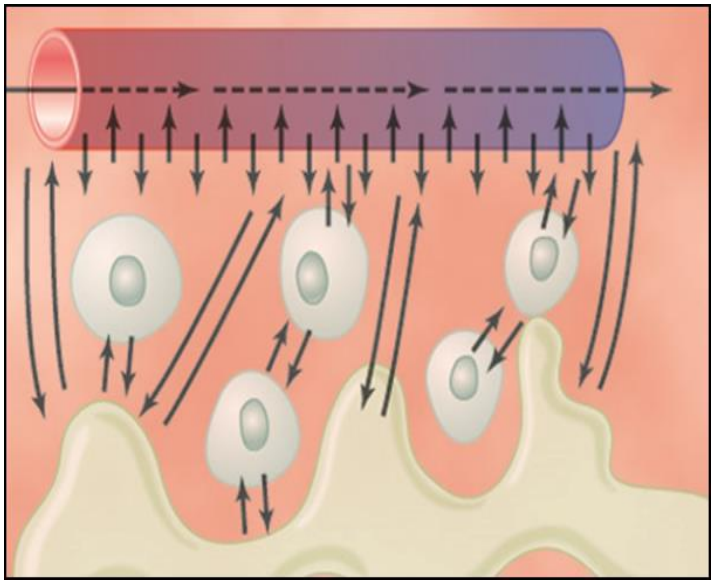
At the venous end, fluid moves in (reabsorption) due to -9 mmHg

On average, about 85% of fluid filtered in reabsorbed

Now most important means by which substances are transferred between plasma and interstitial fluid is by diffusion (which is enhanced by concentration differences across capillary + diffusion depend on the surface area of exchanging, molecules weight and size).

Lipid soluble substances diffuse directly through cell membrane of capillaries (I.E.CO2, O2).

Lipid insoluble substances such as (H2O, Na, Cl, glucose) cross capillary walls via intercellular clefts. (bulk flow)



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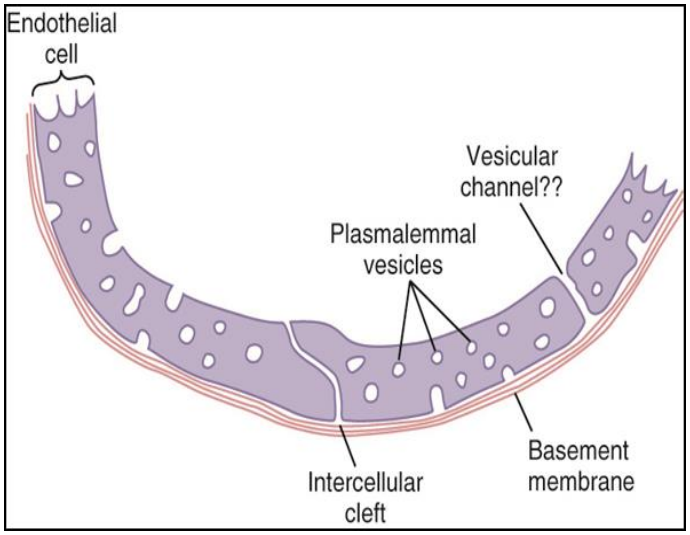
Effect of Molecular Size on Passage Through Capillary Pores

The width of capillary intercellular slit pores is 6 to 7 nanometers.

The permeability of the capillary pores for different substances varies according to their molecular diameters.

The capillaries in different tissues have extreme differences in their permeability.



Relative Permeability of Muscle Capillary Pores to Different-sized Molecules

Substance	Molecular Weight Permeability	Substance
Water	18	1.00
NaCl	58.5	0.96
Urea	60	0.8
Glucose	180	0.6
Sucrose	342	0.4
Insulin	5000	0.2
Myoglobin	17600	0.03
Hemoglobin	69000	0.01
Albumin	69000	0.001

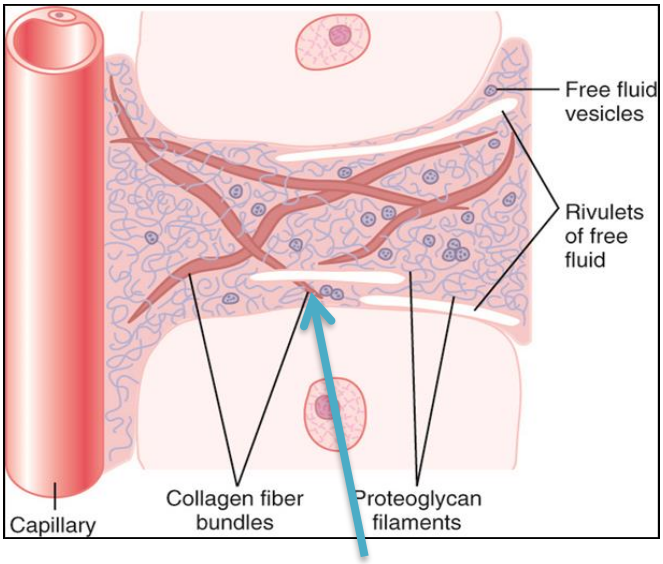
Molecular weight is larger

So very minimal permeability of the membrane to these substances so they cannot pass through pores of the capillary

Space between cells is called interstitium and fluid in this space is called interstitial fluid.

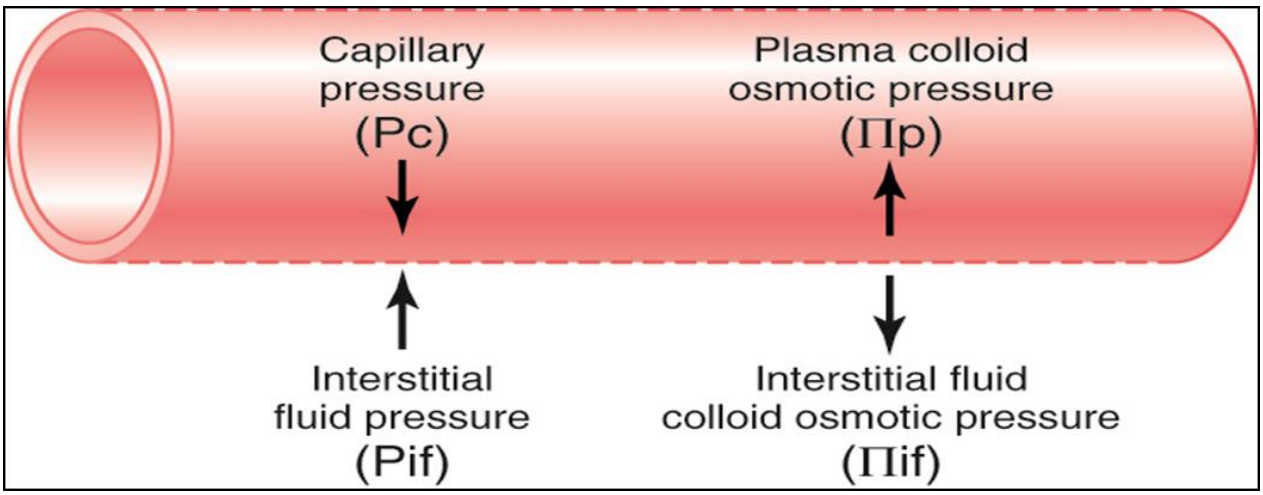
Two major types of solid structures in interstitium are collagen fibers and proteoglycan filaments (coiled molecules composed of hyaluronic acid).

Almost all fluid in interstitium is in form of gel (fluid proteoglycan mixtures); there is very little free fluid under normal conditions.



Interstitial space causes cavities; these cavities might end with negative pressure usually. (it could be positive depending on the type of tissue)

Determinants of Net Fluid Movement across Capillaries



Capillary hydrostatic pressure (Pc)-tends to force fluid outward through the capillary membrane. (causing filtration)

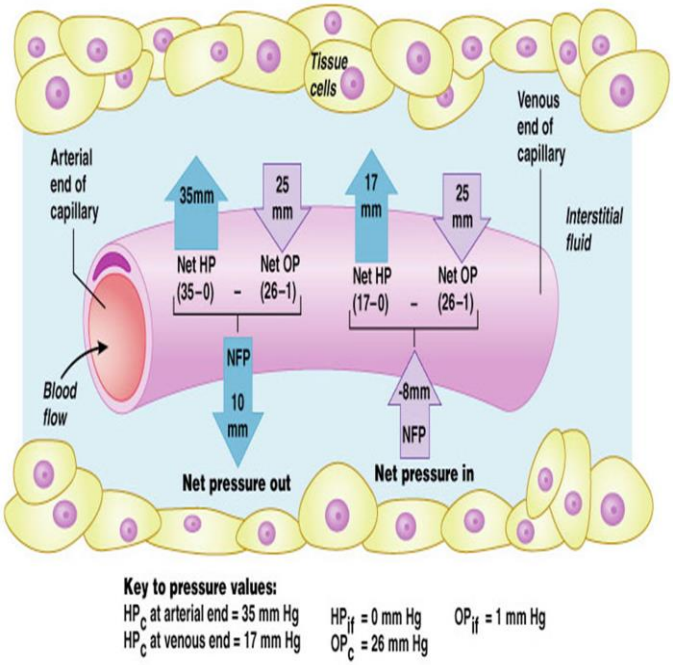
Interstitial fluid pressure (Pif)- opposes filtration when value is positive. (reabsorption)

Plasma colloid osmotic pressure (π c)- opposes filtration causing osmosis of water inward through the membrane. (reabsorption)

Interstitial fluid colloid pressure (π if) promotes filtration by causing osmosis of fluid outward through the membrane. (filtration)

NP = Pc - π c - Pif + π if = (Pc-Pif) – (πc-if) …. يعني Subtract(forces that cause reabsorption) <u>from</u> (forces that cause filtration) --------> and this is starling equation

Net Filtration Pressure (NFP)



We apply the equation on both arterial and venous ends of the capillary

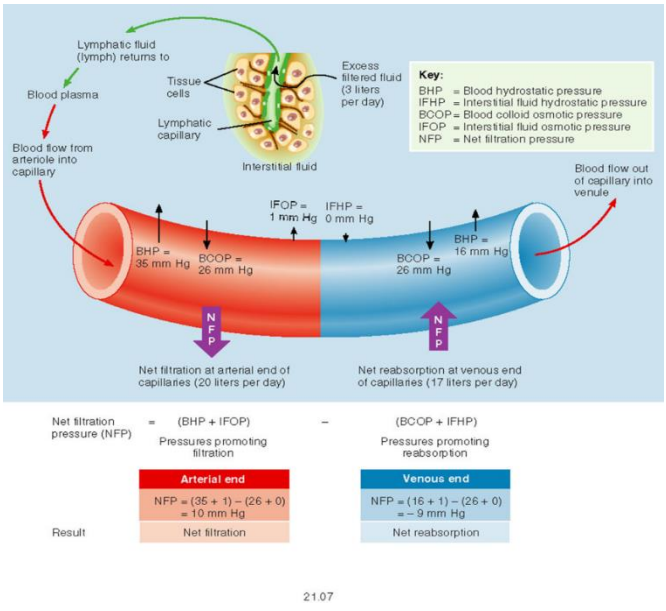
The arterial side:

Forces that cause infiltration minus forces that cause reabsorption:

NP=BHP+IFOP – (BCOP+IFHP)

35+1 – (26+0) = 10 (filtration is more than reabsorption)

And by doing the same in the venous side we end with NP= -8 (negative … so absorption here is more than filtration)



What is extra filter is going to pass through the lymphatics,

The capillary in the lymphatic has large intercellular spaces so can absorb proteins that might pass through the capillary

Remember that the capillary has capacity which is 3L/day

We do the same calculation as in the previous example then …. NF + NR = 10 – 9 = +1 …. positive so filtration is more than reabsorption in this capillary

شطّور يبني خلصت أكتر من نص الشيت هانت قرّبنا

Now normal capillary hydrostatic pressure is approximately 17 mmHg.

Interstitial fluid pressure in most tissues is negative 3. Encapsulated organs have positive interstitial pressures (+5 to +10 mmHg).

Negative interstitial fluid pressure is caused by pumping of lymphatic system or encapsulated organs.

Colloid osmotic pressure is caused by presence of large proteins.

Plasma Proteins and Colloid Osmotic Pressure

we said before that colloid osmotic pressure resulted by protein such as albumin, globulins and fibrinogen. And their conc. between 6-8 g/dl.

- Plasma colloid osmotic = 28mmHg
- Plasma protein conc. = 7.3gm/dl
- 75% of the total colloid osmotic pressure of plasma results from the presence of *albumin* and 25% is due to *globulins.*

	Gm/dl	Πp(mmHg)
Albumin	4.5	21.8
Globulins	2.5	6.0
Fibrinogen	0.3	0.2
Total	7.3	28.0

This colloid osmotic pressure of protein is mainly due to and depends on molecular weight, as an example: m.w of albumin as around 68000 Dalton and m.w for globulins is 240000 and fibrinogen 500000 Dalton.

Question: If we have 1g of albumin and 1g of globulins and dissolved in water, what is the osmotic pressure of them?

We dissolved the same amount but the osmotic pressure of albumin is more than globulin... **why??**

Because of m.w of albumin and m.w of globulin they have the same number of molecules (Avogadro no.), 1 g of albumin has much more molecules than 1 g of globulin,

and you know that osmotic pressure depends on the no. of molecules and not depend on the g concentration.

So, no. of molecules of 1 g of albumin is much more than the number of 1 g of globulin according to m.w.

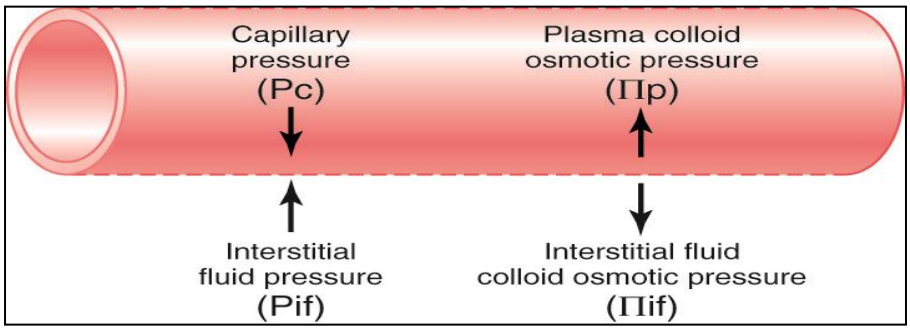
Also, albumin will share much more in colloid osmotic pressure than globulin but also albumin conc. (4.5 gm/dl) is high that why 75% of total colloid pressure is albumin as we wrote above.

When you say there's decrease or increase in colloid osmotic pressure of the plasma mainly due to the albumin not the globulin (25%), fibrinogen has almost no share because it's found very small amount (0.3 g/dl) and m.w is very high (500,000).

Interstitial Colloid Osmotic Pressure

- *Interstitial protein concentration* is approximately 3gm/dl.
- The interstitial colloid osmotic pressure is normally 8mmHg.

Determinants of Net Fluid Movement Across Capillaries



$$\text{Filtration Rate} = K_f\{(P_c - P_{if}) - (\pi_c - \pi_{if})\}$$

- *Filtration rate* = net filtration pressure *(NFP)* multiplied by the filtration coefficient (Kf)
- *Filtration coefficient (Kf)* is a product of and depends on surface area times the hydraulic conductivity or permeability of membrane.

- you want to calculate how much is filtered, you'll multiply NFP with Kf as the equation above. And you'll end by how many ml is filtered per g of tissue per minute.

Note: filtration rate between tissues is different from each other.

Examples: filtration rate is brain is very low otherwise filtration rate in liver is very high also, filtration rate in kidney is measured by glomerular filtration rate معدل الترشيح الكبيبي

Forces Causing Filtration at the Arteriole End of the Capillary.

	mmHg
*Forces tending to move fluid **outward***	
Capillary pressure	30
Negative interstitial free fluid pressure	3
Interstitial fluid colloid osmotic pressure	8
TOTAL OUTWARD FORCE	41
*Forces tending to move fluid **inward**:*	
Plasma colloid osmotic pressure	28
TOTAL INWARD FORCE	28
Summation of forces:	
Outward	41
Inward	28
NET OUTWARD FORCE	13

Arteriole end more filtration

Forces Causing Reabsorption at the Venous End of the Capillary

	mmHg
*Forces tending to move fluid **inward**:*	
Plasma colloid osmotic pressure	28
TOTAL INWARD FORCE	28
*Forces tending to move fluid **outward**:*	
Capillary pressure	10
Negative interstitial free fluid pressure	3
Interstitial fluid colloid osmotic pressure	8
TOTAL OUTWARD FORCE	21
Summation of forces:	
Outward	21
Inward	28
NET INWARD FORCE	-7

Venous end more reabsorption

***The net toward filtration is 6 mmHg.**

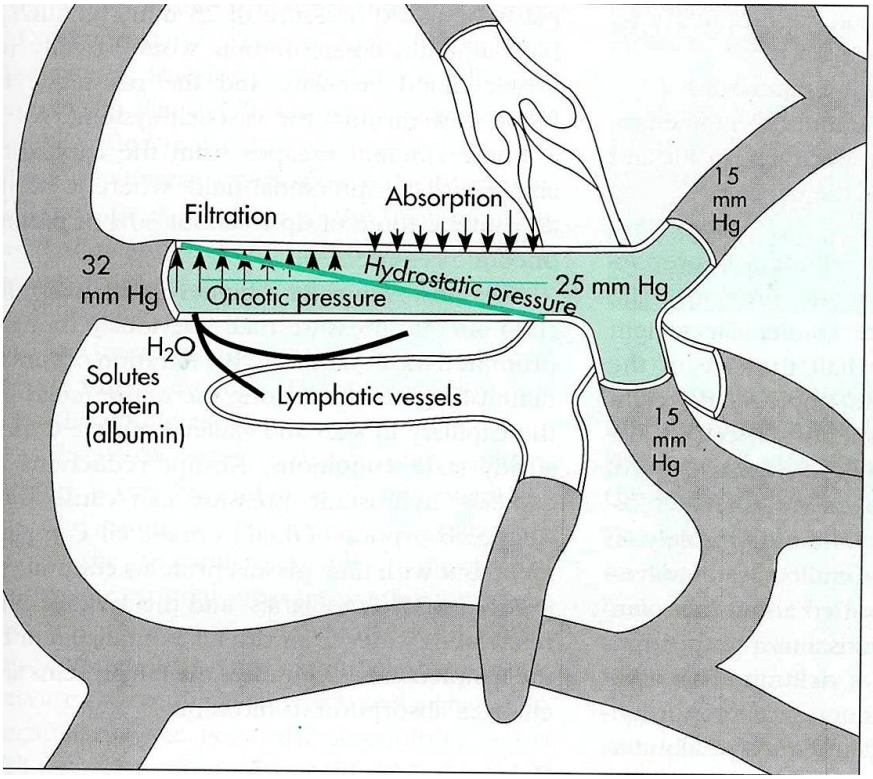


Figure 7-9 ■ Schematic representation of the factors responsible for filtration and absorption across the capillary wall and the formation of lymph.

***About this figure**

25 mmHg → Venous end (reabsorption)

32 mmHg → Arterial end (filtration)

There is extra filter than reabsorb, and the extra filter go to the lymphatic vessels.

The lymphatic vessels have very large intercellular spaces that even can take on the protein and they will oppose formation of edema.

هانت ضايل شوي بس صفحتين

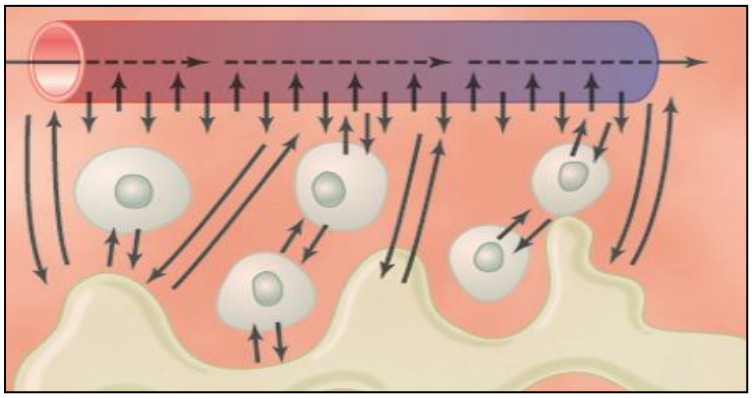
Net Starting Forces in Capillaries

	mmHg
Mean forces tending to move fluid outward:	
Mean Capillary pressure	17.3
Negative interstitial free fluid pressure	3.0
Interstitial fluid colloid osmotic pressure	8.0
TOTAL OUTWARD FORCE	28.3
Mean force tending to move fluid inward:	
Plasma colloid osmotic pressure	28.0
TOTAL INWARD FORCE	28.0
Summation of mean forces:	
Outward	28.3
Inward	28
NET OUTWARD FORCE	0.3 (more filtration), and then goes to lymphatic

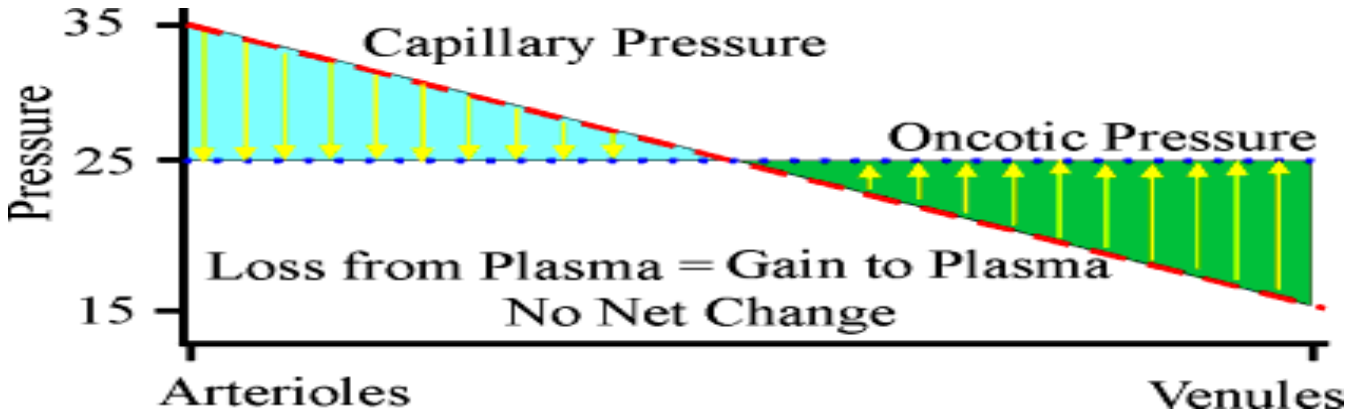
Some notes according what doctor said:

1- Instead of saying that there are a venous and arteriole sides, we can calculate mean capillary pressure.
2- Mean capillary pressure ≠ (arterial end hydrostatic pressure + venous end hp) / 2.
3- Capillary pressure depends on distance.
4- We can calculate it by starling force.

Net Starting Forces in Capillaries



✓ *Net filtration pressure* of 0.3 mmHg x K_f which causes a net filtration rate of 2ml/min for entire body.



On the arteriole end, the hydrostatic pressure is higher than the oncotic, so there is fluid movement from plasma to interstitium. The magnitude of this water flow is indicated by the light blue area on the left (downward arrows). On the venule end, the hydrostatic pressure has dropped below the oncotic pressure. Fluid moves back from the interstitium to the plasma. The magnitude of this reverse flow is indicated by the green area on the right (upward arrows).

Recommended: back to video is better, doctor was drawing on this picture.

Causes of edema

Increased hydrostatic blood pressure (P_c)

- heart failure (left or right),
- excess fluid in the blood

Decreased blood colloid osmotic (oncotic) pressure (π_c)

-Liver, kidney diseases, malnutrition (kwashiorkor), burn injuries

Increased interstitial hydrostatic pressure (P_{if})

(lymphatic capillary blockage)

- breast cancer surgery, elephantiasis

Leaking capillary wall (K_f)

- histamine release during allergic reaction

اعذرونا على طول الشيت و موفقين❤

كل الحب ^_^