physiology

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◉ Sheet ○ Slides

Number

26

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In this sheet we will talk about:

1-Starling forces in different cell types.

2-Edema: causes, types, and safety factors.

Quick Recap:

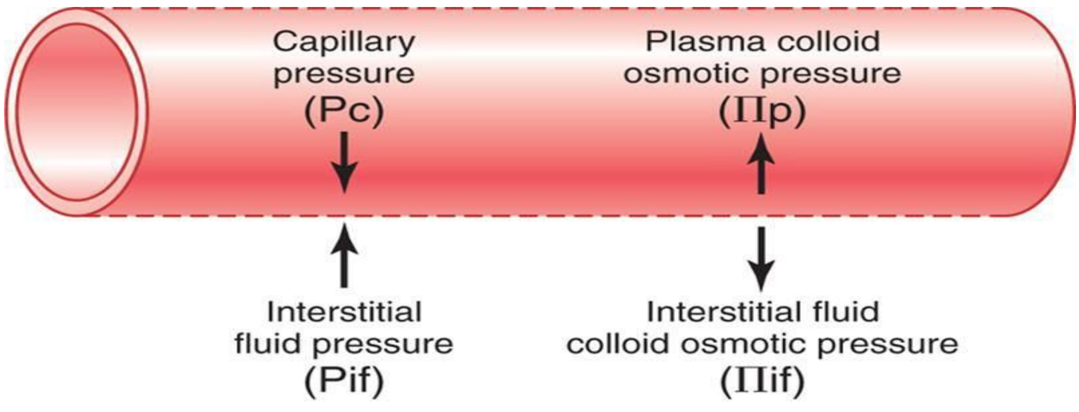
We have **four** primary forces that determine whether fluid will move out of the blood into the interstitial fluid **"filtration"** or in the opposite direction **"reabsorption"**, which are called Starling forces. They are:

1) **Capillary hydrostatic pressure (P_c):** Tends to force fluid outward from the blood "always positive".

2) **Interstitial fluid hydrostatic pressure (P_i):** tends to force fluids inward into the capillary if positive ***"reabsorption"*** and outward if negative ***"filtration".***

3) **Capillary colloid osmotic pressure (π_c):** forces fluids inward into the capillary.

4) **Interstitial fluid colloid osmotic pressure (π_i):** forces fluids outward into the interstitium.



The sum of these forces gives the net pressure, if **positive** there will be net **filtration**, if **negative** there will be net **reabsorption**.

$$\text{Net Force} = P_c - P_i - \pi_c + \pi_i$$

Capillary Hydrostatic Pressure “Pc”:

In general, all capillaries are linked to an arteriole from one end, and a veniole from the other end. As we have studied in physics, resistance is inversely proportional to the cross-section area. So, by vasodilation, we decrease the resistance thus increasing the blood flow, and vice versa. **Be careful!** Dilation and constriction of arterioles and venioles have opposite effects on **Pc**. For instance, arterioles constriction causes less blood flow in the capillary so **Pc** decreases. On the other hand, venioles constriction makes it harder for the blood to get out of the capillary thus increasing **Pc**.

So, you now think that the venous pressure and the arterial pressure contribute to the capillary hydrostatic pressure in the same amount but in opposite sides, right?

No, you’re wrong :(The following equation shows clearly that changing the venous pressure has bigger effect on **Pc** than changing arterial pressure.

$$Pc = \left(\frac{\left\langle \left[\frac{Rv}{Ra} \right] * Pa + Pv \right\rangle}{1 + [Rv / Ra]} \right)$$

$$Rv/Ra = 1/5$$

$$Pc = (1/6)\ Pa + (5/6)Pv$$

Where: Pv = Venous Pressure. **Rv = Venous Resistance.**

Pa = Arterial Pressure. **Ra = Arterial Resistance.**

NOTE: We are only required to know the last equation.

Why do we need to know all that?

In short:

1) Right ventricle failure ➔ Higher pressure at the right atrium ➔ Higher pressure in systematic veins➔ Higher Pc ➔ More filtration ➔ Edema at any part of the body.

For example: Abdomen edema(ascites), Liver edema(hepatomegaly), Lower limb edema, etc.

2) Left ventricle failure ➔ Higher pressure at the left atrium ➔ Higher pressure in pulmonary veins➔ Higher Pc ➔ More filtration ➔ Pulmonary edema (in the lung).

→ Edema is the abnormal accumulation of fluids in the interstitial compartment caused by high filtration.

Colloid osmotic pressure "π":

Molecules or ions that fail to pass through a membrane exert osmotic pressure. Because proteins fail to pass through the capillary, it is proteins of the plasma and interstitial fluid that are responsible for the osmotic pressure exerted on the capillary's membrane **"Colloid osmotic pressure"**.

Note: Total protein concentration in the blood = 6-8 g/dcL.

Blood has two main types of proteins:

1) Albumin 3.5 – 5.5 g/dcL.
2) Globulin 2-4 g/dcL.

The total colloid osmotic pressure of a normal human being is **28 mmHg**. 22 mmHg of this pressure is caused by **Albumin** while the 6 mmHg is caused by **globulin**.
The average molecular weight of albumin and globulin is 70,000 and 140,000 respectively. Therefore, as stated by Avogadro, 1g of albumin contains **more molecules** than 1g of globulin.

Avogadro's law: one mole of any substance in life has 6.022 x 10^{23} particles or molecules.

Osmoles = moles for ions, molecules, and proteins = $\frac{grams}{molar\ mass}$

>> **Albumin** is more important in causing colloid osmotic pressure because it has **higher number of molecules** and its **concentration is twice** the concentration of Globulin.

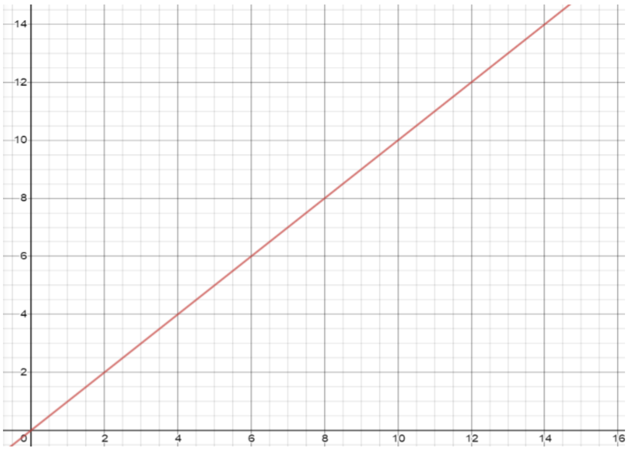
>> Colloid osmotic pressure is directly proportional to **molar** concentration gradient. (There are other factors that we are not going to talk about).

$$\pi \ \alpha \ \Delta C$$

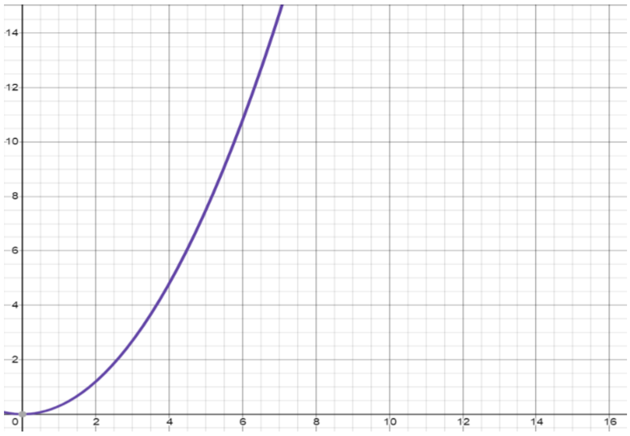
Keep in mind that: Each 1 mOsm of protein causes 19.3 mmHg change in pressure.

*Relationship between the concentration of albumin and the osmotic pressure is not linear as you may think. Albumin causes **higher** osmotic pressure than expected.

Expected



Observed



NOTE: numbers in the previous are arbitrary and not real.

EXTRA INFO: {Why does that happen? Albumin does not act like other proteins.

It's due to many factors such as Gibbs-Donnan effect.**}**

Hypoalbuminemia:

Protein's main source is by **ingesting** it, then it is **reabsorbed** as amino acids in the intestine and then the liver **resynthesizes** the proteins again.

Hypoalbuminemia occurs when the level of albumin in the blood is abnormally low **< 3.5g/dcL.**

NOTE: Albumin **doesn't get filtered** in the kidney; it is not present in the urine.

Hypoalbuminemia is due to:

1) **Malnutrition**: there is no protein intake.
2) **Malabsorption** in the intestine.
3) **Problems in the liver** which synthesizes the albumin.
4) **Kidney failure**: loss of albumin with urine.

>>Hypoalbuminemia causes generalized edema by decreasing the capillary colloid osmotic pressure (π_c) leading to higher filtration.

Types of edema:

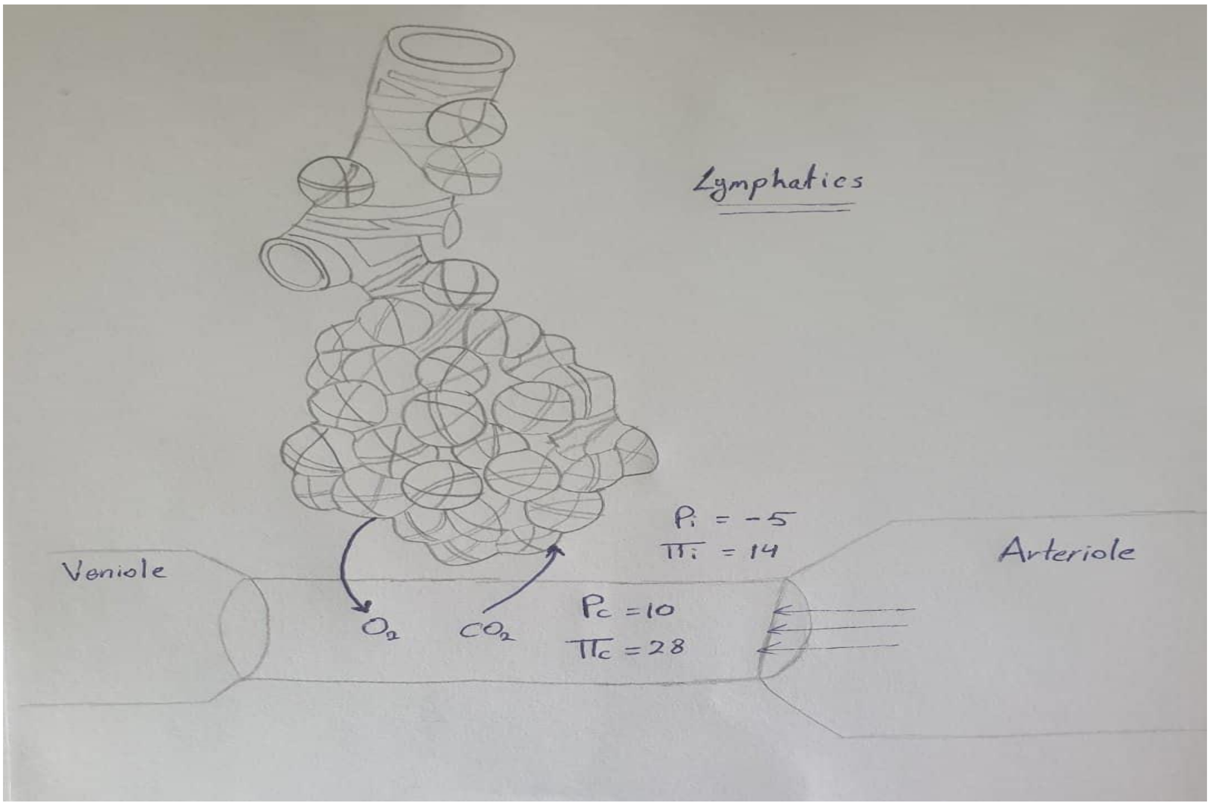
1) **Localized**: edema in a **specific** area. For example: it can occur in pregnant women ***"uterus compresses veins causing high filtration"***, and in lymphatic vessels blockage.

2) **Generalized**: edema happens **all over the body**, as a result of hypoalbuminemia or a right heart failure.

NOTE: Edema can be pitting and non-pitting. Pitting edema, like most types of edema, leaves marks if the skin was touched and it varies between +1 and +4 depending on intensity. Lymphatic edema is a non-pitting edema.

Now let's have a look at the genius design of our body, taking capillaries in lungs and kidneys as example.

1) Lungs: The following figure shows the filtration-reabsorption process in capillaries near the alveoli.



Let's make use of the first equation we've learned today and try to predict what's going to happen.

Net force = $P_c - P_i - \pi_c + \pi_i = 10 - (-5) - 28 + 14 = +1$

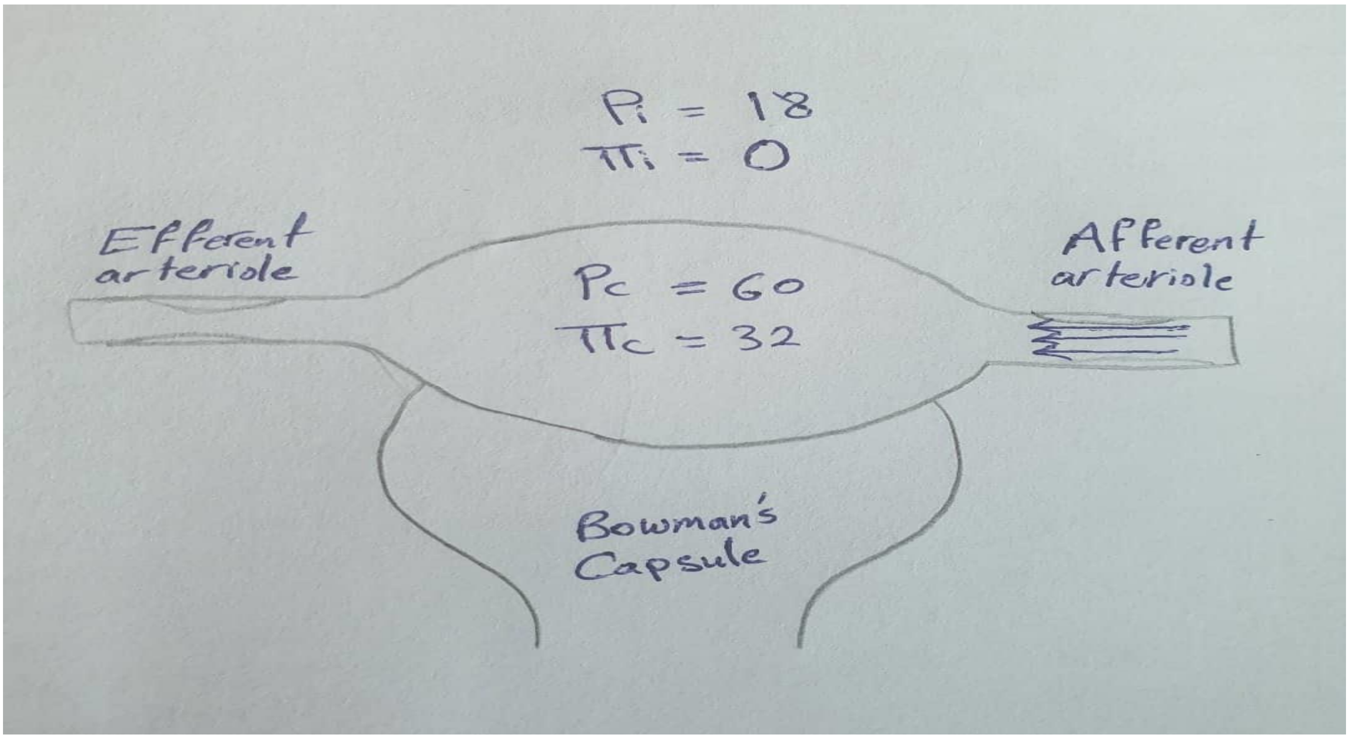
Notice that we here don't care about any of this, we only need that $CO_2 - O_2$ exchange.

So, what to do with that +1 net filtration? Fear not! Our lungs are supplied with high number of lymphatic vessels that can take care of that easily by acting as a vacuum cleaner and sweeping this fluid back to venous circulation.

NOTE: Pulmonary edema safety factor that works against formation of edema is the **high** presence of lymphatic vessels.

Good to know: In the lungs, whilst oxygen is smaller than CO_2, difference in solubility means that **CO_2 diffuses roughly 20x faster than O_2**.

2) Kidneys: Our kidney's main function is filtration. Surprisingly, capillaries there are linked to two arterioles, an **afferent** and an **efferent** one. The efferent arteriole is constricted so that **Pc** can go as high as 60 (instead of 10 in lungs and 30 in muscles).



Using the same equation:

Net force = $P_c - P_i - \pi_c + \pi_i = 60 - 18 - 32 + 0 = +10$

So, we have got a powerful force that favors filtration, and this is what we want.

NOTE: π_c here is higher than usual due to the high filtration rate, where fluid passes outside, and proteins are left behind inside capillaries.

NUMBERS TO BE MEMORIZED

- Total protein concentration in the blood = 6-8 g/dcL.

- Albumin = 3.5 – 5.5 g/dcL and Globulin = 2-4 g/dcL.

- Each 1 mOsm of protein causes 19.3 mmHg change in pressure.

- $P_c = 1/6(P_a) + 5/6(P_v)$.

- The total colloid osmotic pressure of a normal human being is **28 mmHg**. 22 mmHg of this pressure is caused by **Albumin** while the 6 mmHg is caused by **globulin**.

SHORT QUIZ

1) What does 0 pressure in our body mean?

a- There is no pressure.

b- The pressure is less than the atmospheric pressure.

c- The pressure can't be measured.

d- The pressure is equals to the atmospheric pressure.

2) You encountered a patient with edema. You can give him only one mole of a certain substance. Which of the following would you choose to have the best effect?

a- Globulin-1 (Molecular weight = 200k).

b- All have the same effect.

c- Globulin-2 (Molecular weight = 140k).

d- Globulin-3 (Molecular weight = 280k).

3) An old woman is suffering from edema all over the body, what could be the cause?

a- Left ventricle failure.

b- Hyperalbuminemia.

c- Kidney failure.

d- none of the above.

4) A group of researchers got the following information: $P_c=13$, $P_i=6$, $\pi_c=32$, $\pi_i=15$ what body part the data could've been obtained from?

a-Epidermis.

b-Peritubular capillary (part that is responsible for reabsorption in kidneys).

c-Skeletal muscles.

d-a+c

ANSWERS

1-d. When we measure pressure in our body the reference point used is atmospheric pressure.

2-b. The effect (which is basically osmotic pressure that decreases filtration and stops edema formation) depends on number of osmoles (or moles).

3-c. Kidney failure leads to losing Albumin which can cause edema.

4-b. Using our first equation, we can calculate the net force (-10) which means that it favors reabsorption. We are most likely finding it in reabsorption units of the kidney.

Good Luck