Microcirculation and Edema

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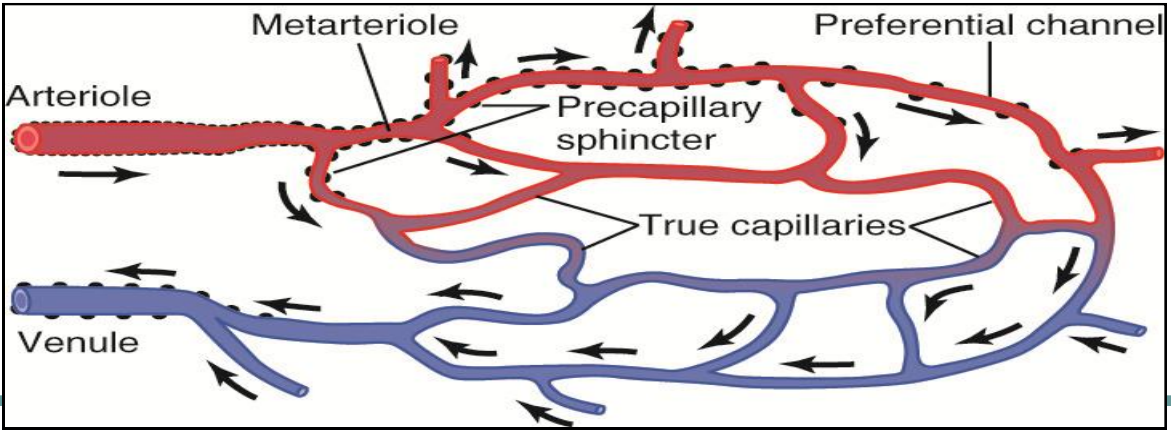
Objectives:

- Point out the structure and function of the microcirculation.
- Describe how solutes and fluids are exchang in capillaries.
- Outline what determines net fluid movement across capillaries.

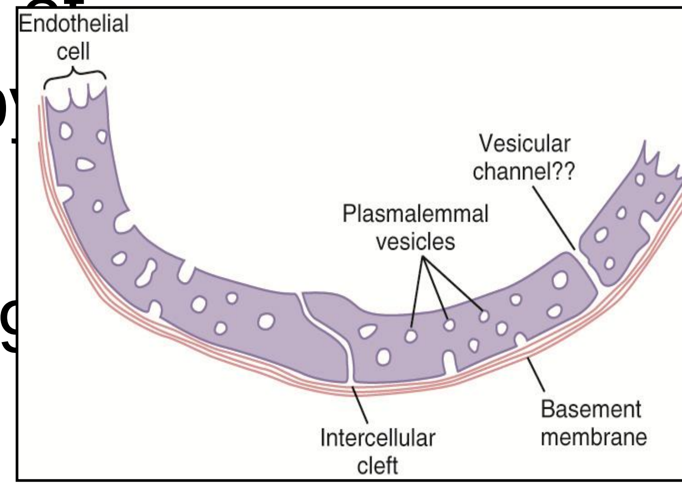
The Microcirculation

- Important in the transport of nutrients to tissues.
- Site of waste product removal.
- Over 10 billion capillaries with surface area of 500-700 square meters perform function of solute and fluid exchange.



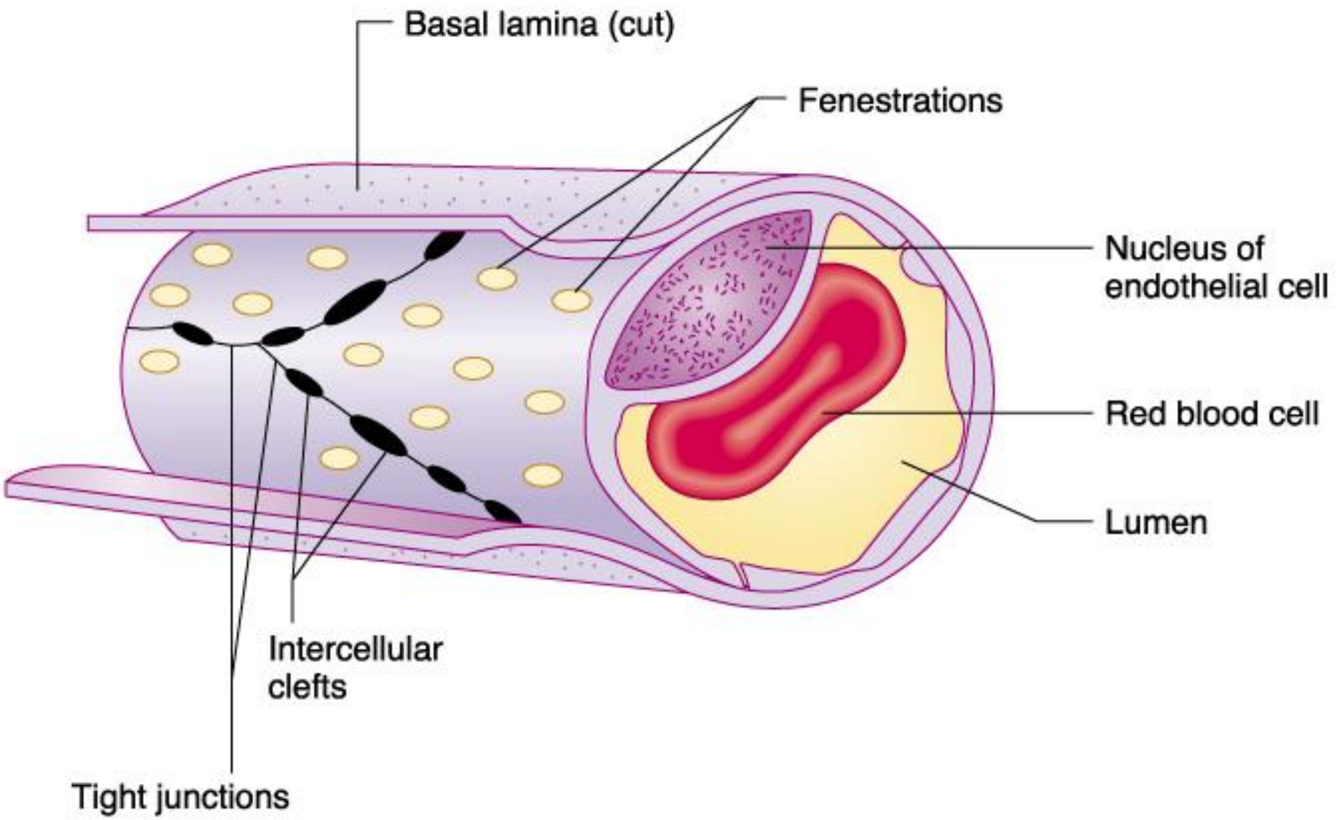
Structure of Capillary Wall

- Composed of unicellular layer of endothelial cells surrounded by basement membrane.

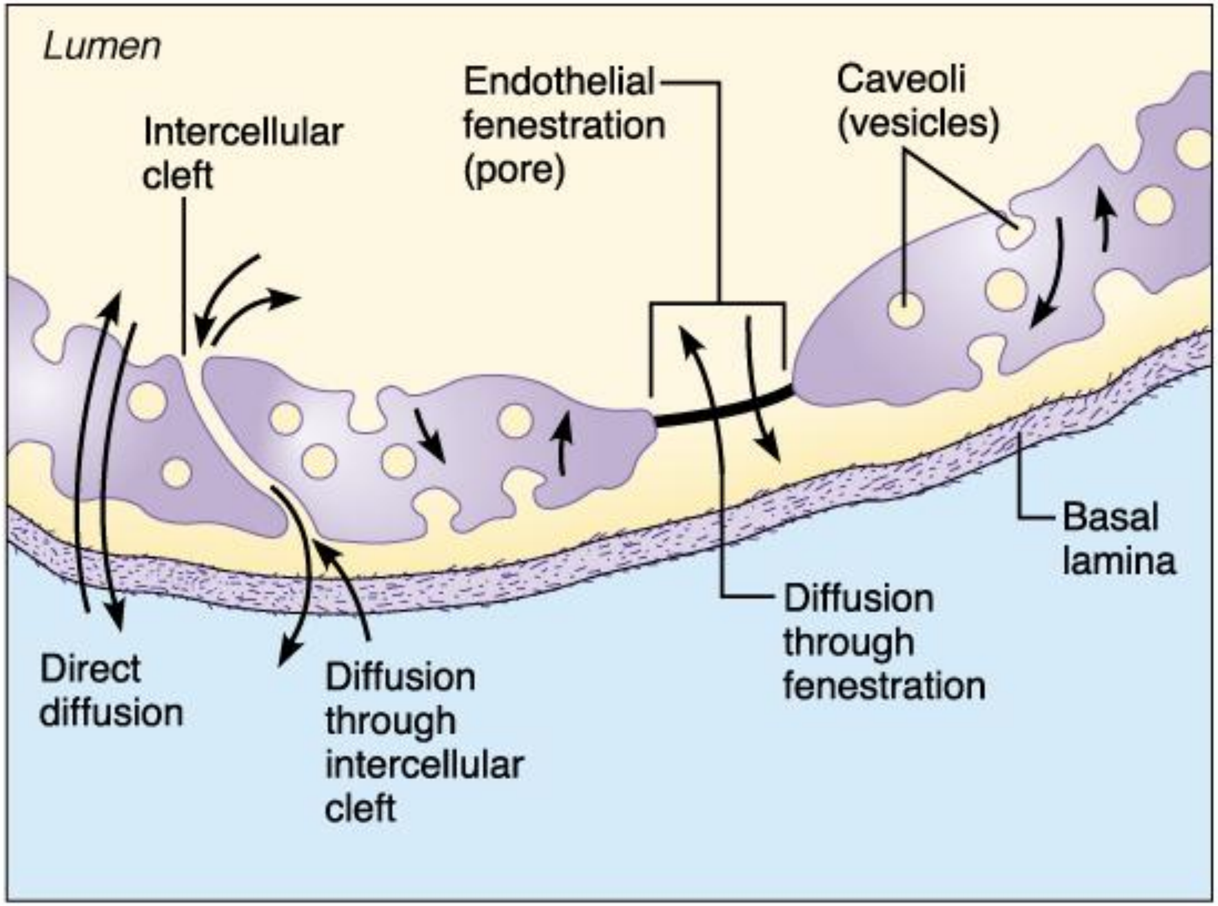


- Diameter of capillaries is 4 to 9 microns.
- Solute and water move across capillary wall via *intercellular cleft* (space between cells) or by *plasmalemma vesicles.*

Capillary Exchange of Respiratory Gases and Nutrients



Capillary Exchange of Respiratory Gases and Nutrients



Capillary exchange

- Movement of substances between blood and interstitial fluid
- 3 basic methods

1. **Diffusion**
2. **Transcytosis**
3. **Bulk flow**

Diffusion

- Most important method
- **Substances move down their concentration gradient**
  - **O_2** and nutrients from blood to interstitial fluid to body cells
  - **CO_2** and wastes move from body cells to interstitial fluid to blood

Diffusion …cont

- Can cross capillary wall **through intracellular clefts, fenestrations or through endothelial cells**
  - **Most plasma proteins cannot cross**
  - **Except in sinusoids** – proteins and even blood cells leave
  - **Blood-brain barrier** – tight junctions limit diffusion

Transcytosis

- Small quantity of material
  - Substances in blood plasma become enclosed within **pinocytotic 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
- Based on pressure gradient
- **Diffusion** is more important for solute exchange
- **Bulk flow** more important for regulation of relative volumes of blood and interstitial fluid
- Filtration – from capillaries into interstitial fluid
- Reabsorption – from interstitial fluid into capillaries

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
2. **Interstitial fluid osmotic pressure** (IFOP) 1 mmHg

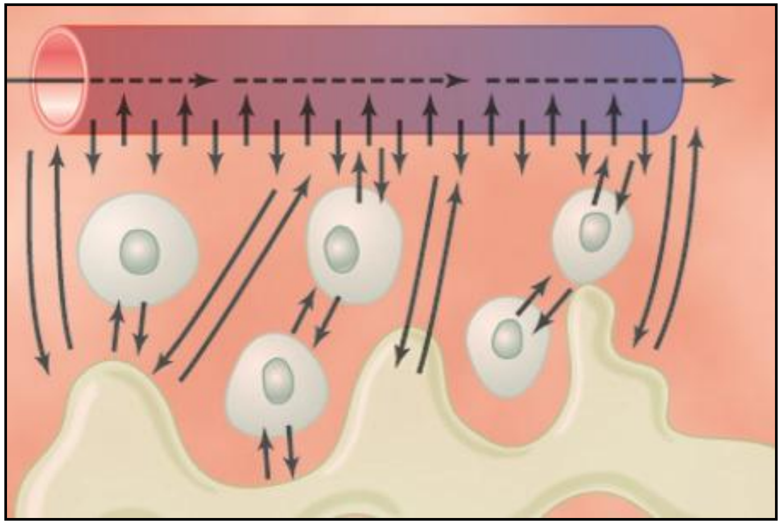
NFP = (BHP + IFOP) – (BCOP + IFHP)

2. Two pressures promote *reabsorption*
   1. **Blood colloid osmotic pressure** (BCOP) promotes reabsorption
      - Averages 36 mmHg
      - Due to presence of blood plasma proteins to large to cross walls
   2. **Interstitial fluid hydrostatic pressure** (IFHP)
      - Close to zero mmHg

Starling's Law

- Nearly as much reabsorbed as filtered
  - 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 reabsorpbed
  - Excess enters lymphatic capillaries (about 3L/day) to be eventually returned to blood

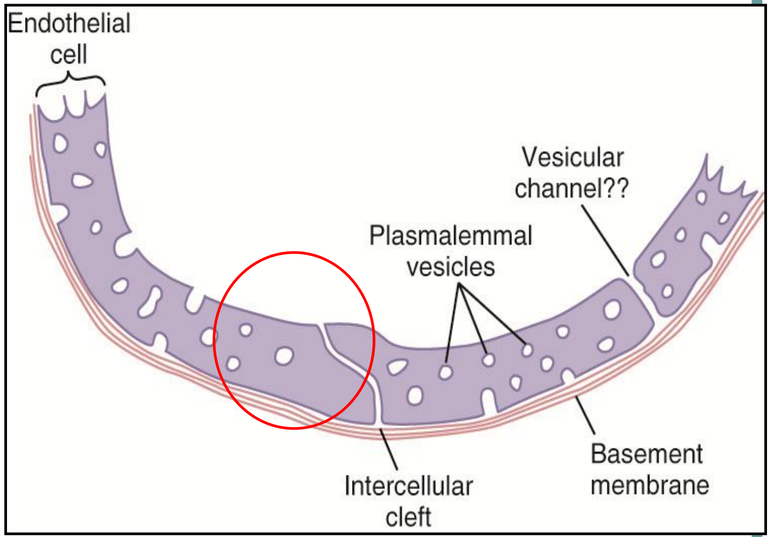
Solute and Fluid Exchange Across Capillaries



- Most important means by which substances are transferred between plasma and interstitial fluid is by *diffusion.*
- *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.
- *Concentration differences* across capillary enhances diffusion.

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 permeabilities.



Relative Permeability of Muscle Capillary Pores to Different-sized Molecules

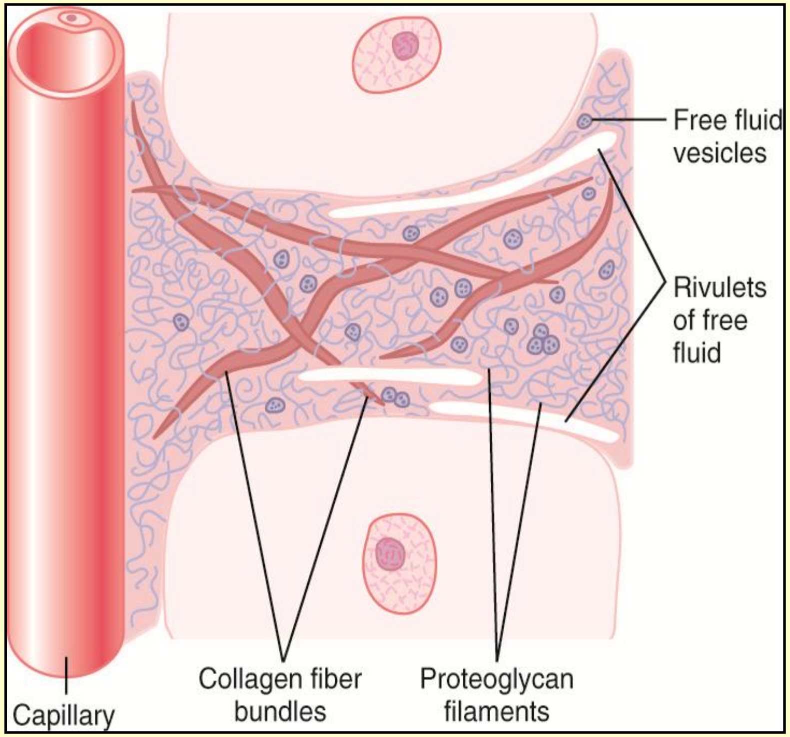
Substance	Molecular Weight	Permeability
Water	18	1.00
NaCl	58.5	0.96
Urea	60	0.8
Glucose	180	0.6
Sucrose	342	0.4
Insulin	5000	0.2
Myoglobin	17,600	0.03
Hemoglobin	69,000	0.01
Albumin	69,000	.0001

Interstitium and Interstitial Fluid

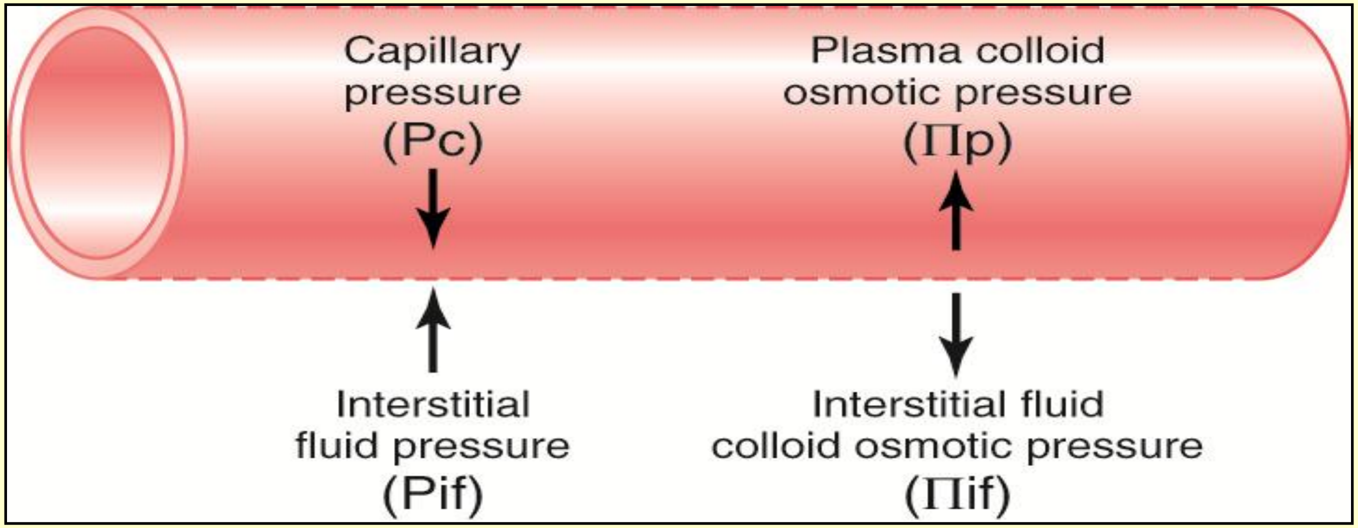
- Space between cells is called *interstitium*; fluid in this space is called *interstitial fluid.*

- 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.

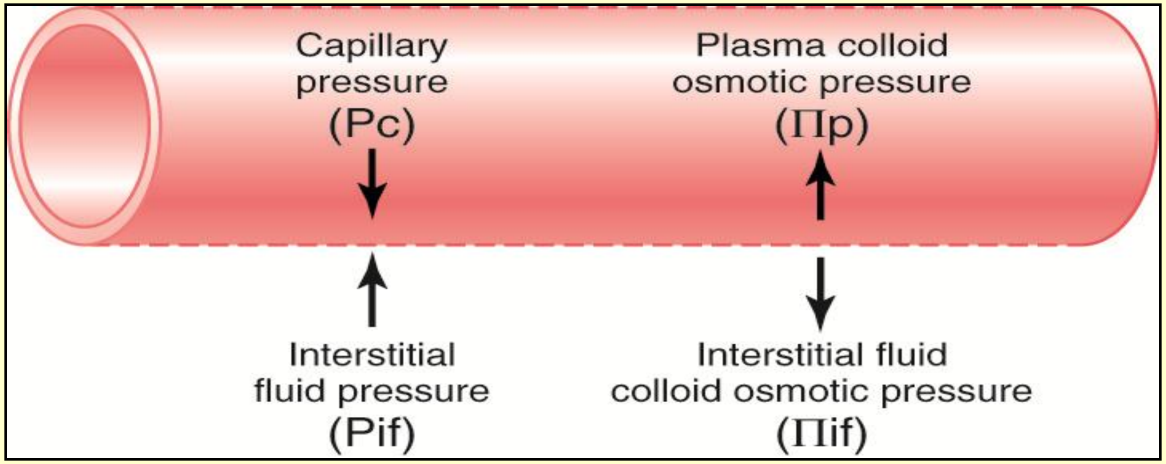


Determinants of Net Fluid Movement across Capillaries



- *Capillary hydrostatic pressure* (P_c)-tends to force fluid outward through the capillary membrane.
- *Interstitial fluid pressure* (P_{if})- opposes filtration when value is positive.

Determinants of Net Fluid Movement across Capillaries

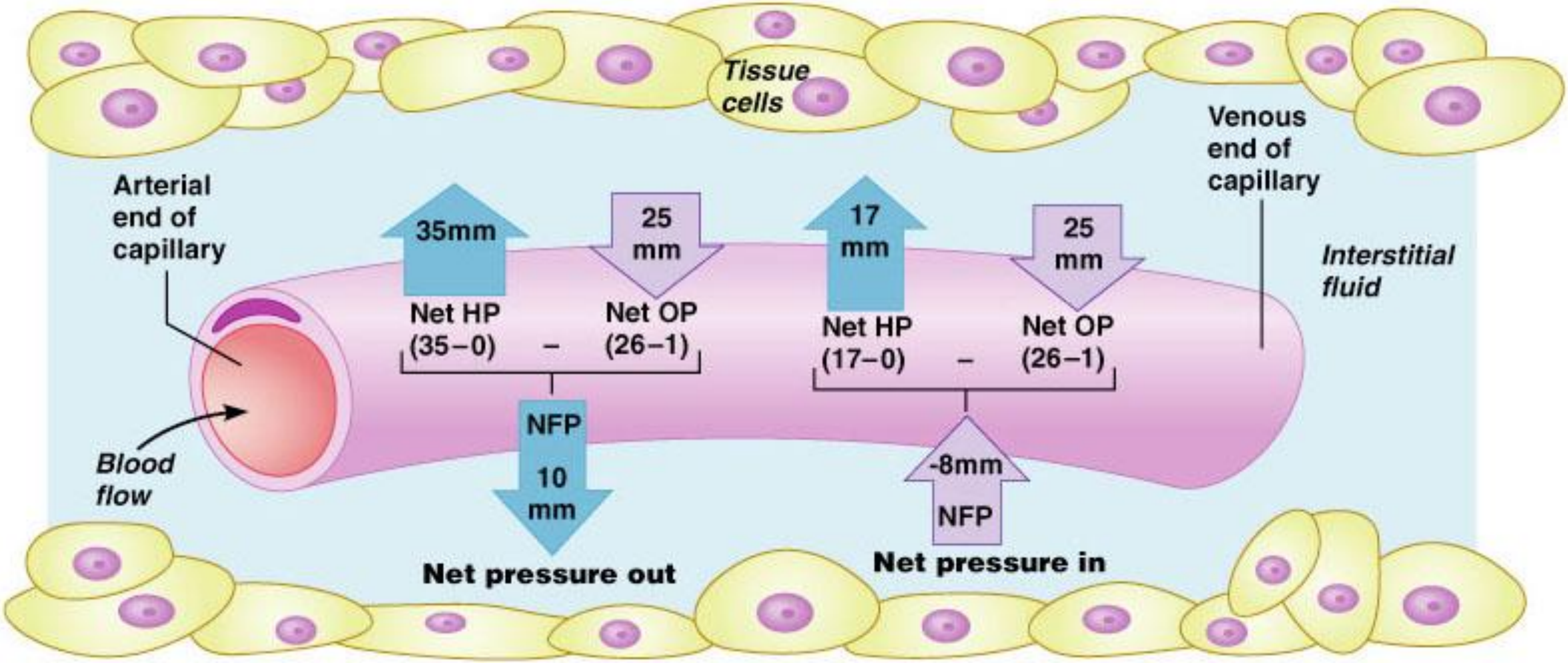


- *Plasma colloid osmotic pressure* ($\boldsymbol{\pi}_c$)- opposes filtration causing osmosis of water inward through the membrane

- *Interstitial fluid colloid pressure* ($\boldsymbol{\pi}_{if}$) promotes filtration by causing osmosis of fluid outward through the membrane

$$NP = P_c - \boldsymbol{\pi}_c - P_{if} + \boldsymbol{\pi}_{if} = (P_c - P_{if}) - (\pi_c - \pi_{if})$$

Net Filtration Pressure (NFP)



Key to pressure values:

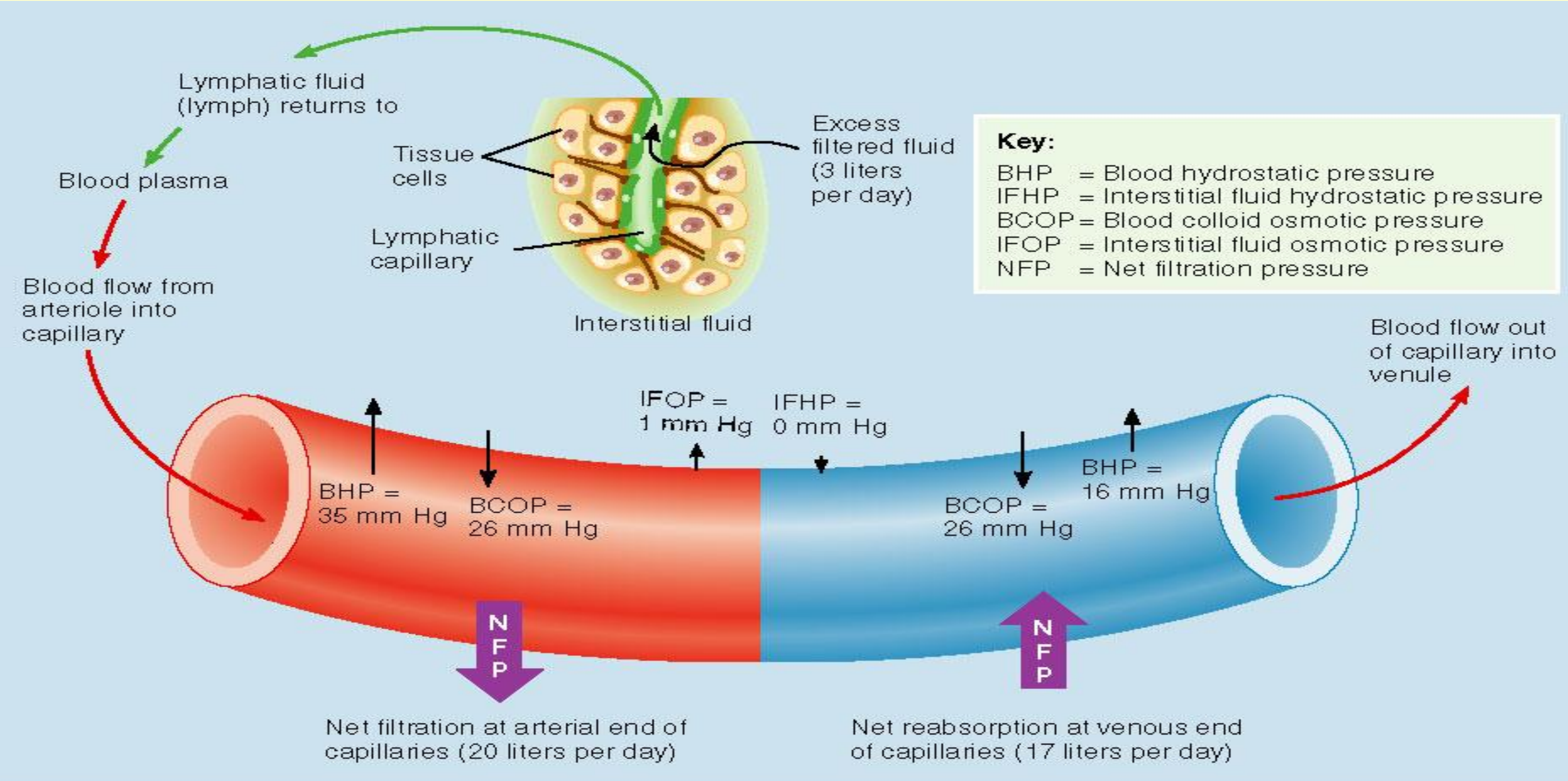
HP_c at arterial end = 35 mm Hg

HP_c at venous end = 17 mm Hg

HP_{if} = 0 mm Hg

OP_c = 26 mm Hg

OP_{if} = 1 mm Hg



Net filtration pressure (NFP) = (BHP + IFOP) – (BCOP + IFHP)

Pressures promoting filtration – Pressures promoting reabsorption

	Arterial end	Venous end
	NFP = (35 + 1) – (26 + 0) = 10 mm Hg	NFP = (16 + 1) – (26 + 0) = – 9 mm Hg
Result	Net filtration	Net reabsorption

21.07

Starling Forces

- 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.*
- *Colloid osmotic pressure* is caused by presence of large proteins.

Plasma Proteins and Colloid Osmotic Pressure

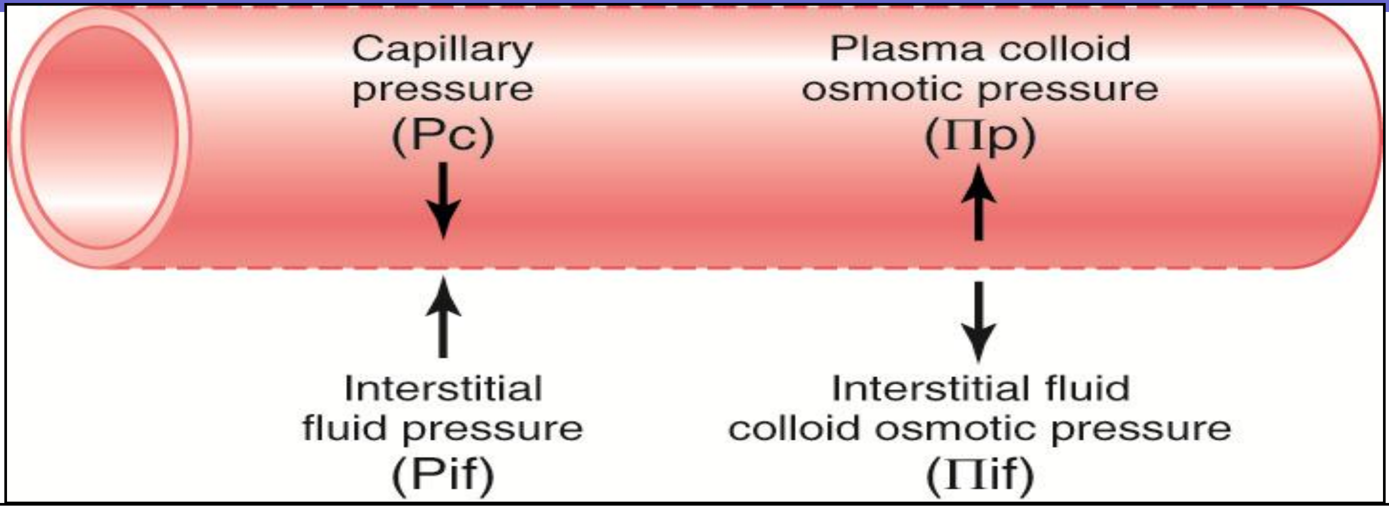
- Plasma colloid osmotic = 28mmHg
- Plasma protein conc. = 7.3gm/dl
- 75% of the total colloid osmotic pressure of plasma results from the presence of *albumin* and 25% is due to *globulins.*

	gm/dl	*πp(mmHg)*
Albumin	4.5	21.8
Globulins	2.5	6.0
Fibrinogen	0.3	0.2
Total	7.3	28.0

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 surface area times the hydraulic conductivity of membrane

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

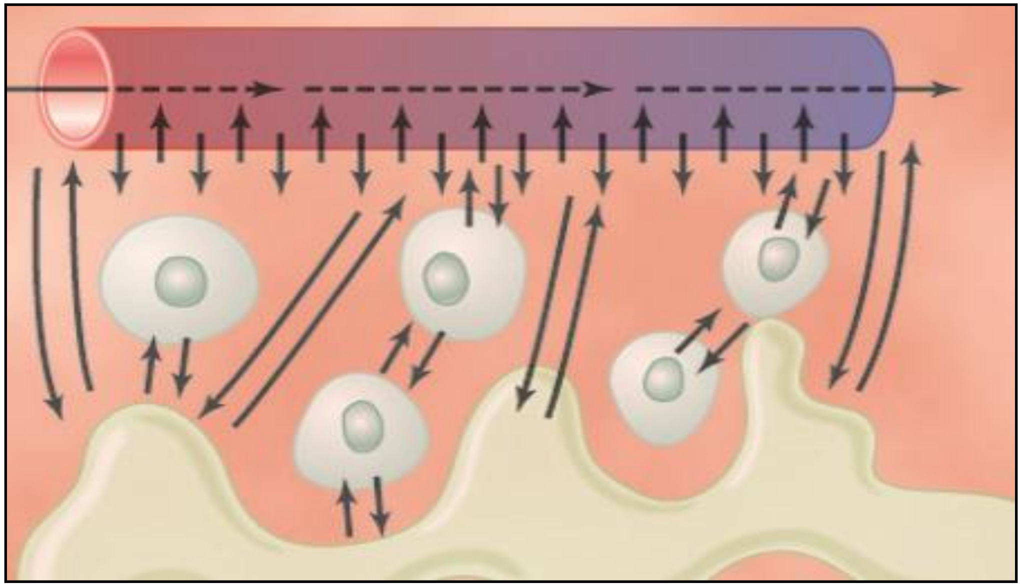
Forces Causing Reabsorption at the Venous End of the Capillary

	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

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	28.0
NET OUTWARD FORCE	0.3

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.

Causes of edema

1. Increased hydrostatic blood pressure (P_c) - heart failure (left or right), - excess fluid in the blood 2. Decreased blood colloid osmotic (oncotic) pressure (π_c) -Liver, kidney diseases, malnutrition (kwashiorkor), burn injuries	3. Decreased interstitial hydrostatic pressure (P_{if}) (lymphatic capillary blockage) - breast cancer surgery, elephantiasis 3. Leaking capillary wall (K_f) - histamine release during allergic reaction

Capillary Exchange of Respiratory Gases and Nutrients

- Oxygen, carbon dioxide, nutrients, and metabolic wastes diffuse between the blood and interstitial fluid along concentration gradients
  - Oxygen and nutrients pass from the blood to tissues
  - Carbon dioxide and metabolic wastes pass from tissues to the blood
  - Water-soluble solutes pass through clefts and fenestrations
  - Lipid-soluble molecules diffuse directly through endothelial membranes

Capillary Exchange: Fluid Movements

- Direction of movement depends upon the difference between:
  - Capillary hydrostatic pressure (HP_c)
  - Capillary colloid osmotic pressure (OP_c)
- HP_c – pressure of blood against the capillary walls:
  - Tends to force fluids through the capillary walls
  - Is greater at the arterial end of a bed than at the venule end
- OP_c– created by nondiffusible plasma proteins, which draw water toward themselves

Net Filtration Pressure (NFP)

- NFP – considers all the forces acting on a capillary bed
- $NFP = (HP_c - HP_{if}) - (OP_c - OP_{if})$
- At the arterial end of a bed, hydrostatic forces dominate (fluids flow out)
- At the venous end of a bed, osmotic forces dominate (fluids flow in)
- More fluids enter the tissue beds than return to the blood and the excess fluid is returned to the blood via the lymphatic system

Thank You