physiology

premed 2018 - JU

◉ Sheet ○ Slides

Number

25

Done by:

شُعبة أربعة اللّطيفة

Corrected by:

Ibrahim Elhaj

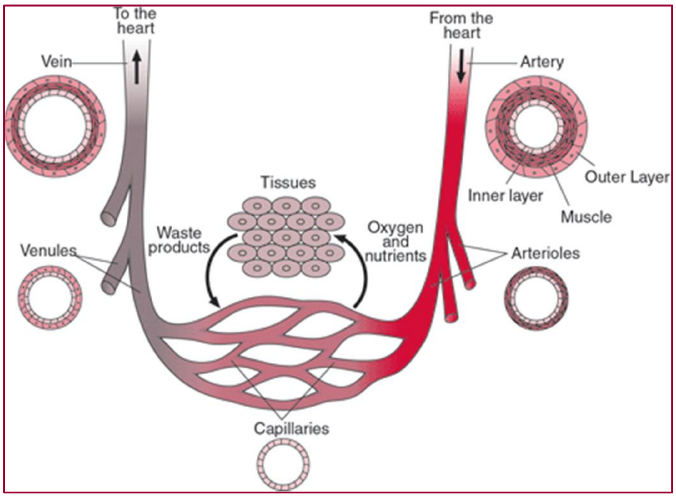
Doctor

Dr. Yanal Shafagoj

“When the heart speaks, the mind finds it indecent to object.”

Microcirculation and capillary exchange, lecture three.

In order to understand the flow of blood in the body and capillary exchange, you need to take in some new terms and visualize the structure of the microcirculation and capillary system.

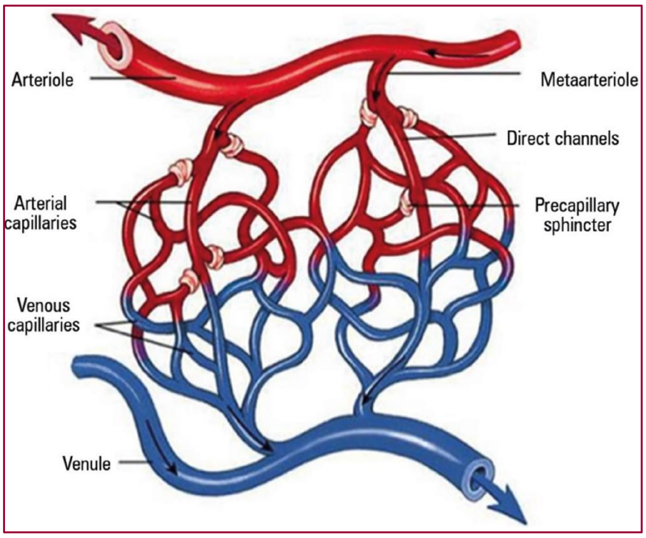


-Components of microcirculation:

1) Arterioles.

2) Venules.

3) Capillaries.



The microcirculation of each organ is organized to serve the organ’s specific needs.

In general, an **artery** is a blood vessel that carries blood **away from the heart**, where it branches into ever-smaller vessels.

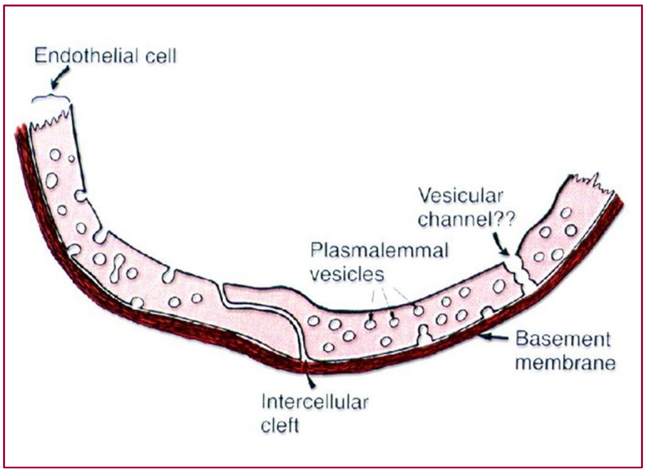
Eventually, the smallest arteries, vessels called **arterioles**, further branch into tiny **capillaries**, where nutrients and wastes are **exchanged**.

Capillaries come together to form **venules**, small blood vessels that carry blood to **a vein**; a larger blood vessel that returns blood to the heart.

The arterioles are highly muscular, and their diameter can change manifold. At the point where each true capillary originates from an arteriole, **a smooth muscle fiber usually encircles the capillary**. This structure is called ***pre-capillary sphincter***. **This sphincter can open and close the entrance to the capillary.**

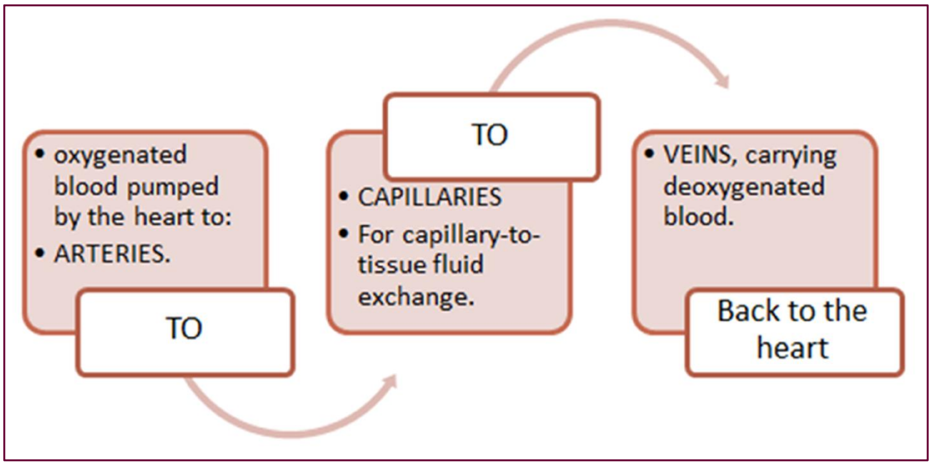
The structure of the capillary

The capillary wall is composed of a single layer of **endothelial cells** and it is surrounded by a thin basement membrane on the outside of the capillary. The cells show ***intercellular clefts, intracellular gaps***, and ***intracellular fenestrations***; which are small passageways connecting the **interior of the capillary with the exterior**, and through which **fluid** can percolate **freely**.



Capillaries do **not** have smooth muscle in their walls, and thus they **cannot** change their diameter. However, blood flow through them can be controlled by larger vessels that feed them.

Blood volume



Arteries and veins transport blood in two distinct circuits: the **systemic circuit** and the **pulmonary circuit**. **Systemic arteries** provide blood **rich in oxygen** to the body's tissues. The blood returned to the heart through **systemic veins** has less oxygen, since much of the oxygen carried by the arteries has been delivered to the cells. In contrast, in the pulmonary circuit, **arteries** carry blood low in oxygen exclusively **to the lungs** for gas exchange. **Pulmonary veins** then return **freshly oxygenated** blood **from the lungs to the heart** to be pumped back out into **systemic circulation**. Although arteries and veins differ structurally and functionally, they share certain features.

Blood distribution for a 70-kg adult ♂:

Systematic circulation (4100 mL).	Systematic arteries (750 mL).
	Systematic veins (3000 mL).
	Systematic capillaries (350 mL).
Pulmonary circulation (500 mL).	Pulmonary arteries.
	Pulmonary veins.
	Pulmonary capillaries.
Heart chambers (350 mL).	Ventricles and atrium.

*Note: numbers are approximate and we only care about the blood volume in systematic capillaries (350 mL).

-The average blood volume of adults is about 7% **(5 Liters in a 70-kg adult male)** of body weight. About 55% **(3 Liters)** of the blood is plasma and 45% **(2 Liters)** is red blood cells, but these percentages can vary considerably in different people, depending on gender, weight, and other factors.

-Plasma is mostly **water** (up to 92% by volume), and contains dissolved proteins (e.g. serum albumins, globulins, and fibrinogen), glucose, electrolytes (Na^+, Ca^{2+}, Mg^{2+}, HCO_3^-, Cl^-, etc.), hormones, carbon dioxide and oxygen **(8%)**.

Interstitial fluid: it is the fluid in the interstitium which is the space between cells.

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

-Recall that total body water in a 70-kg adult male is about **60%** of the body weight **(42 Liters)**, **28** of the **42** Liters of fluid in the body are intracellular. Thus, the **intracellular constitutes about 40%** of the total body weight. All the fluids outside the cells are collectively called the extracellular fluid. Together **these fluids account for about 20%** of the total body weight (**14 Liters**).

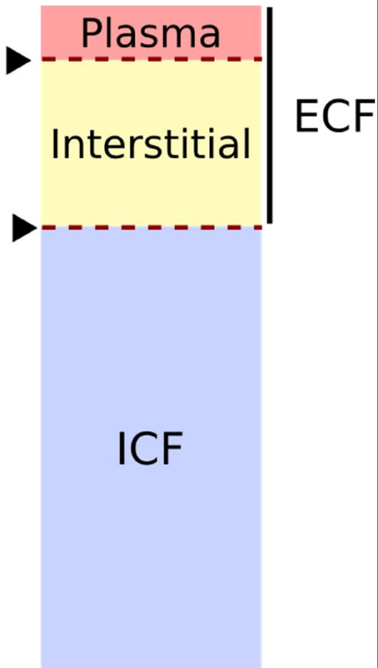
The two largest compartments of the extracellular fluid are the plasma which makes up almost **one fourth of the extracellular fluid (3 Liters),** and the **interstitial fluid** which makes up more **than three fourths** (**11 Liters**) of the **extracellular fluid**; **10 Liters in the gel form, and 1 Liter as a free fluid.**

-Note1: blood cells **do not move** across the capillary wall during capillary-to-tissue fluid exchange, it's only the plasma and its contents.

-Note2: Almost **all fluid** in the interstitium is in form of ***gel*** (fluid proteoglycan mixtures); there is very little free fluid under normal conditions.

-Note3: Selective barriers allow fluid compartments to differ in composition; the ionic composition of the extracellular fluid does differ markedly from the intracellular. However, water can diffuse rapidly by osmosis which in turn maintains the same osmolarity in all of the three compartments (300 mOsm).

Cardiac output (CO):



It is the volume blood pumped by the heart per unit time, and it equals ≈ 5 Liters\min, and because plasma makes up about 55% of the total blood volume; the amount of plasma volume pumped per minute ≈ 3 Liters.

For the whole day:

(3Liters\min)*(60min\hour) * (24 hours\ day) = 4000 Liters plasma\ day.

So as mentioned above, cardiac output is **the volume of blood pumped by each ventricle per minute (not the total amount of blood pumped by the heart).**

Keep in your mind that blood flow through a vessel depends on the pressure gradient and vascular resistance.

Flow rate: The volume of blood passing through a vessel per unit of time. It is **directly** proportional to the pressure and **inversely** proportional to vascular resistance.

F = Δ P/R

F= flow rate of blood through a vessel

ΔP=pressure gradient

R= resistance of blood vessel

- ✓ **Pressure gradient:** the difference in pressure between the beginning and end of a vessel. Blood flows from an area of higher blood pressure to an area of lower blood pressure down a pressure gradient.
- ✓ Contraction of heart imparts pressure to the blood, which is the main driving force or flow through the vessel.
- ✓ Because of frictional losses (resistance), the pressure drops as blood flows throughout the vessel's length. Accordingly, pressure is higher at the beginning than at the end of the vessel, establishing a pressure gradient for forward flow of blood through the vessel.
- ✓ **Resistance :** the measure of the hindrance or opposition to blood flow through the vessel caused by **friction** between the moving fluid and the **stationary vascular walls**, as resistance to flow **increases** it is more **difficult** for blood to pass through the vessel , so flow rate **decreases** (as long as the pressure gradient remains unchanged).

- ✓ A slight change in the radius of a vessel brings about a notable change in flow, because the resistance is **inversely** proportional to the fourth power of the radius.

  (R α 1/r)^4

- ✓ Thus, doubling the radius reduces the resistance to 1/16 its original value and increases flow through the vessel 16 times (at the same pressure gradient).The converse is also true, only 1/16th as much blood flow through a vessel at the same driving pressure when its radius is halved.

We need to clarify a potentially confusing point. The term Flow can be used in two different contexts – flow rate and flow velocity.

The flow rate refers to the **volume** of blood per unit of time (this is the flow we have been talking about in relation to the pressure gradient and resistance).

The velocity flow is the **distance** per unit time, with which blood flow forward through a given segment of the circulatory system.

Very important to understand:

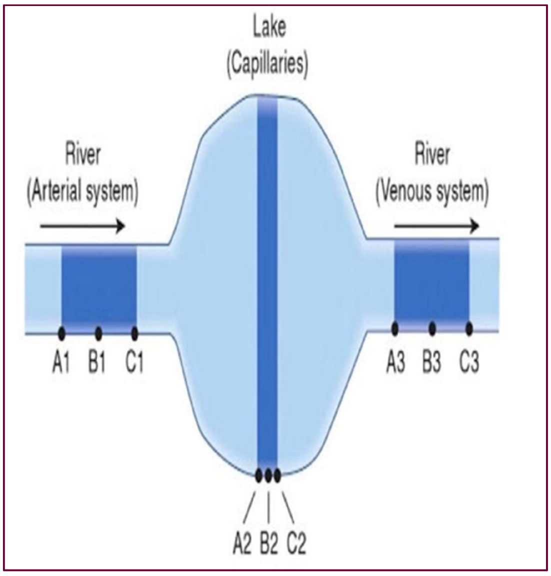
The circulatory system is a close system; the volume of blood flowing through any level of the system must equal the **cardiac output**.

For example if the heart pumps out 5L/min , and 5L/min return to the heart , then 5 L/min must flow through the arteries , arterioles, capillaries, and veins. The flow rate is the same at all levels of the circulatory system.

However, the velocity varies, blood slows considerably as it passes through the capillaries, this slow velocity allows **adequate** time for exchange of nutrients and metabolic end products between blood and tissue cells, which is the **sole purpose of the entire circulatory system**.

For a better understanding:

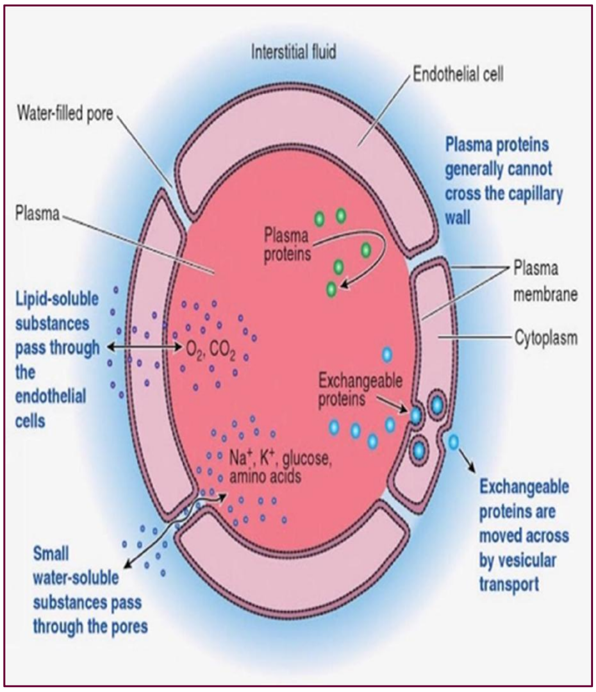
The figure shows three dark areas represent equal volumes of water.



During one minute, this volume of water moves forward from points A to points C. Therefore, an identical volume of water flows past points B1, B2, and B3 during this minute. That is the flow rate is the same at all points. However during that minute the identical volume of water moves forward a much shorter distance in the wide lake (A2 TO C2) than in the much narrower river (A1 to C1 and A3 to C3).Thus the velocity of flow is much slower in the lake than in the river. Similarly, velocity of flow is much slower in the capillaries than in the arterial and venous system.

The permeability of a capillary:

Water-filled capillary pores permit passage of small, water-soluble substances. The single **endothelial layer cells** are continuous or closely joined, with only narrow water filled clefts or Pores at the junction between cells.



We know that permeability K= 1/R so we can say;

Flow= driving force (pressure gradient) × K

Permeability of the capillary can change, for example histamine increases capillary permeability by triggering contractile response in endothelial cells to widen the intercellular gaps (pores). This is **NOT a muscular contraction** because no smooth muscle cells are present in capillaries, because of these enlarged pores, the affected capillary wall is leakier. **As a result, normally retained plasma proteins** escape into the surrounding tissue exerting **osmotic** effect. Resulting in local fluid retention which contributes to **inflammatory swelling. See the figure in the previous page.**

Recall that flow is the product of the driving force (∆P) and the permeability (K);

Flow = cardiac output = Q =∆P * k

And K = 1/ R

So Q= ∆P/R , note that we have restated Ohm's law (I=V/R) ✓

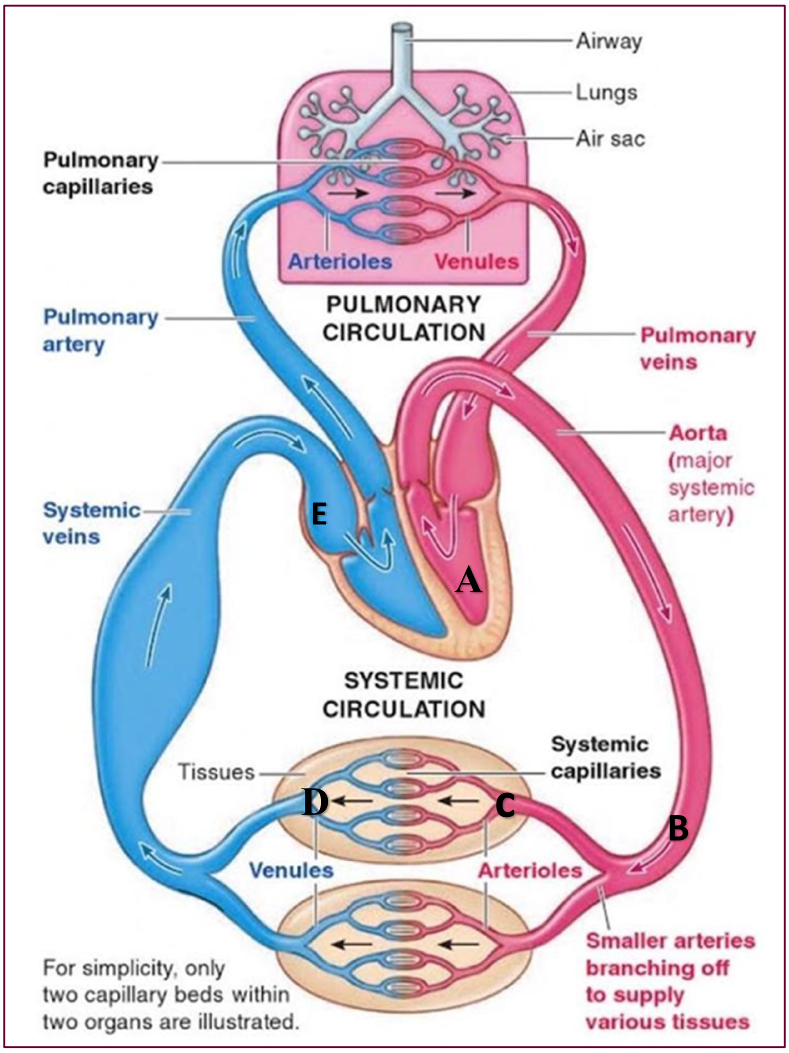
It is hard to measure the resistance of blood vessels directly. But we know that the **flow** in all of the vessels is equal to the cardiac output (1 unit).

Looking at the circulatory system as a whole , flow through all vessels is equal to the cardiac output. 5L/min which will be considered as a single unit (1 unit= cardiac output).

Pressure gradient can be easily measured between any two different points. So, from the previous equation we know that the **pressure gradient must equal the resistance in order to permit the flow of the same cardiac output as a single unit**, so we can measure the resistance **indirectly.**

- ✓ Pressure at point A (left ventricle) = 100 mmHg
- ✓ Pressure at point B (end of the artery)= 85 mmHg
  - Δ P (A to B) = 100-85 = 15mm Hg
  - Q= 5L=1 unit
  - 15/R=1
    R= 15
- ✓ Pressure at point C= 40mmHg
- ✓ Δ P (B to C) = 85-40 =45mmHg
  - R=45 (arterioles are the **major resistance** vessels in the vascular tree).
- ✓ Pressure at point D=20mmHg
- ✓ ΔP (C to D) = 40-20 =20mmHg
  - R= 20
- ✓ Pressure at point E (right atrium)=0mmHg
- ✓ ΔP (D to E) = 20-0=20mmHg
  - R=20

- ✓ ΔP equals the difference in pressure between the beginning and end of the systemic circulatory system. The beginning pressure is the mean arterial pressure as the blood leaves the left ventricle at an average of 93-100 mmHg. The end pressure in the right atrium is 0 mmHg. Therefore ΔP= 100-0=100 mmHg, which is equivalent to the mean arterial pressure.



Accordingly, R = 100 in the whole circulatory system.

Exchanges across the capillary wall between plasma and interstitial fluid are largely passive. Capillary walls are highly permeable, so the interstitial fluid takes on essentially the same composition as incoming arterial blood, with the exception of the large plasma proteins that usually do not escape from the blood.

Bulk flow across the capillary wall:

A volume of protein-free plasma actually filters out of the capillary, mixes with the surrounding interstitial fluid, and then reabsorbed. This process is called Bulk flow.

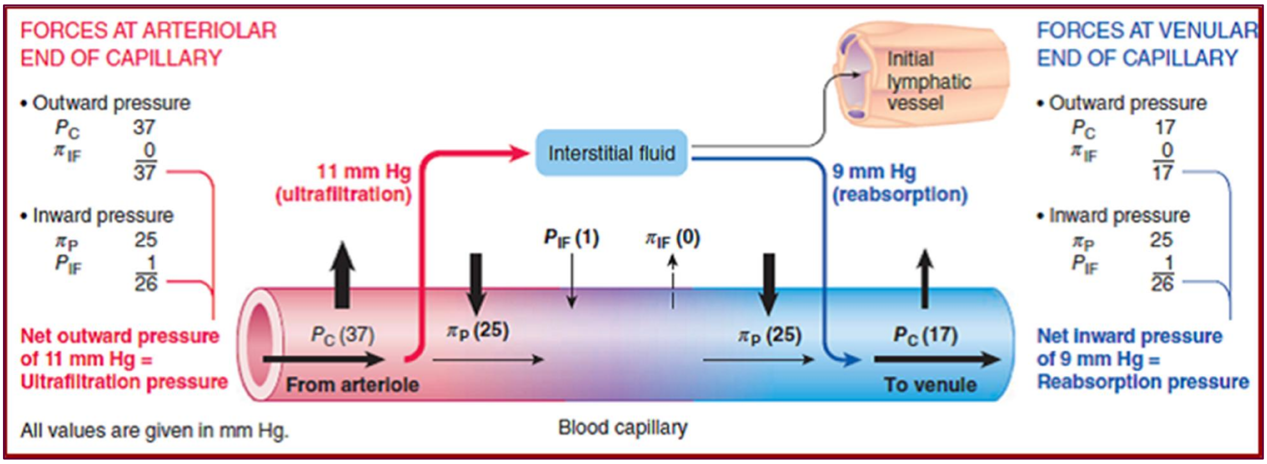
- ✓ When pressure inside the capillary exceeds pressure on the outside, fluid is pushed out through the pores in a process known as ***Filtration.***
- ✓ When inward-driving pressures exceed outward pressure across the capillary wall, net inward movement of fluid from the interstitial fluid into the capillaries takes place through the pores, a process known as ***Reabsorption***.

- ✓ **Forces influencing bulk flow :**
  Bulk flow occurs because of differences in the hydrostatic and colloid osmotic pressures between plasma and interstitial fluid.
- ✓ **1.Capillary blood pressure (Pc)** is the fluid or hydrostatic pressure exerted on the inside of the capillary walls by blood. This pressure tends to force fluid out of the capillaries into the interstitial fluid. By the level of capillaries blood pressure is dropped .On average, the hydrostatic pressure is 37 mmHg at the arteriolar end ,it declines to 17 mmHg at the venular end .
- ✓ **2.Plasma-colloid osmotic pressure (∏p)** also known as oncotic pressure, a force caused by colloidal dispersion of plasma proteins. It encourages fluid movement into the capillaries.
  - **Plasma osmotic pressure averages 25-28mmHg**

- ✓ **3.Interstitial fluid hydrostatic pressure (Pif)** the fluid pressure exerted on the outside of the capillary wall by interstitial fluid ,this pressure tends to force fluid into the capillaries (if +ve).The actual value of the pressure is a controversial issue , it is either at slightly above or slightly below atmospheric pressure . We will assume it is 1 mmHg .above atmospheric pressure .
- ✓ **4.Interstitial fluid colloid osmotic pressure (∏if)** The small fraction of plasma proteins that leak into the interstitial space are normally returned to the blood by lymphatic system .Therefore the Interstitial colloid osmotic pressure is very close to zero .If plasma proteins pathologically leak into the interstitial fluid, as they do when histamine widens the capillary pores during tissue injury, the leaked proteins exert osmotic effect the tends to move fluids out of the capillaries.
- ✓ **Two pressures tend to force fluid out of the capillary :**
  - Capillary blood pressure (Pc).
  - Interstitial fluid colloid osmotic pressure (∏if).
- ✓ **The two opposing pressures that tend to force fluid into the capillary :**
  - Plasma-colloid osmotic pressure (∏p).
  - Interstitial fluid hydrostatic pressure (Pif).
- ✓ **Net exchange pressure** =(Pc+∏if)-(∏p+ Pif) = Outward-inward

- *At the arteriolar end of the capillary ,the outward pressure totals 37mmHg (37+0) , whereas the inwards pressure totals 26 mmHg (25+1), A net outward pressure of 11 mmHg .Filtration takes place at the beginning of the capillary as this outward pressure gradient forces a protein-free filtrate through the pores*

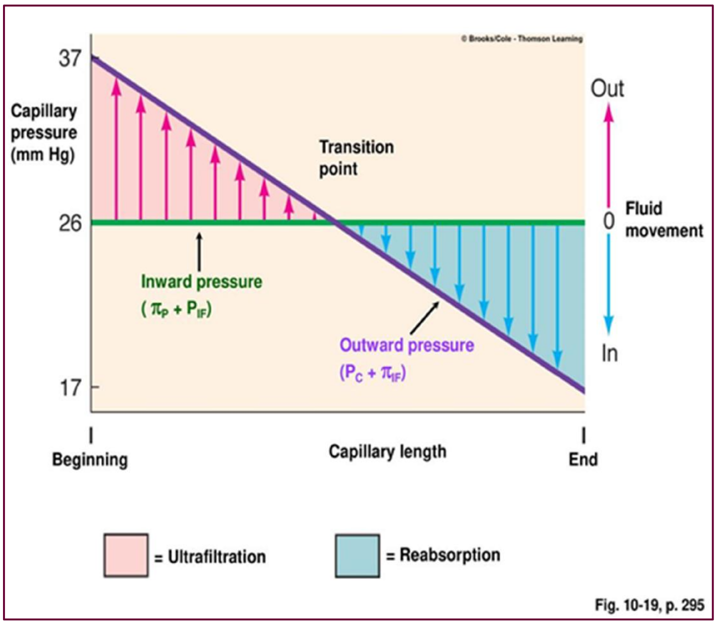
- *By the time the venular end is reached ,the capillary blood pressure has dropped, but the other pressures have remained essentially constant. The outward pressure has fallen to 17mmHg ,whereas the total inward pressure is still 26 mmHg ,for a net inward pressure of 9 mmHg .Reabsorption of fluid takes place as this inward pressure gradient forces fluid back into the capillary at its venular end .* ***Note: You can notice that the previously mentioned numbers are not for memorizing ,and they may also differ from the ones mentioned by Dr.Yanal during lectures, I only mentioned them to clarify how these forces influence fluid movement .***



To sum up, filtration occurs at the beginning of the capillary because capillary blood pressure exceeds plasma-colloid osmotic pressure ,whereas by the end of the capillary ,reabsorption takes place because blood pressure has fallen below osmotic pressure.

NOTE: it is important to realize that we have taken "snapshots" at two points-at the beginning and at the end- in a hypothetical capillary. Actually, blood pressure gradually *diminishes* along the length of the capillary.

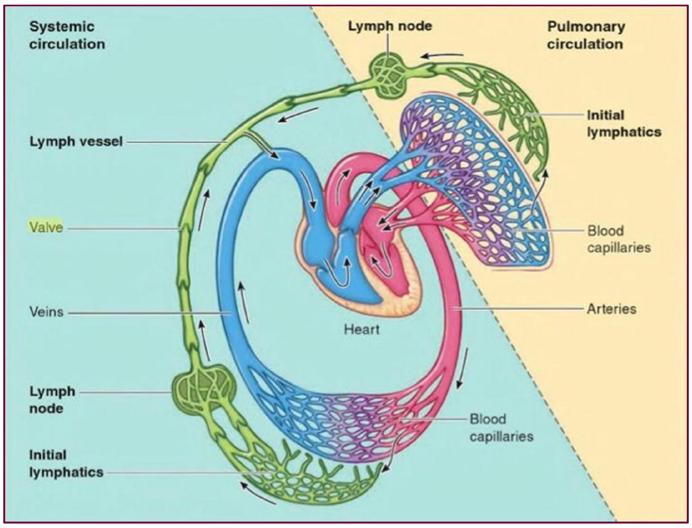
The figure shows that the inward pressure (∏p+ Pif) **remains constant** (26mmHg) throughout the length of the capillary, whereas the outward pressure (Pc+∏if) progressively **declines** throughout the capillary's length.



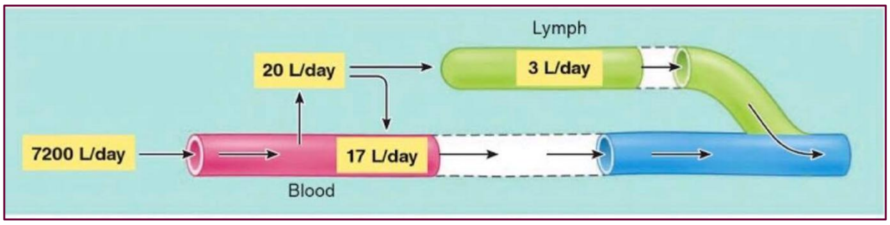
In the first half of the vessel where the **declining outward pressure still exceeds the constant inward pressure**, fluid is filtered out (upward red arrows).
In the last half of the vessel, fluid is reabsorbed (downward blue arrows) as the **declining outward pressure falls further below the constant inward pressure**.

Lymphatic system

Normally, capillary filtration exceeds reabsorption by about **3** liters per day (20 liters filtered, 17 liters reabsorbed. Even though only a small fraction of the filtred fluid is not reabsorbed by the blood capillaries, the cumulative effect of this process being repeated with every heartbeat results in the equivalent of more than the entire being left behind plasma volume



the interstitial fluid each **day.**



Obviously, this fluid must be returned to the circulating plasma, and this task is accomplished by the lymph vessels.

Lymph vessels can carry **<u>proteins</u> and <u>large</u>** particulate matter away from tissue spaces, neither of which can be removed by absorption directly into the blood capillaries. This return of proteins to the blood from the interstitial spaces is essential function without it we would die within about 24 hours. ☹

Test your understanding

1) When considering the forces that govern fluid movement across the capillary wall, which of the following is/are correct?

A) A positive net filtration pressure refers to a condition that favors the movement of fluid out of the capillary lumen and into the surrounding interstitial fluid.

B) A negative net filtration pressure refers to a condition that favors the movement of fluid out of the capillary lumen and into the surrounding interstitial fluid.

C) A positive net filtration pressure refers to a condition that favors the movement of surrounding interstitial fluid into the capillary lumen.

D) A negative net filtration pressure refers to a condition that favors the movement of surrounding interstitial fluid into the capillary lumen.

2) In a typical capillary, the net filtration pressure is positive throughout the entire length of the capillary.

A) True.

B) False.

3) In the kidney glomerular capillaries, the net filtration pressure is positive throughout the entire length of the glomerular capillary.

A) True.

B) False.

4) In an average adult male (60 kg in weight), approximately what is the volume of his blood?

A) 4

B) 6

C) 3

5) Plasma comprises approximately ________% of total blood volume.

A) 55%

B) 20%

C) 60%

6) This physical barrier separates the interstitial fluid compartment from the intravascular fluid compartment.

A) Arteriolar wall.

B) Dense connective tissue.

C) Plasma membrane.

D) Capillary endothelium.

7) Hydrostatic blood pressure is lowest in the:

A) Arteries.

B) Arterioles.

C) Veins.

D) Capillaries.

8) Hydrostatic blood pressure is highest in the:

A) Arteries.

B) Arterioles.

C) Veins.

D) Capillaries.

Answers:

1	2	3	4	5	6	7	8
A and D	B	A	A	A	D	C	A