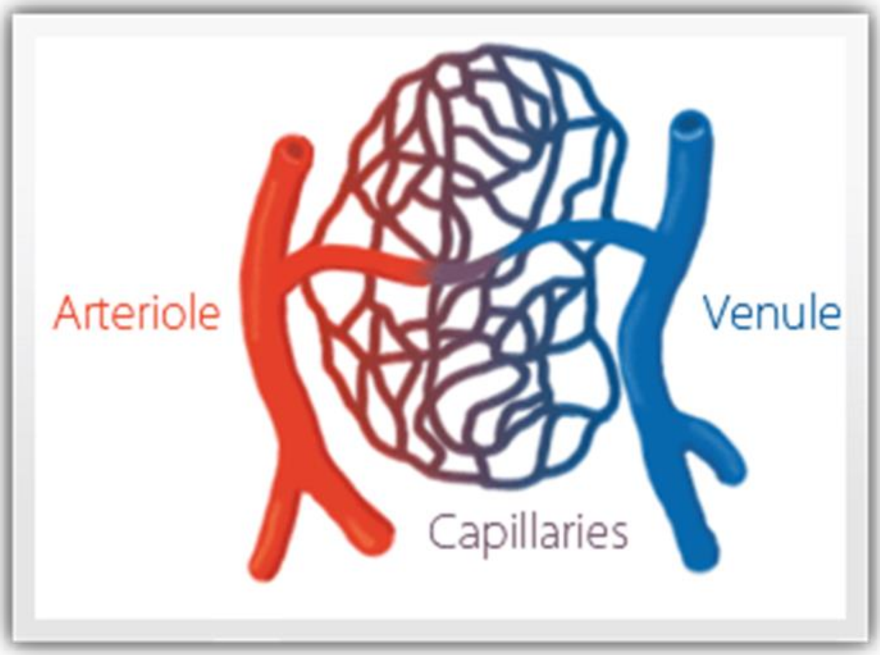
Introduction to Physiology

Final Exam Material

Dr. Yanal Shafagoj

Lecture 3

“Microcirculation and Edema”



Comprehensive File

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The lecture should start with the experiment of culturing 5 lymphoma cells in a beaker with proper medium. After 3 days the cells will die because of accumulation of waste products and lack of nutrients. The cells of our body have ICF (intracellular fluid) and are bathed in ISF (interstitial fluid). The bathing medium is not enough to keep cell survival for appreciable time. Thus, ISF (ECF) is not a good reservoir and will not maintain homeostasis. We need to refresh ISF with new nutrients and continuously remove the waste products exactly as we do in cell culture. This can be achieved by plasma, and thus it is important to understand how plasma flow to the tissue is regulated.

Cells are surrounded by Interstitial fluid (ISF) and separated by 20 – 30 micrometers (no direct contact) from the surrounding capillaries (small blood vessels surrounding cells) where filtration and reabsorption occurs.

Filtration is the flow of fluids from the capillaries to the ISF.

Reabsorption is the flow of fluids from the ISF to the capillaries.

Both contribute to the refreshment of the ISF.

Suppose a human whose total body mass is 70 kg.

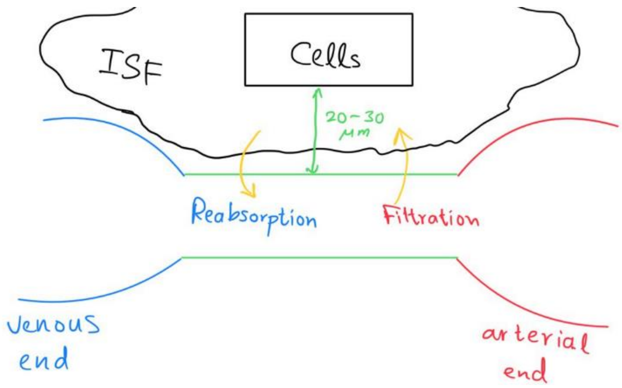
Fluids in the body (≈ 60% of total body mass = 42 L) are divided into:

1. Extracellular fluids (one third of 42 L → 14 L)
2. Intracellular fluids (two thirds of 42 L → 28 L)

Extracellular fluids contain ISF which surrounds the cells is divided into:

(1) ISF volume → 11 L; (2) Intravascular fluids → 3 L (plasma).

Each capillary has two ends – an arterial end and a venous end.



The ISF is the medium where cells live, and it must be refreshed continuously, and this is why we have the blood cycle.

The cycle starts at the heart (LV) → aorta (major artery) → other arteries (and arterioles) → capillaries → veins → back to the heart (RA). This is the systemic circulation.

The average cardiac output of blood is 5 liters per min divided into:

1. Kidneys (≈1L, actually, it is 1250 ml/min)
2. The rest (4 L) are divided as follows:
   a. Plasma (2L) which will refresh the ISF surrounding the cells.
   b. Cells and other formed elements (2L).

The cardiac plasma output from the heart per day:

$$2\frac{L}{min} * 60\frac{min}{hour} * 24\frac{hour}{day} = 2880 \approx 3000\frac{\mathrm{L}}{day}.$$

The ISF is renewed 3000/11 ≈ 300 times each day (artificial cells cultures have their surrounding media renewed one time every 72 hours); therefore, in our body 300 times/d is a huge number.

This is necessary to maintain homeostasis at the medium surrounding the cells (ISF).

Capillaries are divided functionally into 3 types:

1. Only filtration: glomerular capillaries in kidneys
2. Only reabsorption: GIT capillaries
3. Ideal capillaries (such as in skeletal muscles) which show filtration at the arterial end and reabsorption at the venous end.

Typically, 20 L/day are filtered at the arterial end of the capillary, and only 17 L/day are reabsorbed at the venous end.

The ISF volume is increased by 3 L/day (20 – 17 = 3) and this leads to an increment in the ISF volume.

How can the body get this excess volume out of the ISF?

Excess fluids are returned to the bloodstream by lymphatics which act as a vacuum cleaner (scavengers of our body).

1. Remove excess fluids.
2. Remove cells debris which attracts bacteria and causes infection. (two different terms)
3. Remove large macromolecules (such as proteins) which can't pass through the walls of the capillaries.

Lymphatics return all the above to the bloodstream via systemic veins such as right and left subclavian veins.

If filtration increases by a small amount (say 20 → 25), lymphatics can deal with this change by increasing lymphatic activity (3 → 8). . During exercise lymph flow increases 20-30 times.

However, if filtration increases by a huge amount (say 20 → 30), not all excess fluids (13 L in this case) can be returned by lymphatics.

This leads to accumulation of fluids in the interstitial space which is called edema.

Edema can be localized in a specific place or generalized throughout the whole body.

Edema can be life threatening (mainly the 4 types below):

1. Pulmonary edema:

For the lung to operate efficiently, it must be in dry conditions.

Pulmonary edema will cause excess fluids in the interstitial space of the lungs, and excess fluids will interfere with gas exchange (O_2, CO_2).

Pulmonary edema is considered a top medical emergency as the patient may die within 1 or 2 hours.

2. Brain edema:

Because the brain is surrounded by the skull (cranium), it can't expand if excess fluids accumulate. This will compress the neurons destroying them and causing death since neurons are irreplaceable.

3. Laryngeal edema (especially in children as they have a soft larynx):

It causes the closure of the airway causing death by suffocation.

4. Cardiac edema:

Pericardial effusion (or excess fluids in the pericardial cavity) causes compression on the heart causing difficulty in expansion preventing enough refilling of the heart chambers with blood.

We need to insert a needle in the pericardial cavity to drain excess fluids.

Other non-life-threatening types of edema includes:

1. Upper or lower limb edema
2. Face edema
3. Abdominal edema (ascites) which can occur due to liver cirrhosis causing accumulation of fluids (10 – 15 L) in the abdominal cavity.

The flow of blood is the volume of blood moving per unit time.

$$Flow = \frac{volume}{time} = DF\ (Driving\ Force)\ *\ K\ (Permeability)$$

The driving force in this case is the pressure difference (ΔP):

ΔP can have 4 forms called the 4 starling forces which are responsible for the movement of fluids from the capillary to the ISF or vice-versa.

2 of the forces are inside and 2 are outside the capillaries.

Some Starling forces favor filtration while others favor reabsorption.

The 4 forces will be discussed in this lecture and the one after.

Edema happens due to excess flow of fluids out of the capillaries.

It may be due to increased DF (such as the increase of the capillary pressure) or increased K (such as the effect of histamine after a bee sting for example). We use antihistamines to reduce inflammation.

Pressure is measured in mmHg, and we report pressure values with respect to a reference point of 760 mmHg which is the atmospheric pressure at sea level. If we have a pressure of 860 mmHg, we say it is 100 mmHg.

Let's discuss the first starling force – the capillary pressure (P_c).

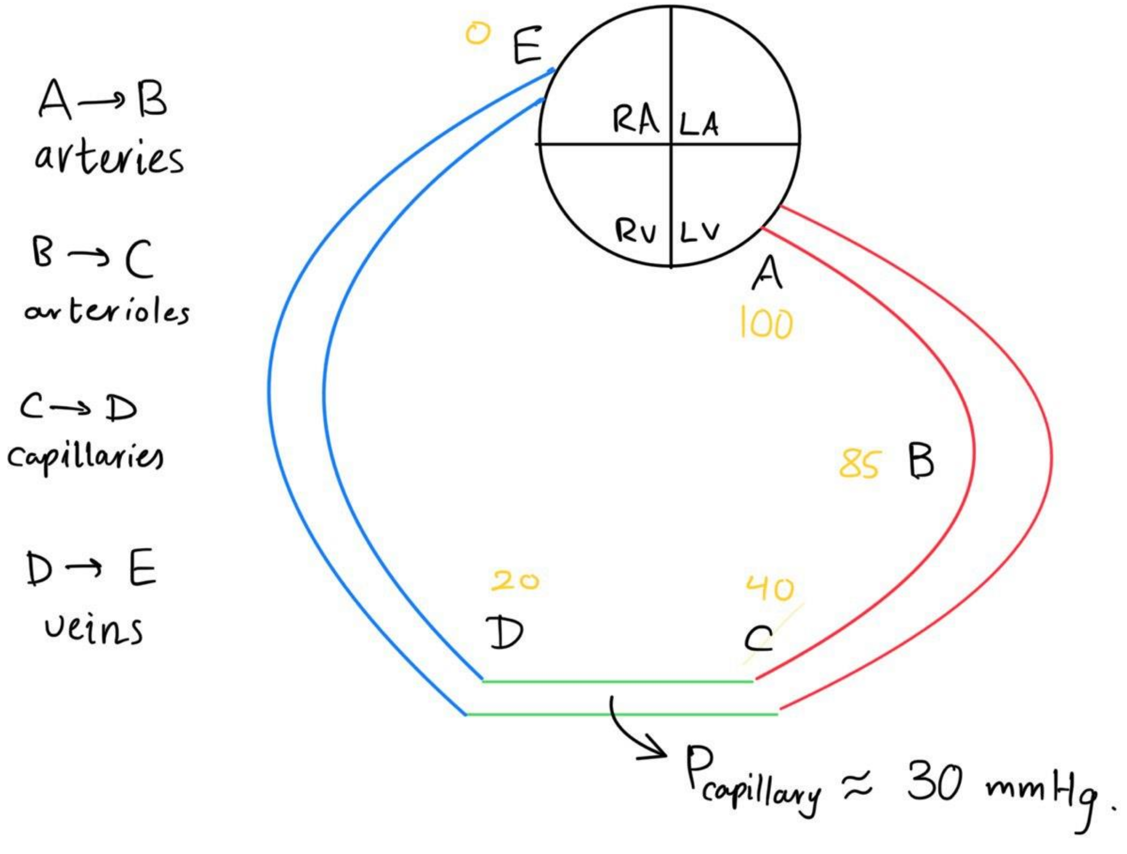
P_c: Hydrostatic pressure of the blood flowing inside capillaries, and this force favors filtration (force and pressure are used interchangeably).

The more P_c, the more filtration will occur and that is why we have different values for P_c depending on the location of the capillary in the body:

1. In Lungs (low filtration): 7 mmHg
2. In Skeletal muscles: 30 mmHg
3. In kidneys, glomerular capillaries (high filtration): 60 mmHg

Systemic cycle: pumping oxygenated blood from the heart to capillaries.

Pressure Map of the Systemic Cycle



The average capillary pressure (between C and D) is 30 mmHg.

Let's discuss blood volume distribution throughout the body.

$$Total\ Blood\ Volume\ (in\ L) \approx 7\% * Total\ Mass\ (in\ kg)$$

Let's assume someone whose mass is 70 kg → Total Blood Volume ≈ 5 L.

Because the blood density is 1.060 kg/L, the volume occupied by 1 kg of blood is approximately 1 liter, and this is why we obtain values for blood volume in liters from the equation above.

We have two cycles in which blood flows – systemic and pulmonary cycles.

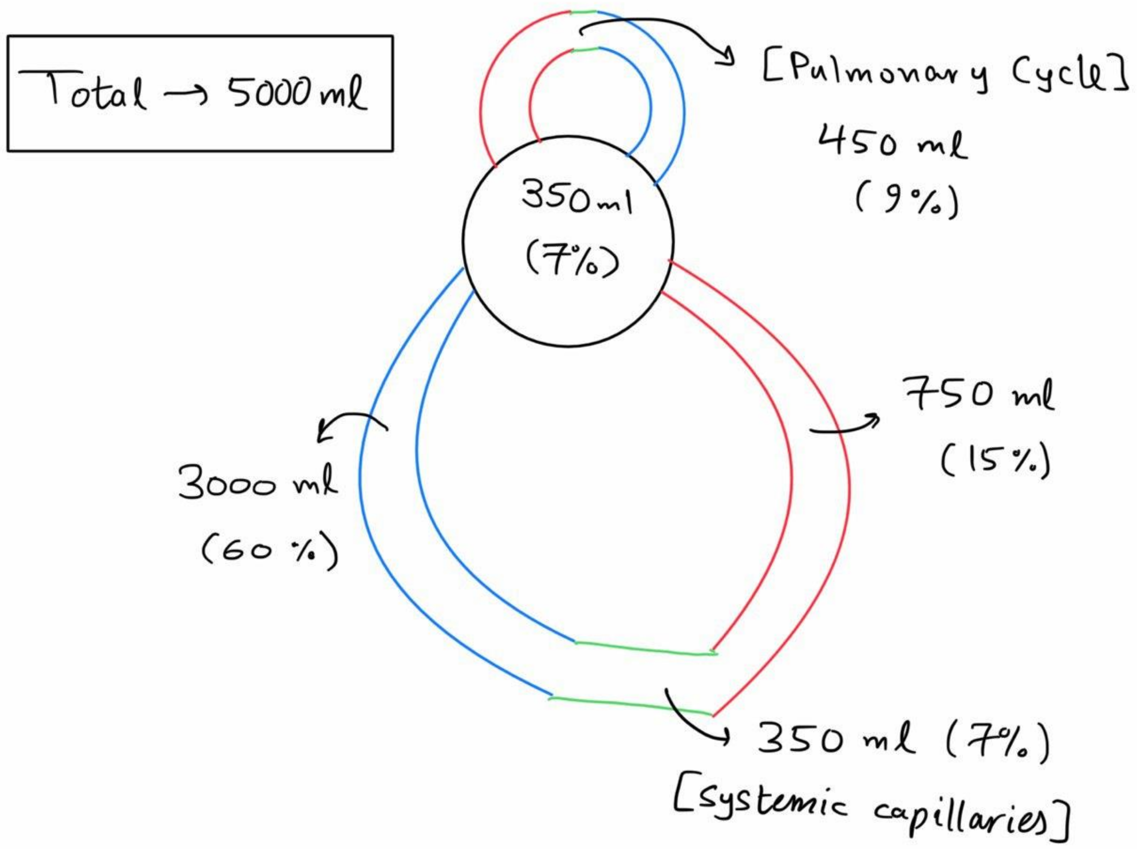
A) Systemic cycle:

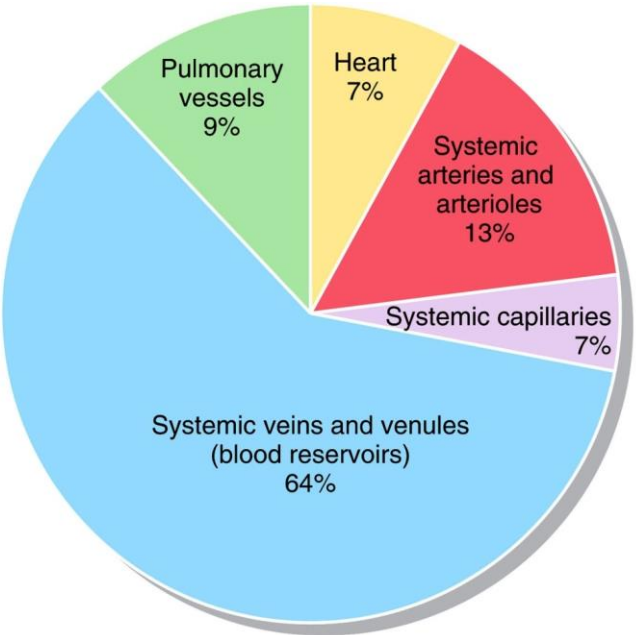
   Starts from the left ventricle → arteries → systemic capillaries → veins → right atrium.

B) Pulmonary cycle:

   Starts from right ventricle → lungs → left atrium.

Distribution of Blood Volume in the Blood Cycles





Systemic veins are considered blood reservoirs as they contain most of the blood (≈ 60%).

Our focus will be on systemic capillaries (7% of blood) because this is where exchange with cells occurs.

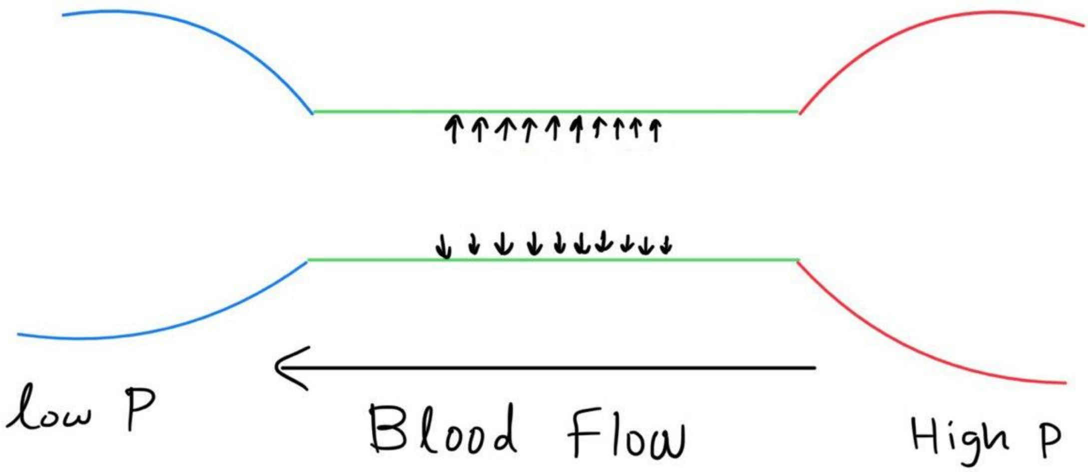
Other parts (93% of blood) serve these capillaries:

1. Arteries: supply blood from the heart
2. Veins: return blood to the heart
3. Heart: pumps blood
4. Lungs: where gas exchange occurs

Net flow of fluids is determined by the summation of the 4 starling forces.

If filtration is increased → more ISF volume → edema.

If filtration is decreased → less ISF volume → dehydration.



$$P = \frac{F}{A}$$

Since the capillaries are lined only by a single layer of epithelial cells and they don't contain smooth muscles (no dilation or constriction). The cross-sectional area (A) won't change and thus the force (F) is the only determining factor of the pressure.

The force (capillary hydrostatic pressure (P_c)) is due to the presence of a volume of blood pushing against the walls of the capillaries.

A change in the volume will lead to a change of pressure, for example:

We can increase the pressure by arteriodilation which will increase the volume of blood entering the capillary.

We can also increase the pressure by venoconstriction which will allow less blood to exit, increasing the volume of blood inside the capillary.

In general, if we need more blood in a certain location, arteries leading there will dilate (decreasing resistance) causing more blood to flow into that location.

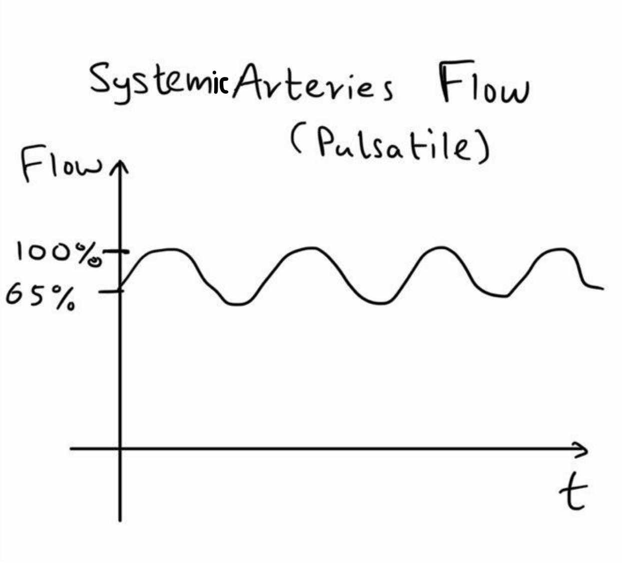
Conversely, if we don't need much blood in a certain location, arteries leading there will constrict (increasing resistance) causing blood to flow to other parts if the body.

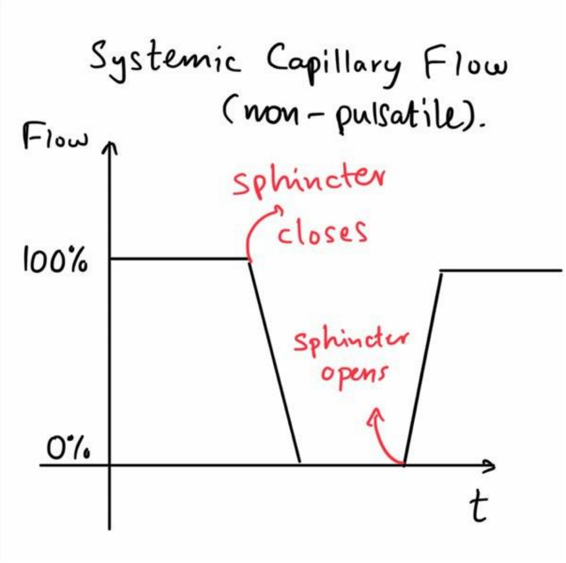
On the arterial end of a capillary, there is a sphincter (smooth muscle ring that opens and closes). Sphincter contraction will close the capillary.

Since the capillary has a sphincter, its flow is not pulsatile but intermittent, meaning that it is independent of the cardiac cycle (0.3 systole + 0.5 diastole).

If the capillary blood flow was pulsatile, capillaries will receive blood mainly during the systolic phase of the cycle.

Instead, the blood flow in the capillaries depend on the activity of the sphincter which is present on the arterial end of the capillary.





As mentioned before P_c can be increased by either arteriodilation or venoconstriction.

The following equation summarizes the effects of changing the pressure on one side of the capillary (arterial or venous) on P_c:

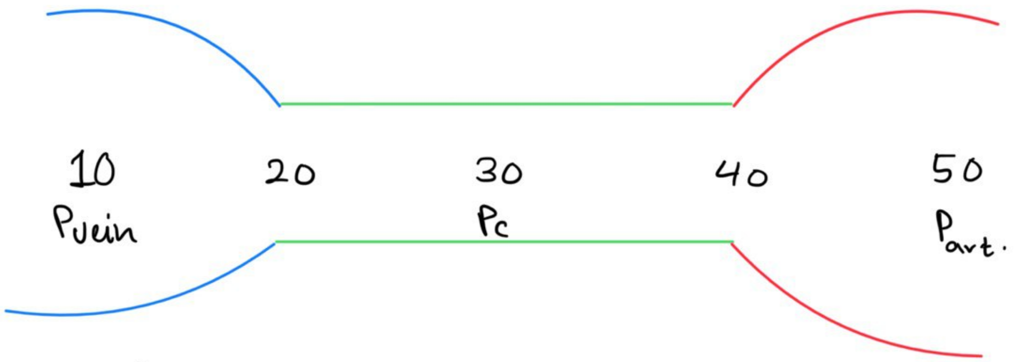
$$P_c = \frac{\frac{R_v}{R_a} * P_a + P_v}{\frac{R_v}{R_a} + 1} ; \textit{the ratio } \boldsymbol{\frac{R_v}{R_a}} \textbf{ \textit{is typically equal to} } \boldsymbol{\frac{1}{5}}$$

"R" is for resistance, "P" for pressure, "v" for veins, and "a" for arteries.

We only need to memorize the final form of the equation below.

The equation becomes: $P_c = \frac{1}{6}P_a + \frac{5}{6}P_v$

As we see, the effect of increasing P_v is stronger than the effect of increasing P_a.



if $P_{art.}$ $(50 \rightarrow 70$, change $= 20)$,

$\Rightarrow P_c = 30 + \frac{1}{6}(20) \approx 33$ mmHg (+3)

if P_{vein} $(10 \rightarrow 30$, change $= 20)$,

$\Rightarrow P_c = 30 + \frac{5}{6}(20) \approx 47$ mmHg (+17)

The blood, to maintain normal flow, the arterial end of the capillary must have a higher pressure than the venous end.

If, for example, $P_a = P_v$, there will be no pressure difference across the capillary → no blood flow → cardiac arrest → death.

In the case of right ventricular failure, blood accumulates in the right atrium causing increased pressure in the systemic veins leading to increased P_c (30 → 40) and increased filtration → edema.

Because the failure is in the heart, the edema is generalized.

An example of localized edema is when the pregnant uterus presses on pelvic veins decreasing its radius.

$$R \propto \frac{1}{r^4}, (Poiseuille's\ equation\ from\ physics\ 105)$$

Decreased radius (r) → very high resistance (R).

$$Flow = \frac{DF}{R}, (Ohm's\ law)$$

High resistance → we need more pressure (DF) to maintain enough flow.

More pressure in veins → very high P_c → more filtration → edema.

The edema in this case is localized in the region below the pelvic veins.