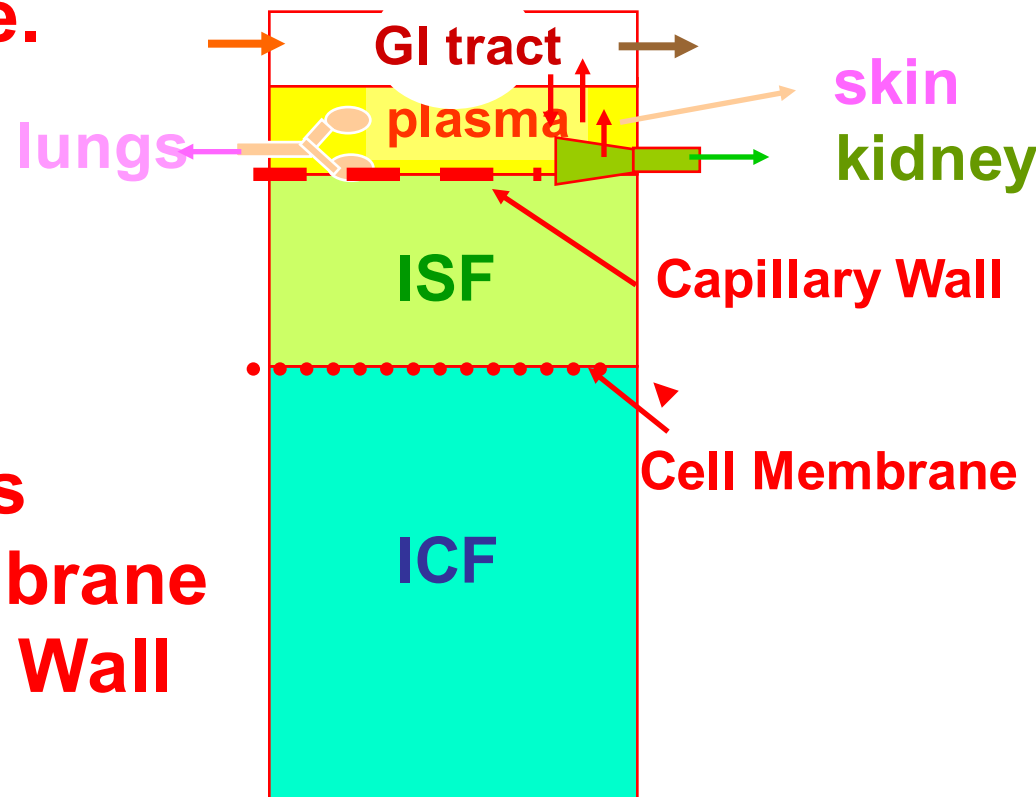


SUMMARY last few lectures

Homeostasis & Milieu Interieur

Body Fluid Compartments & Subcompartments

Communication with External Environment and within the Internal one.

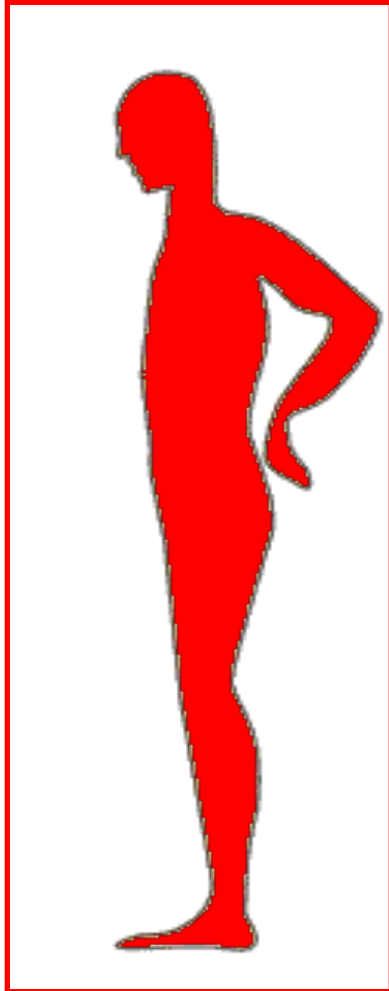


Transport Mechanisms

a) across Cell Membrane

b) across Capillary Wall

BLOOD –



- supporter of life – “lifeblood”
- associated with emotions
 - “bad blood”
- reflective of relationship
 - “blood brothers”

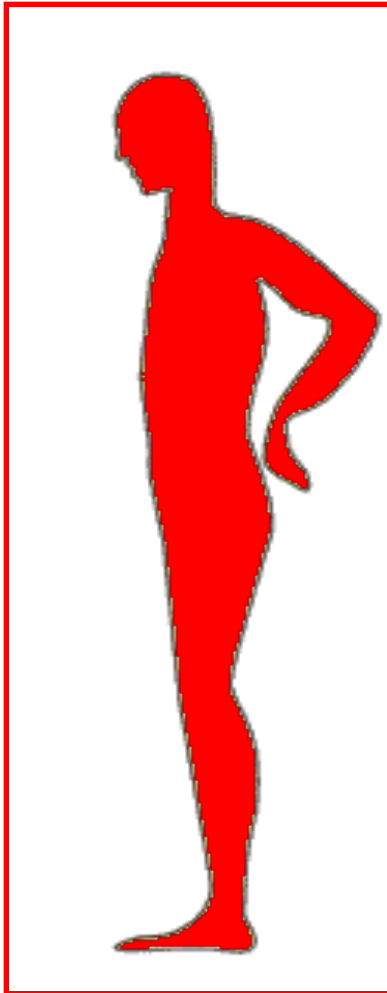
Ancient Chinese Medicine- blood linked to energy flow

Ancient Greece – advocated bleeding as treatment for many diseases

Medieval Western Medicine – blood inhabited by good and evil spirits

Modern days - carrier of diseases

BLOOD –



It comprises both **ECF** (plasma) and **ICF** (inside Blood Cells)

May be studied *in vivo* and *in vitro*

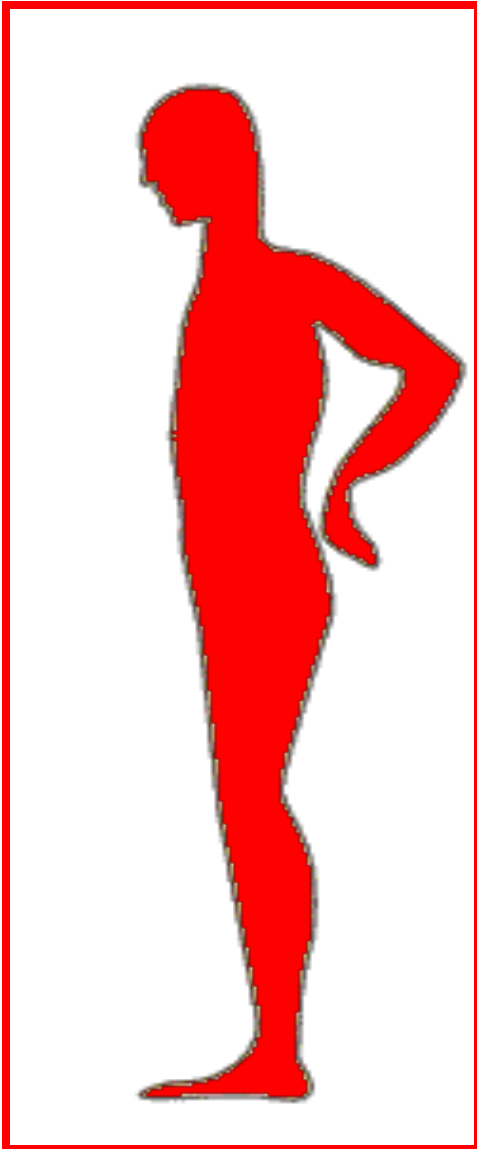
It accounts for ~ **7%** of Body Mass = ~ 5L

Normal Blood Volume = NORMOVOLEMIA

Lower Blood Volume = HYPOVOLEMIA

Higher Blood Volume = HYPERVOLEMIA

BLOOD FUNCTIONS



1. Transport:

Nutritive

Respiratory

Excretory

Hormone Transport

Temperature Regulation

2. Acid-Base Balance

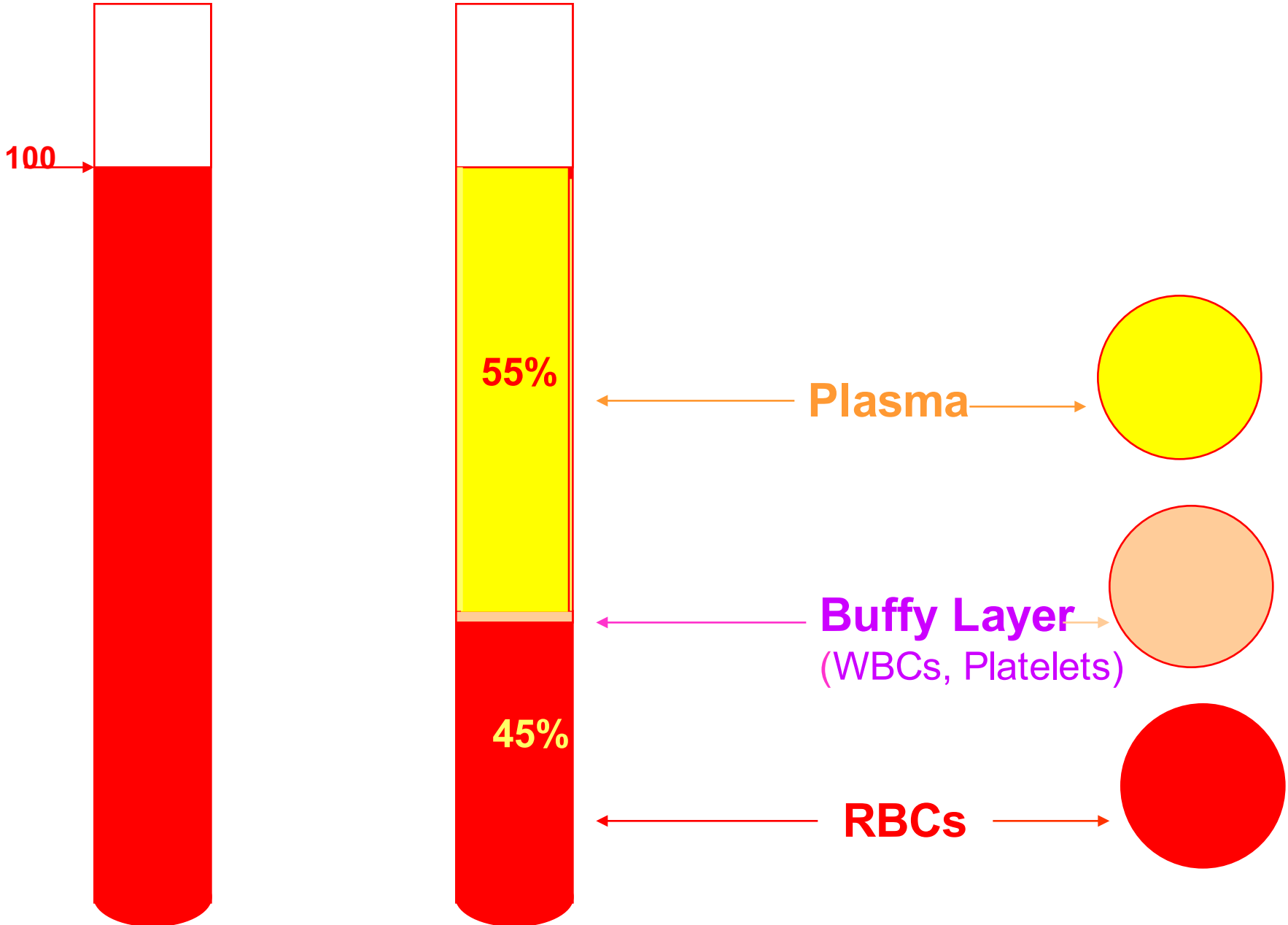
Normal pH range 7.30-7.45

3. Protective

**Whole
Blood**

**Centrifuged
Blood**

p.354¹²; 363-64¹³ Vander



HEMATOCRIT

It is that **percentage** of Blood Volume that is occupied by **Red Blood Cells**

$$\text{Ht} = \frac{\text{Height of erythrocyte column}}{\text{Height of whole blood column}} \times 100$$

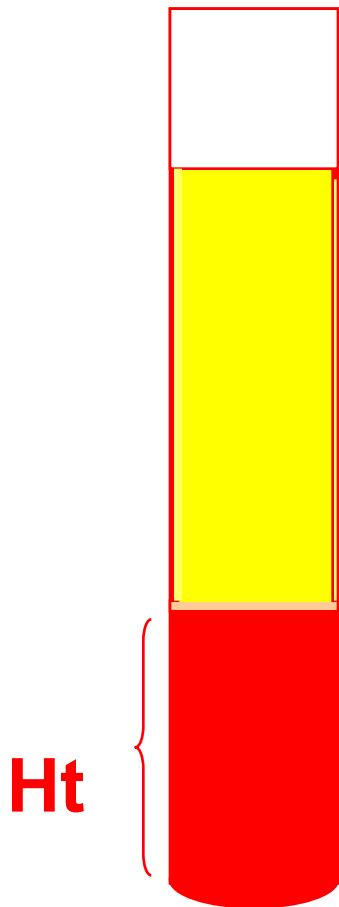
Normal Value: ~ 45%

Blood Volume = ~7- 8 % of Body Weight
5 – 5.5 L (70 Kg male)

If Hematocrit (% of blood volume occupied by RBCs) is 45%,

Total Blood Volume occupied by RBCs = ~2.25L

Total Blood Volume occupied by Plasma = ~ 2.75L



COMPOSITION OF PLASMA

(similar to that of ISF)

1. > 90% water

2. **Na⁺**, K⁺, (Ca⁺⁺, Mg⁺⁺)
Cl⁻, HCO₃⁻, (PO₄⁻⁻)

May be approximated by physiological saline: 0.9g/dl NaCl

3. Glucose, amino acids, lipids, O₂, CO₂

4. **PROTEINS (colloids) = 7g%**

ALBUMINS

GLOBULINS

FIBRINOGEN

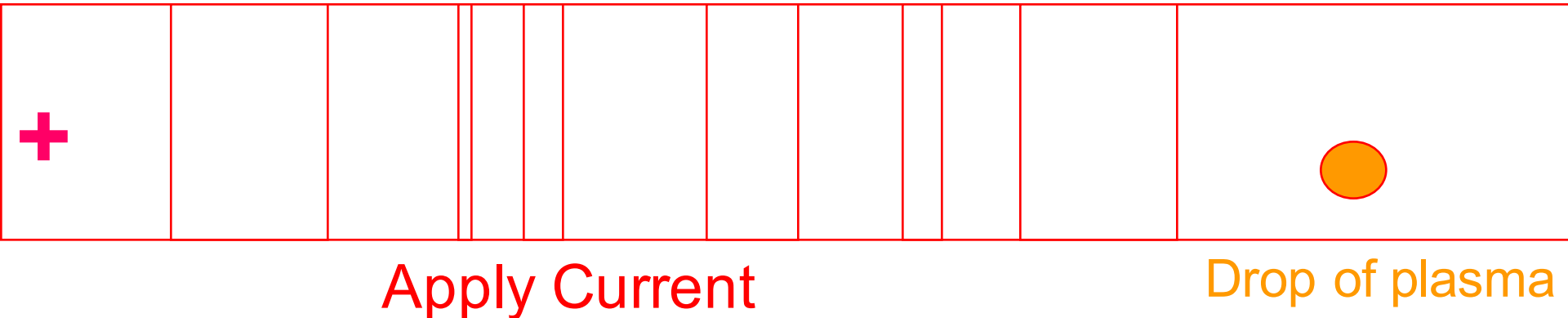
SEPARATING PLASMA PROTEINS

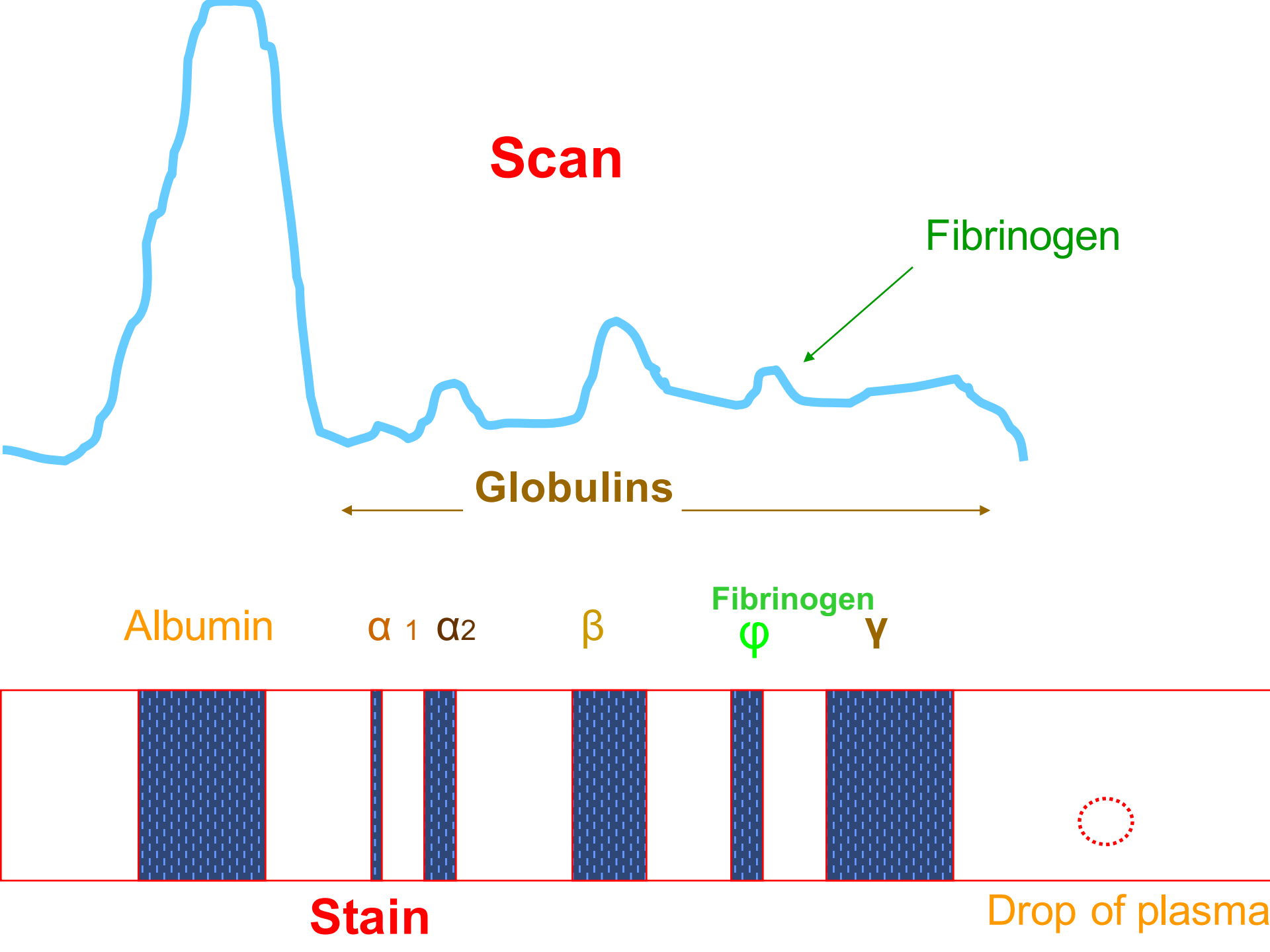
1. Differential Precipitation by Salts
2. Sedimentation in Ultracentrifuge
3. Electrophoretic Mobility
4. Immunological Characteristics

ELECTROPHORESIS — fractionation method based on movement of charged particles along a voltage gradient

Rate of migration is influenced by the number and distribution of charges and by the MW of each protein.

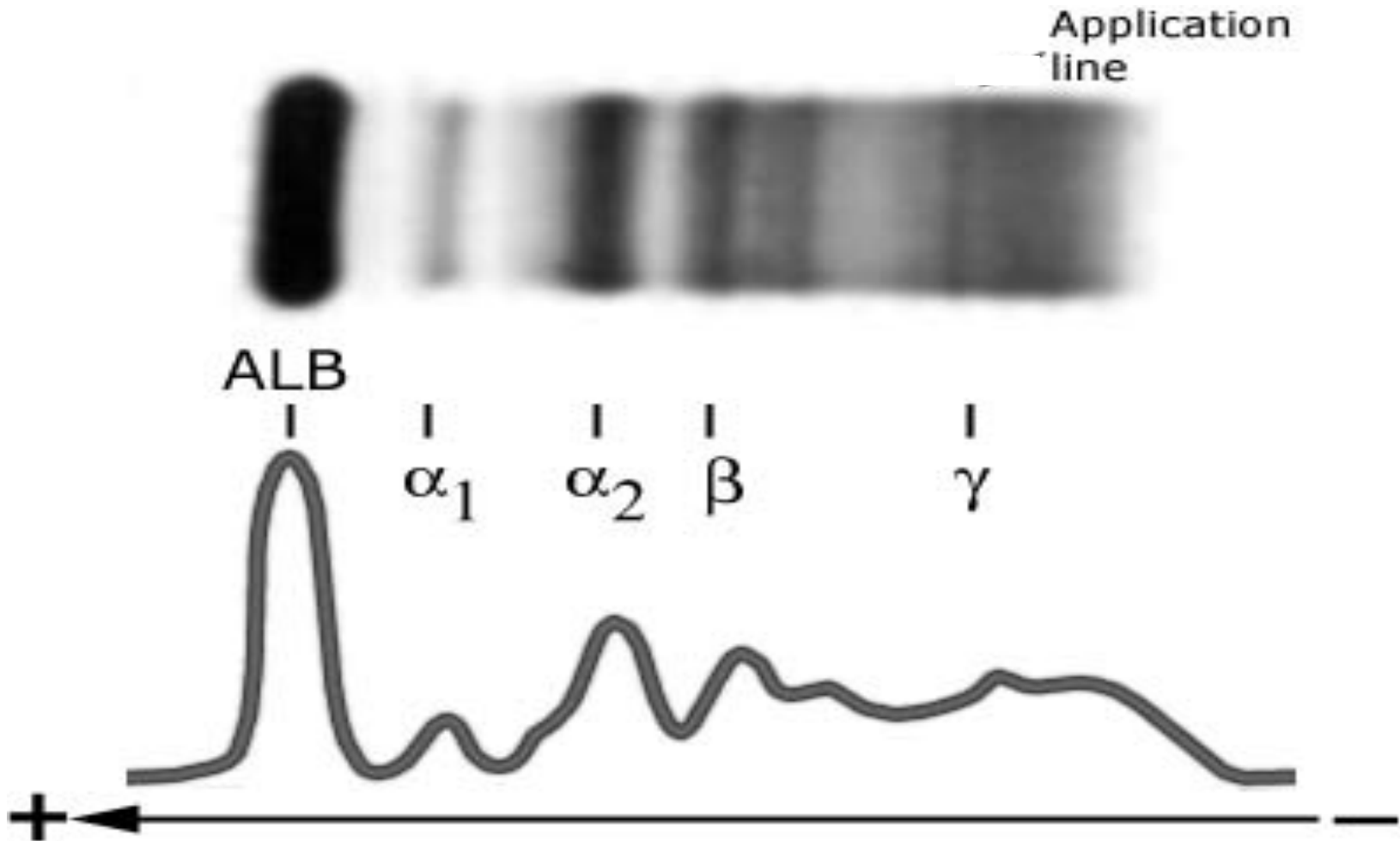
Each protein migrates at its own characteristic rate.



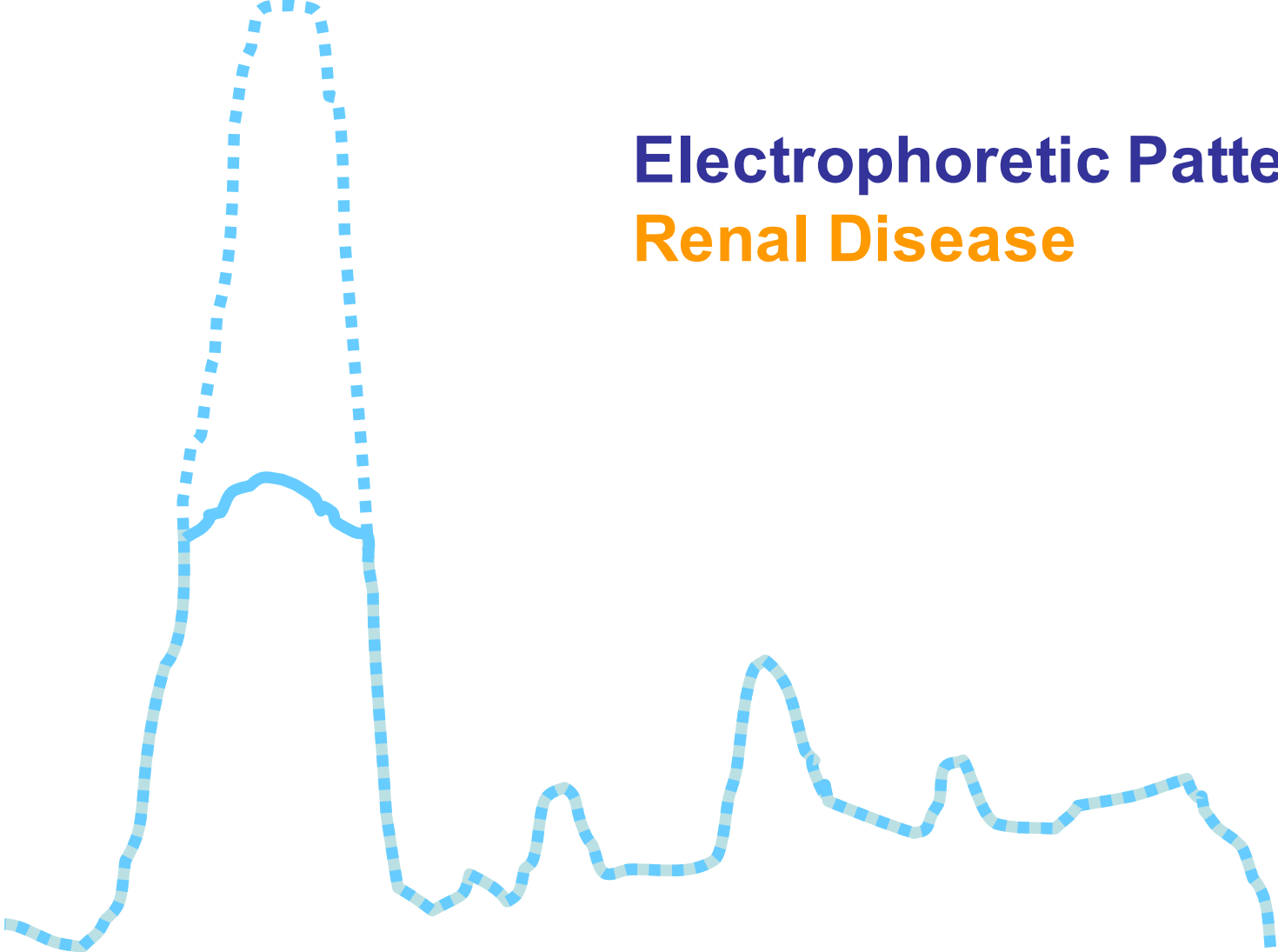


Serum Electrophoretic Pattern

(Note absence of Fibrinogen (ϕ) peak – why?)



Electrophoretic Pattern in Renal Disease



Fibrinogen



Albumin

$\alpha 1$

$\alpha 2$

β

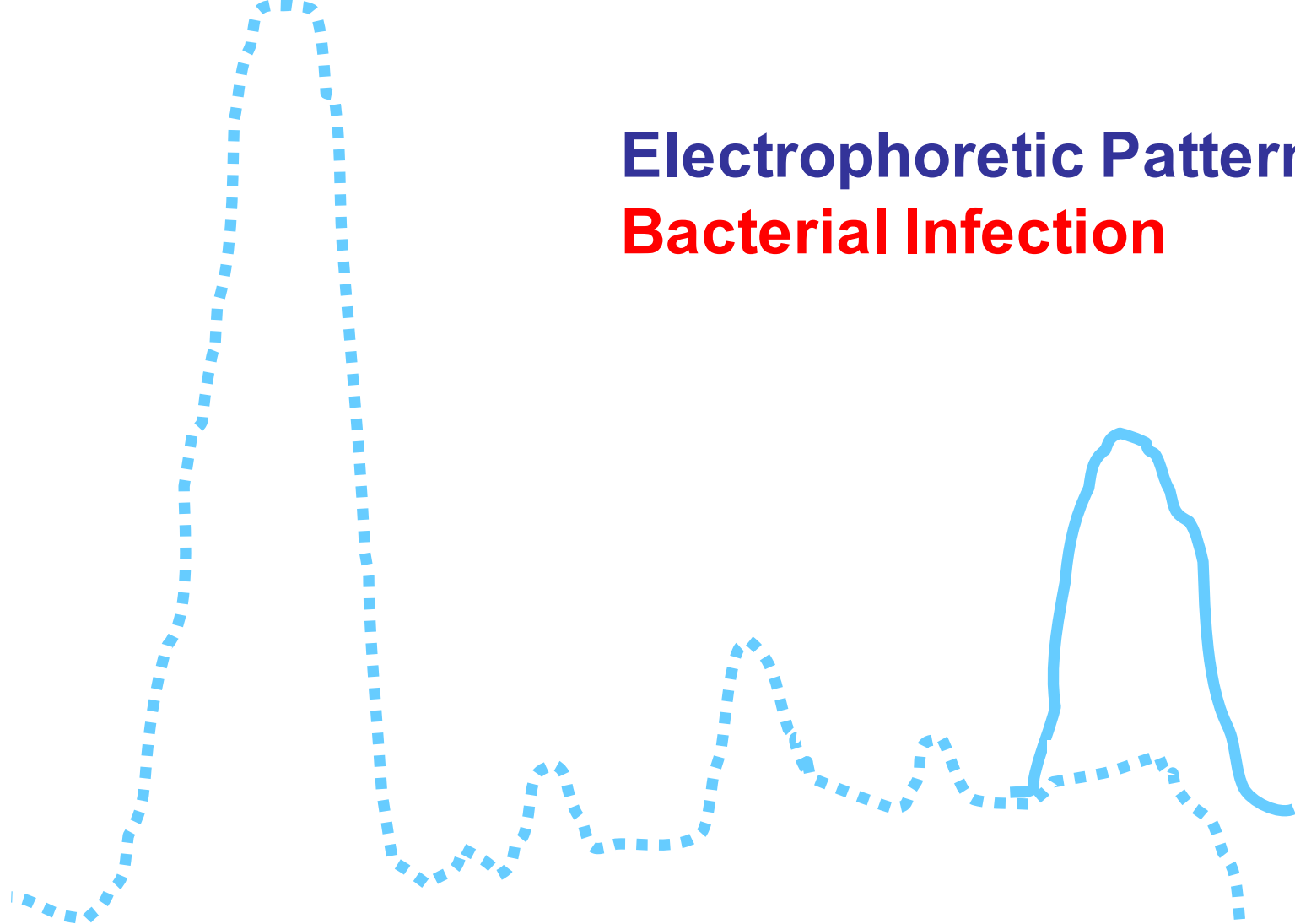
Φ

γ

Globulins



Electrophoretic Pattern in Bacterial Infection



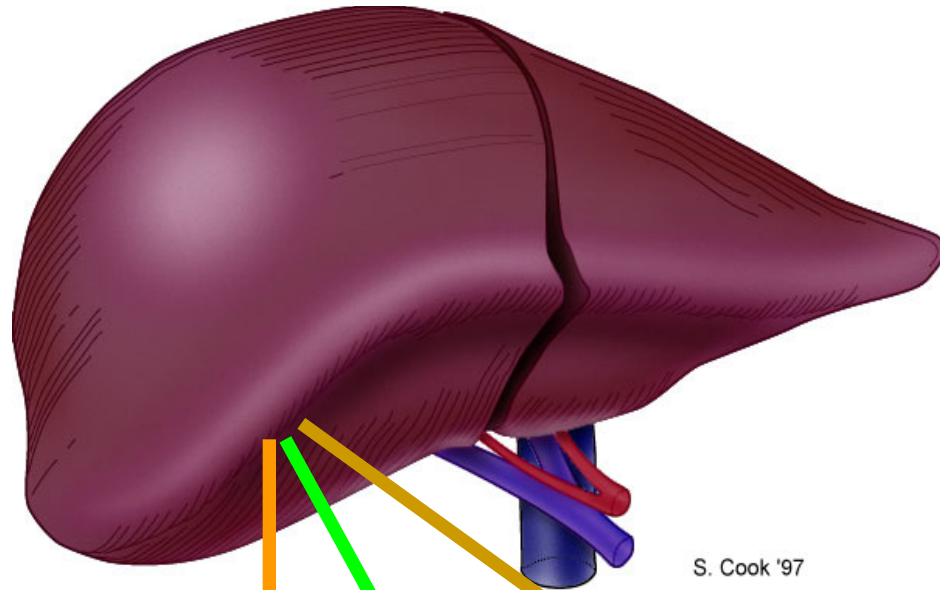
Fibrinogen



← Globulins →

Origin of Plasma Proteins

p. 417¹²; p. 428¹³ Vander



LYMPHOID TISSUE


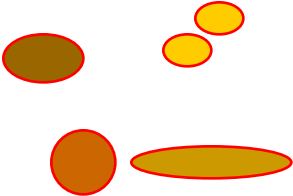
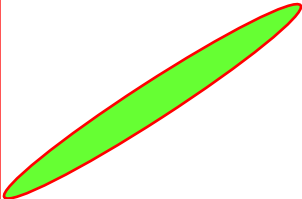
Albumin

Fibrinogen

α_1 , α_2 , β
Globulins

γ Globulin

Plasma Protein Properties

Protein	Shape	Molec.Wt. (K)	Conc'n (g%)	
Albumin		69	4	
Globulins		90-800	2.7	
Fibrinogen		350	0.3	

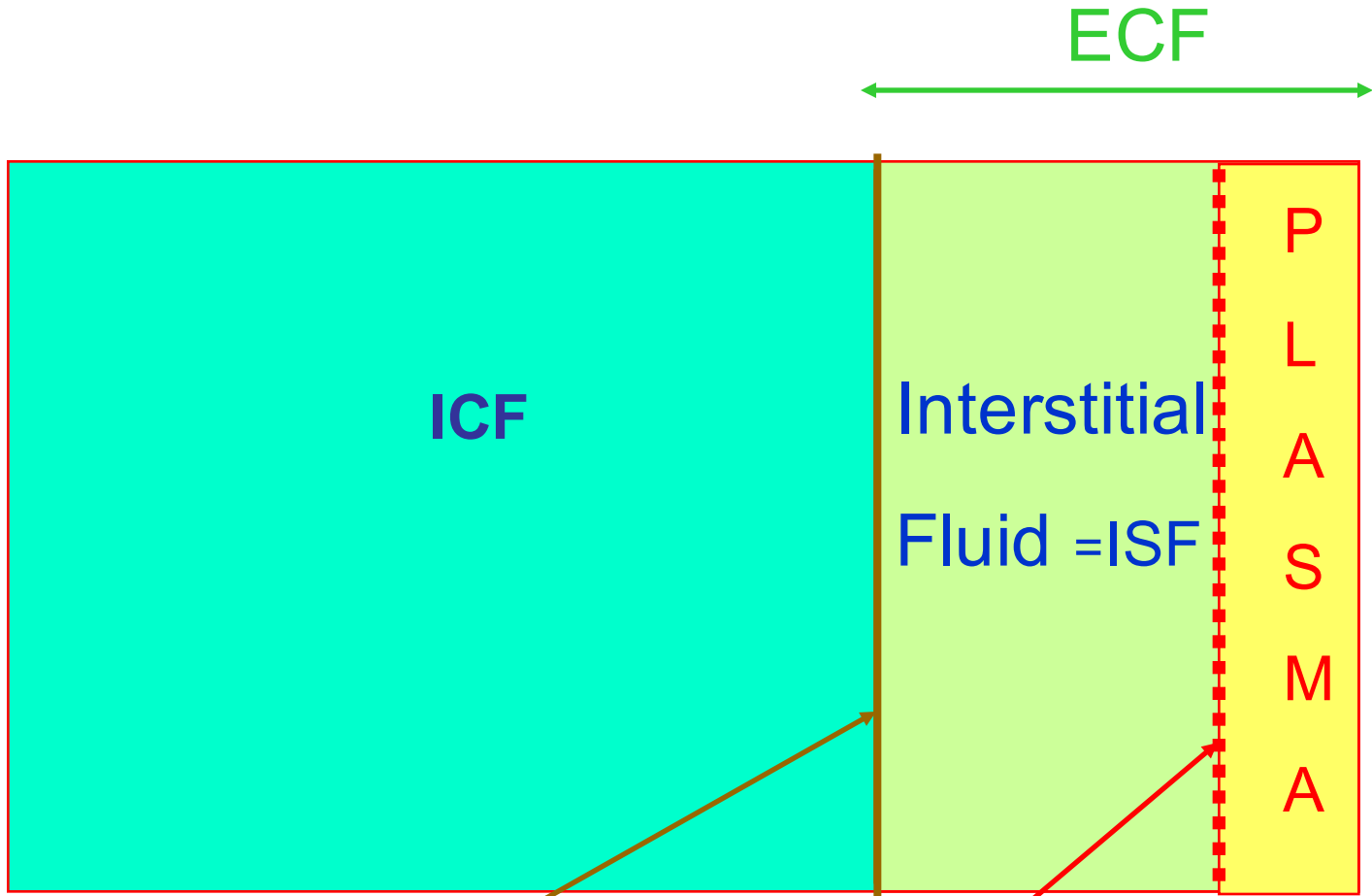
Role of Plasma Proteins

1. Major role in determining the **distribution** of fluid between **the plasma** and the **ISF** compartments by controlling **transcapillary dynamics**



See pp. 389-391¹² (398 –402¹³) in Vander

Body Water Compartments and Major Subcompartments

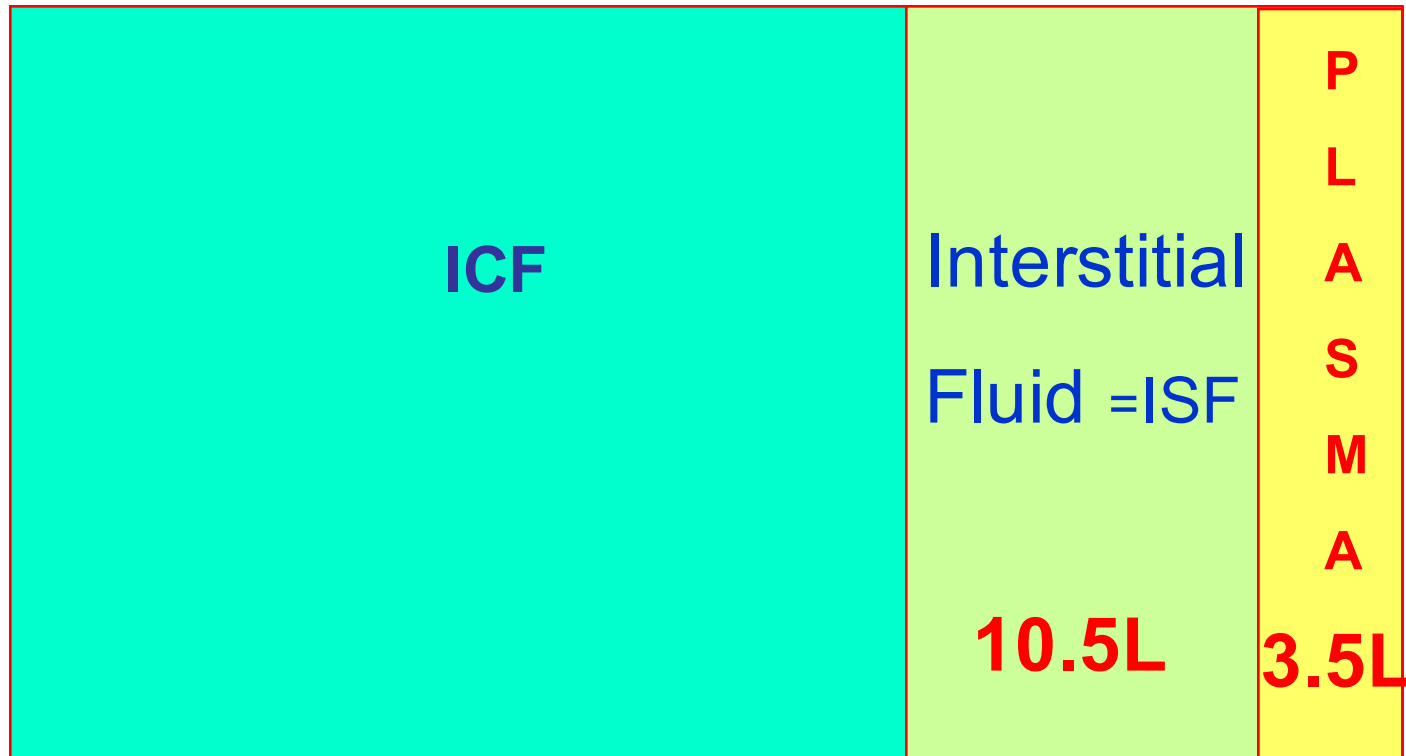


Cell membrane – relatively impermeable to ions

Capillary Wall – freely permeable to H₂O and ions

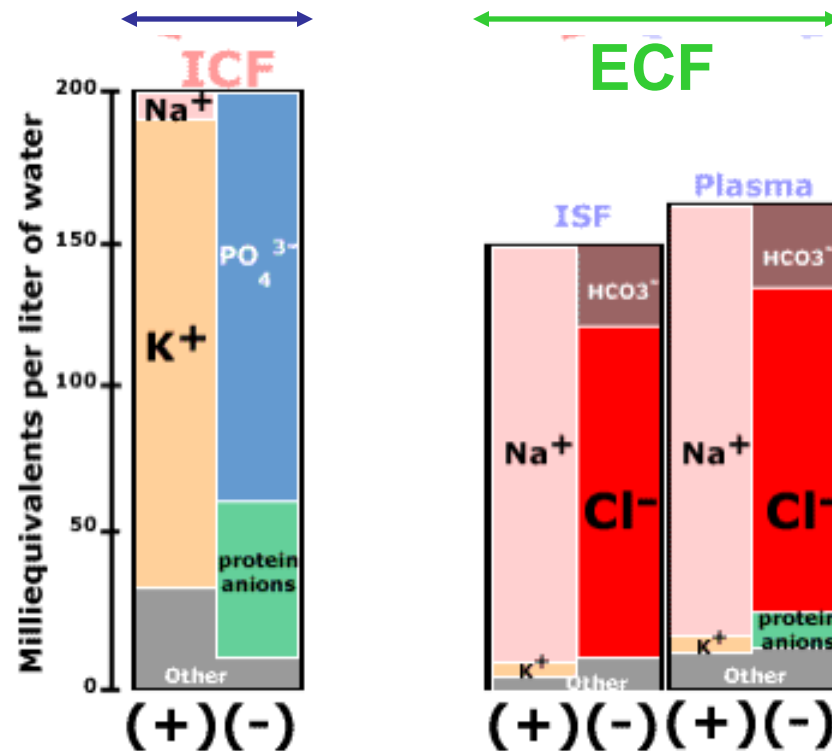
Body Water Compartments and Major Subcompartments

← ISF = 15% ▶ 5%



← ICF = 40% of Body Mass → ← ECF = 20% →

Body fluids – ionic composition



The ECF may be approximated by a 0.9% solution of NaCl

= 300mOsm

ISF

0.9% NaCl

300 mOsm

o.p. = 6.7 atms

= 5100 mm Hg

PLASMA

0.9% NaCl

300 mOsm

o.p. = 6.7 atms

= 5100 mm Hg

← capillary wall

For a net flow of water between compartments, there has to be a difference in osmotic pressure

Only **NON-DIFFUSIBLE** solutes contribute to the effective o.p. of a solution

Diffusible solutes do **NOT** contribute, since they become equally distributed on the 2 sides of the membrane

PLASMA PROTEINS are **NON-DIFFUSIBLE**

therefore, they can exert an osmotic effect

This effect is known as the **COLLOIDAL OSMOTIC (ONCOTIC) PRESSURE (C.O.P.) OF PLASMA**

= 25 mm Hg

ISF

0.9% NaCl

300 mOsm

o.p. = 6.7 atms

= 5100 mm Hg

PLASMA

0.9% NaCl

300 mOsm

o.p. = 6.7 atms

= 5100 mm Hg

Colloidal Osmotic Pressure
(C.O.P.) or Oncotic Pressure due
to plasma proteins

= 25 mm Hg

If the COP increases, more water will flow into plasma

If the COP decreases, more water will flow into ISF

Transport across Capillary Wall (1)

There are two major forms of fluid transport across the capillary wall

1. The C.O.P. of plasma determines **how much water** will flow into or out of capillaries



Transport across Capillary Wall (2)

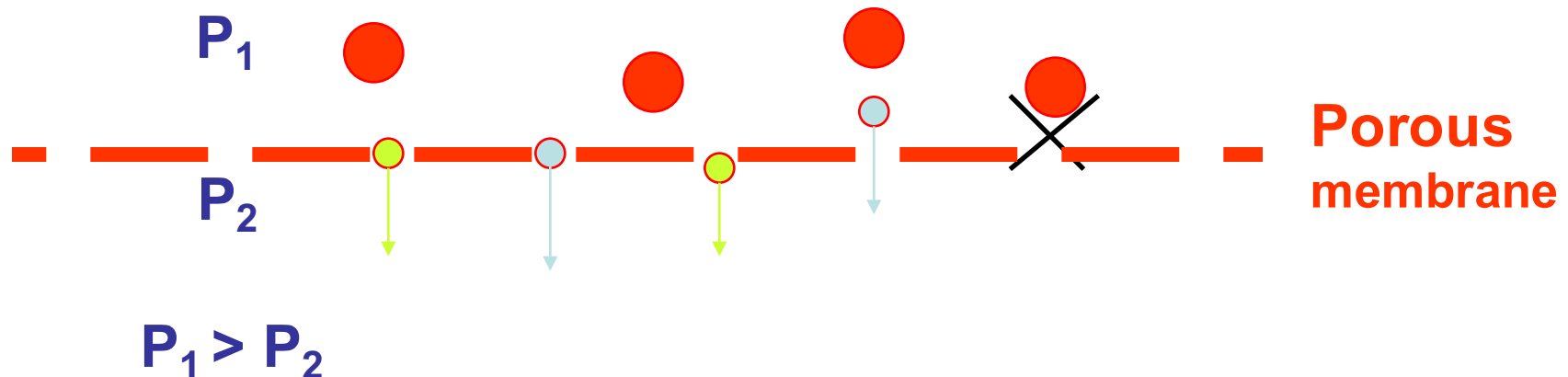


BULK FLOW – flow of molecules subjected to a pressure difference

Magnitude of bulk flow \propto hydrostatic pressure difference



FILTRATION – bulk flow across a porous membrane (which acts as a “sieve”, withholding some particles)



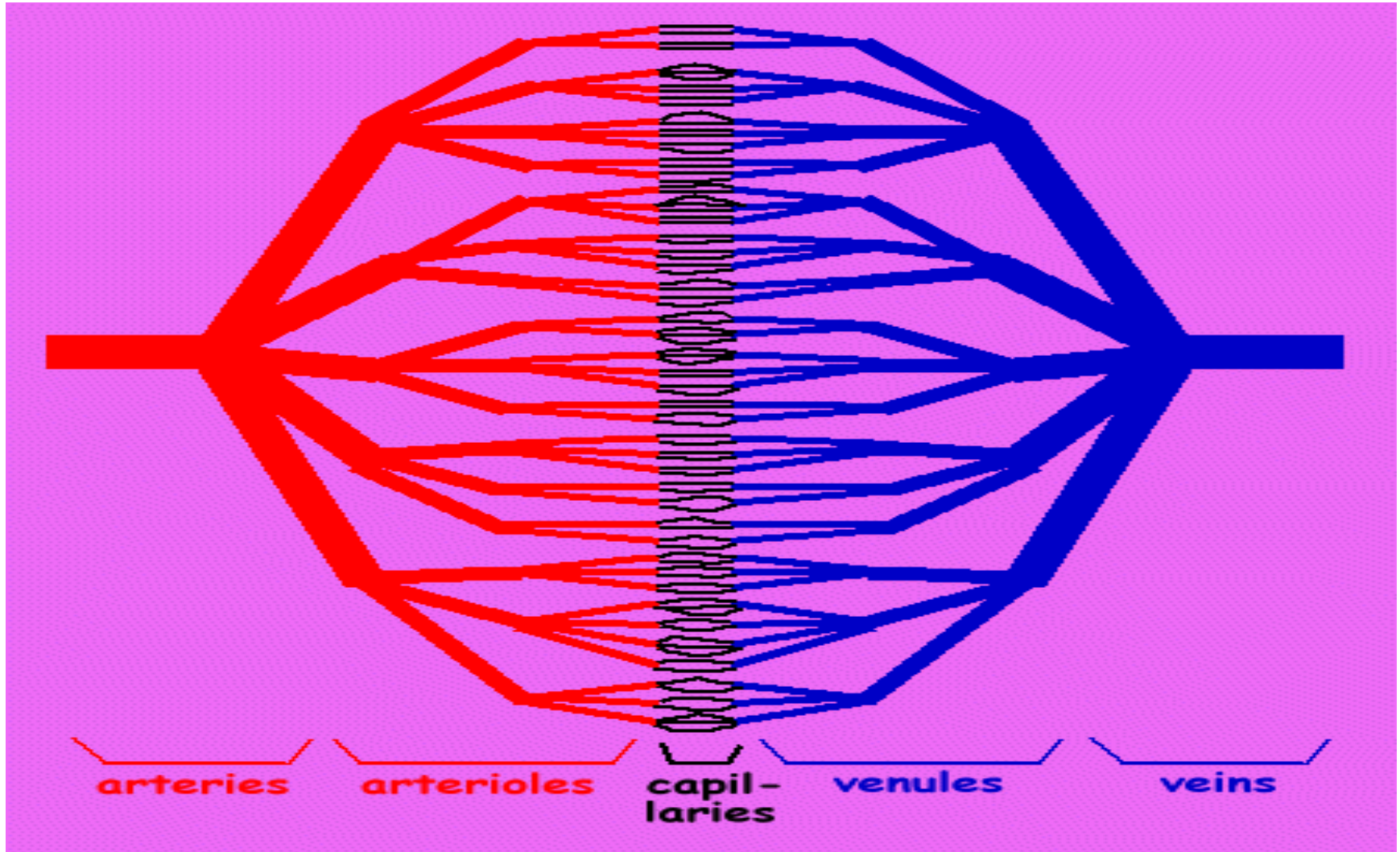
Two important transport mechanisms across capillaries:



- 1) Filtration – tends to “push out” the fluid from inside the capillaries
- 2) Osmotic Flow – tends to “pull in” or retain fluid inside the capillaries

1) and 2) = **STARLING FORCES**

CAPILLARY BED- site where exchanges take place between plasma and ISF



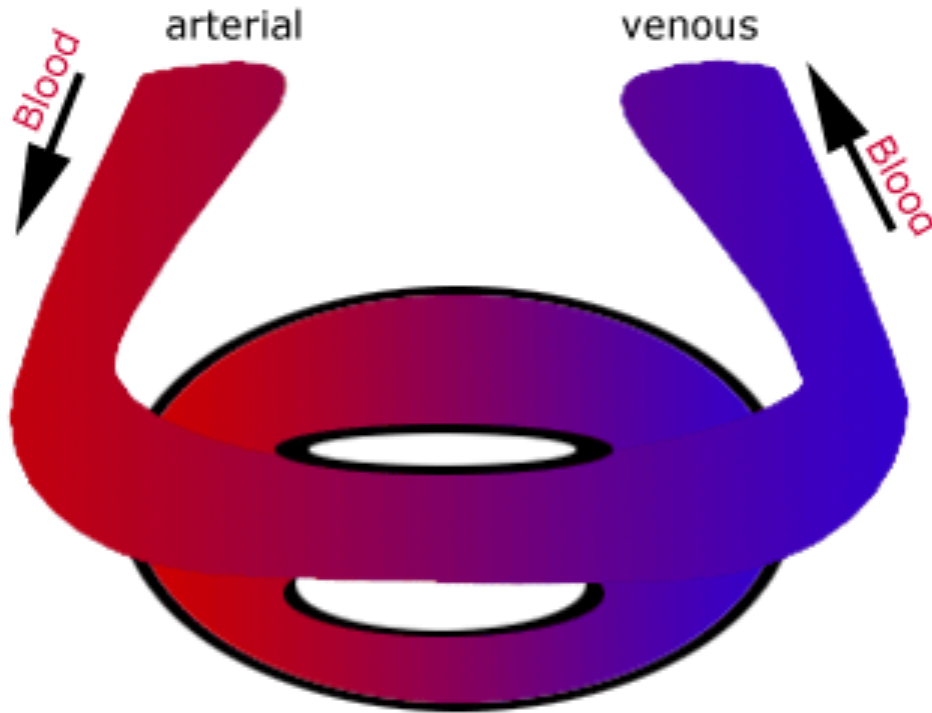
DIFFUSION is responsible for the exchange of nutrients, gases, and wastes across the capillary wall

The **STARLING FORCES** determine the distribution of **ECF** volume between **Plasma** and **ISF**



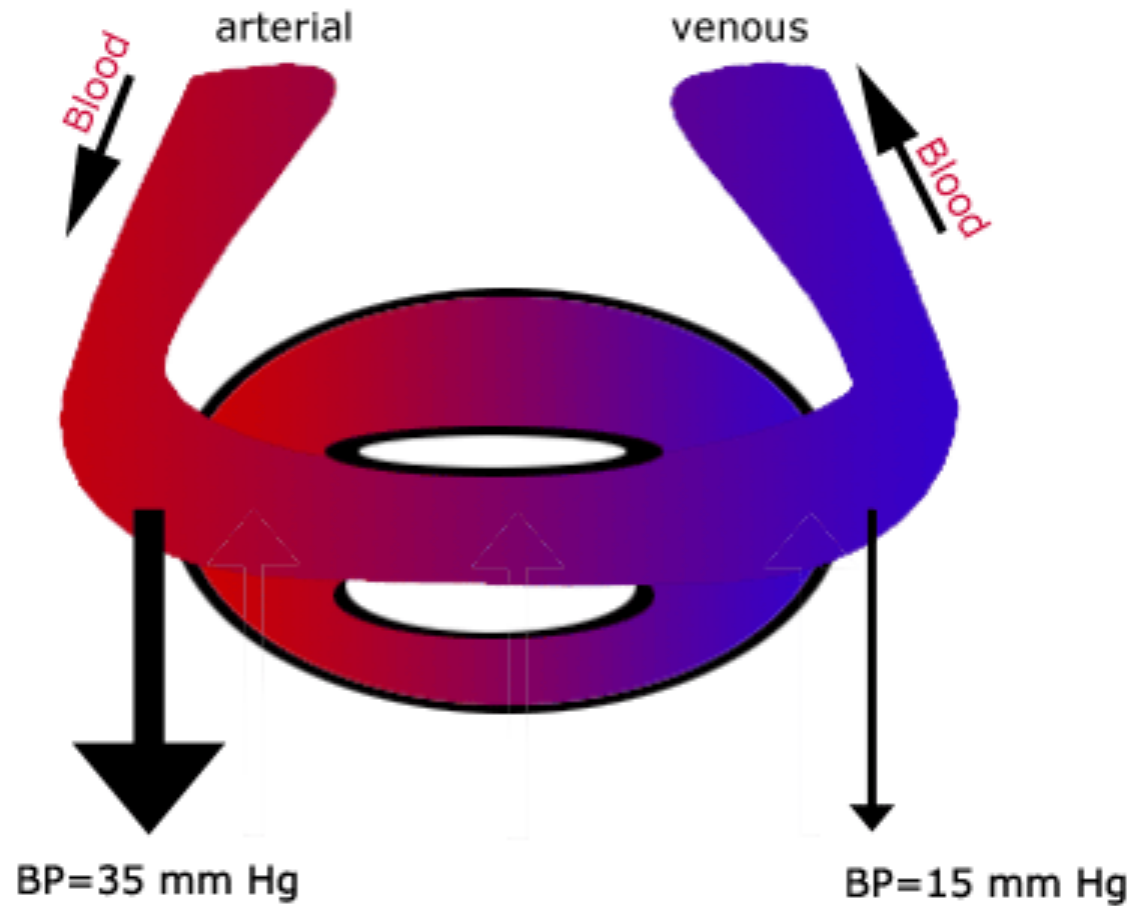
- 1) **Filtration** – tends to “push out” the fluid from inside the capillaries
- 2) **Osmotic Flow** (due to plasma proteins) – tends to “pull in” or retain fluid inside the capillaries

Starling's Transcapillary Dynamics

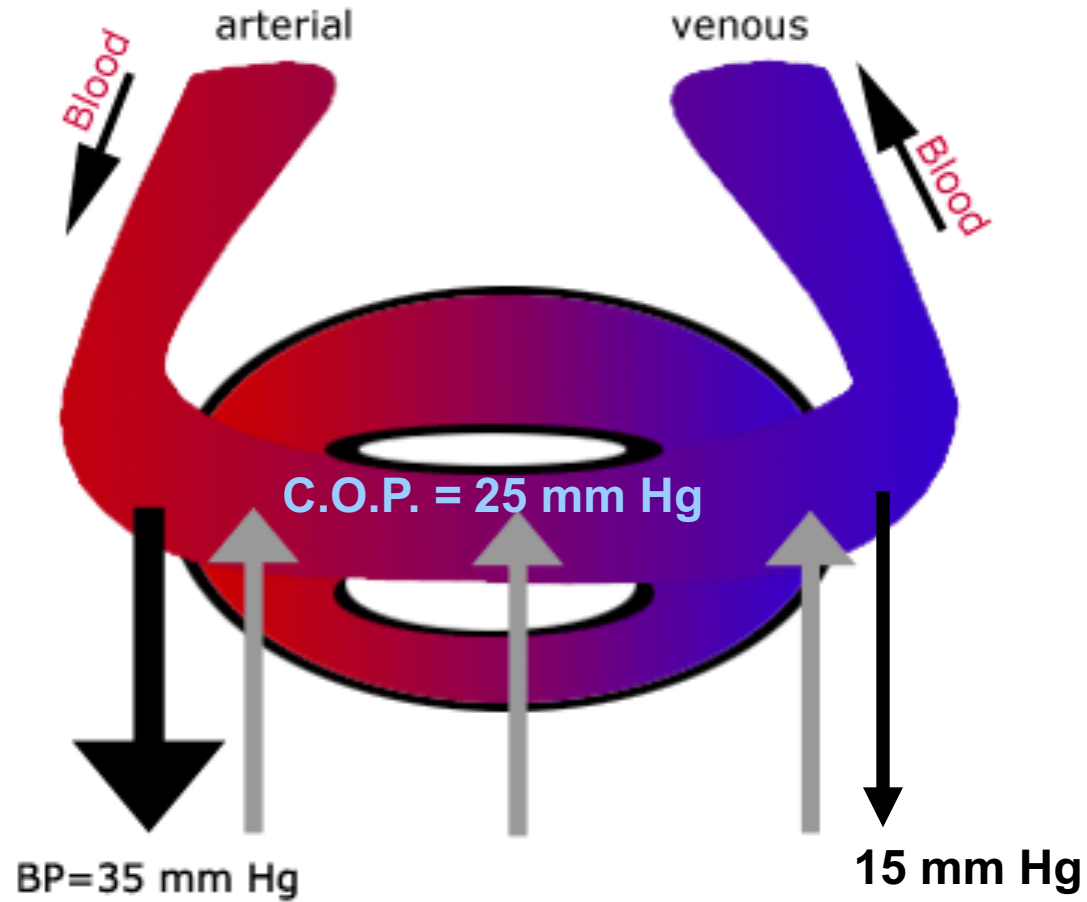


Read pp. 388-392¹² (399 – 402¹³) Vander

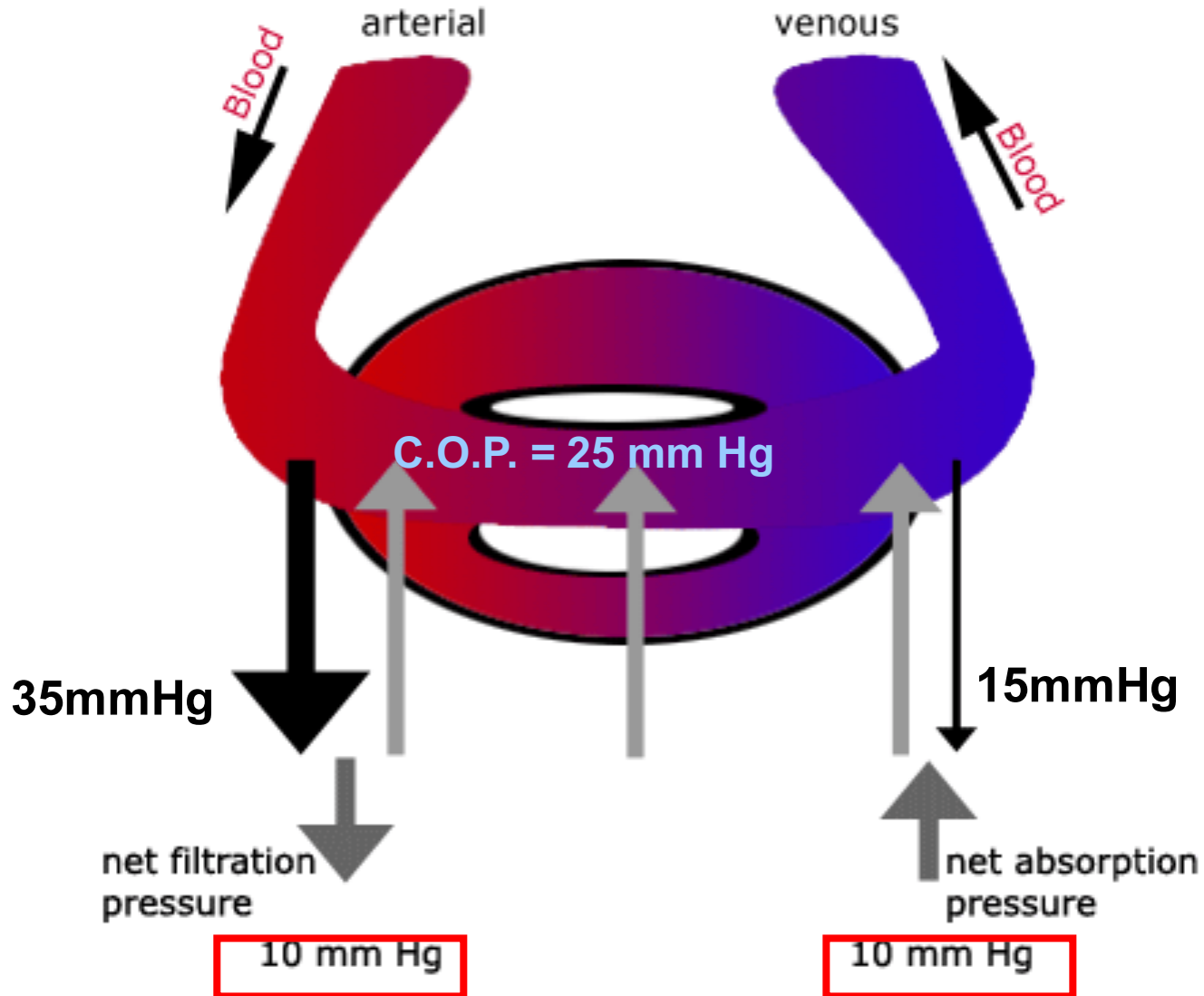
Starling's Transcapillary Dynamics



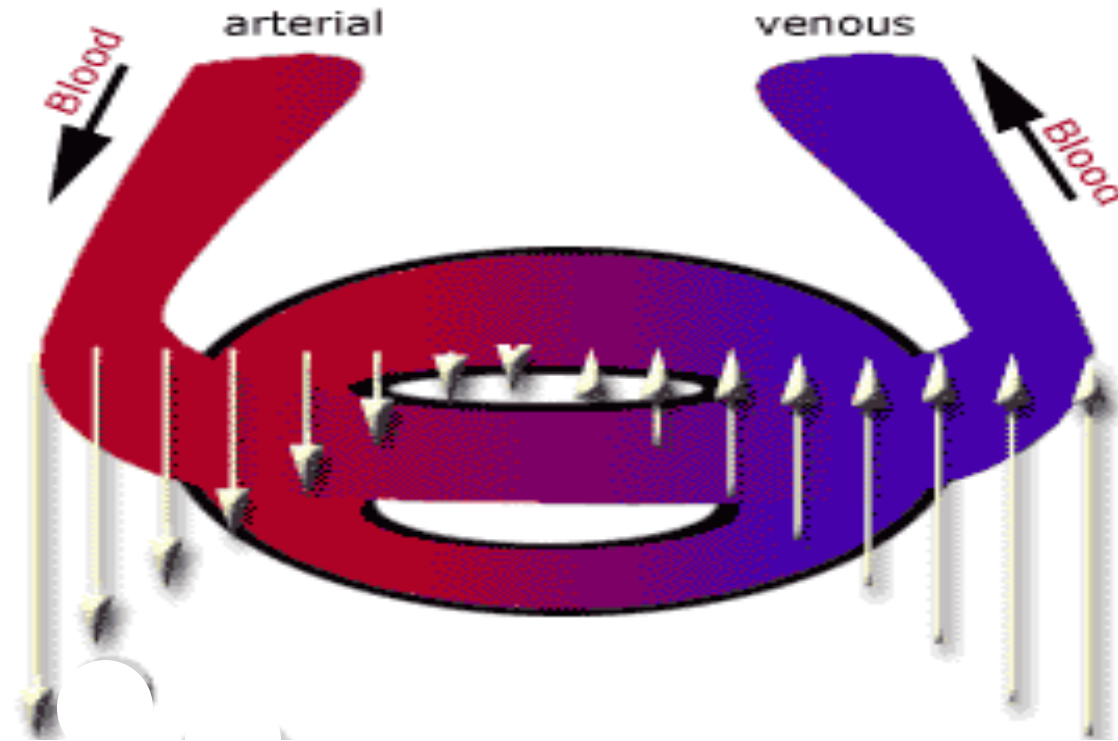
Starling's Transcapillary Dynamics



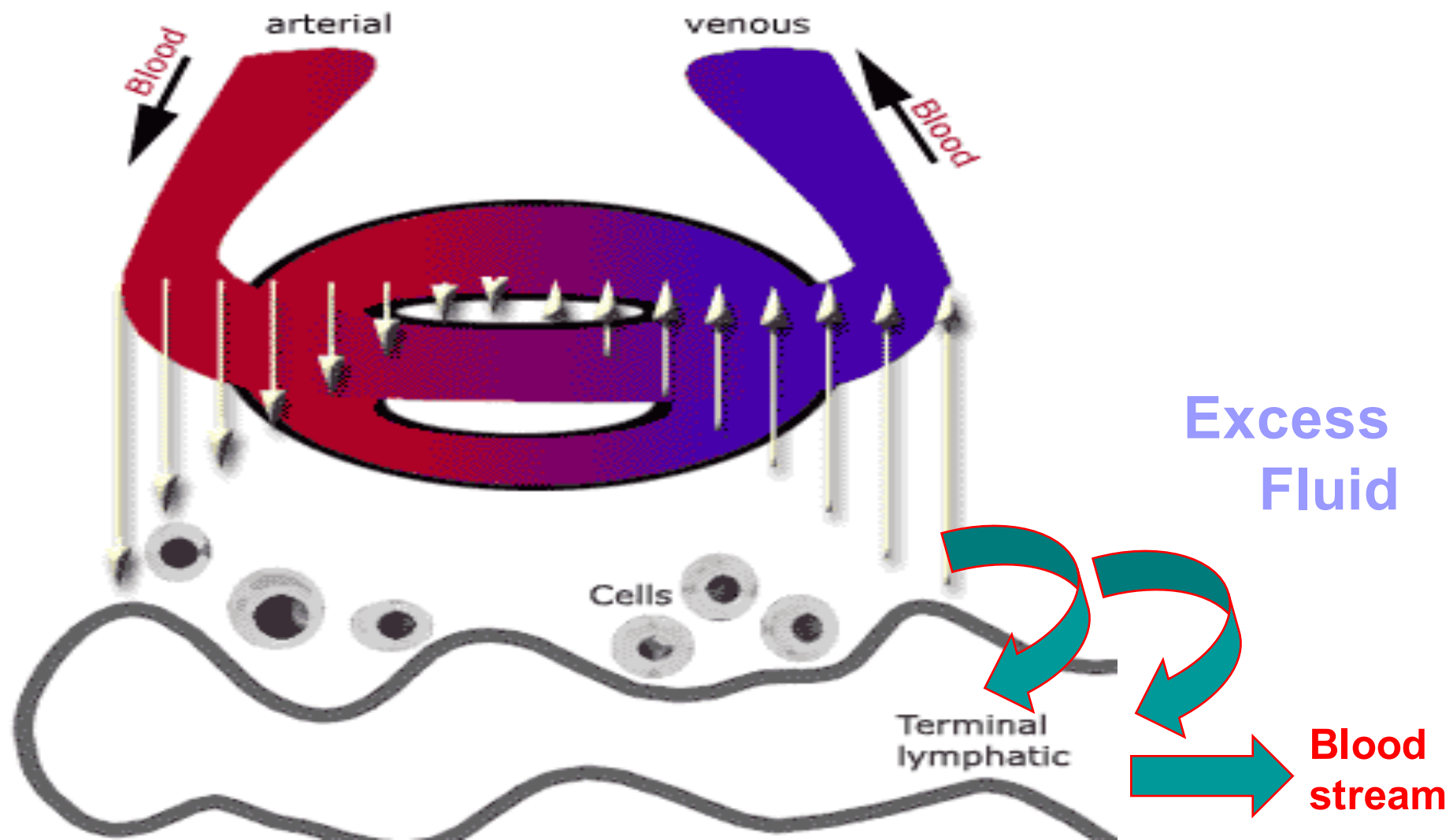
Starling's Transcapillary Dynamics



Starling's Transcapillary Dynamics

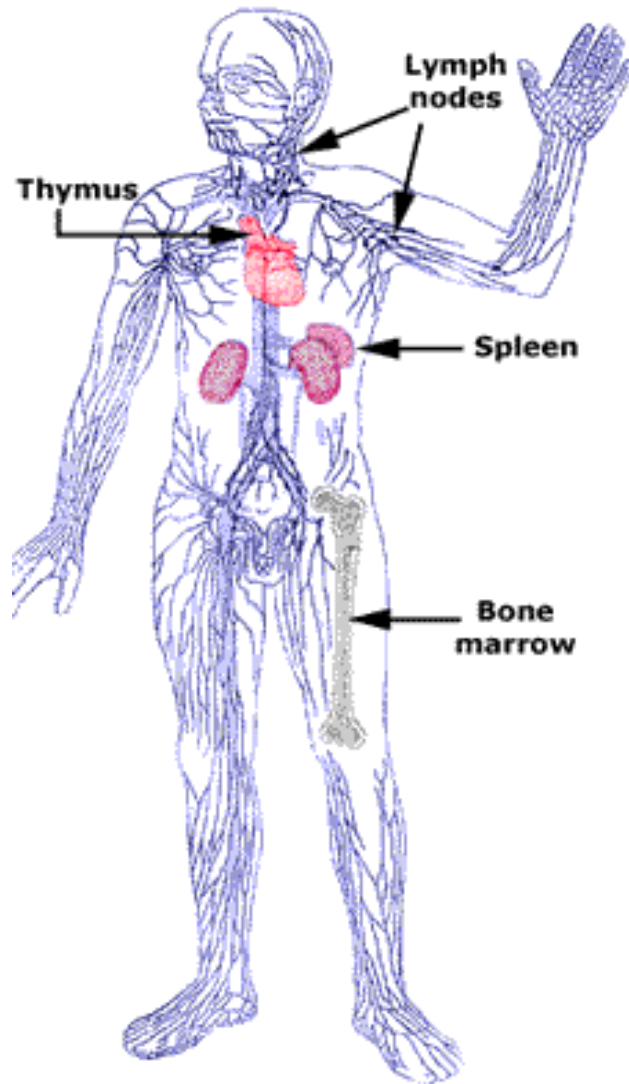


1. Exchanges (filtration/absorption) take place **along the whole length of the capillary** (not just at the 2 ends)



2. Only ~ 90% of the fluid filtered out is reabsorbed directly back into the capillary. 10% is drained by the lymphatic vessels.

Lymphatic System



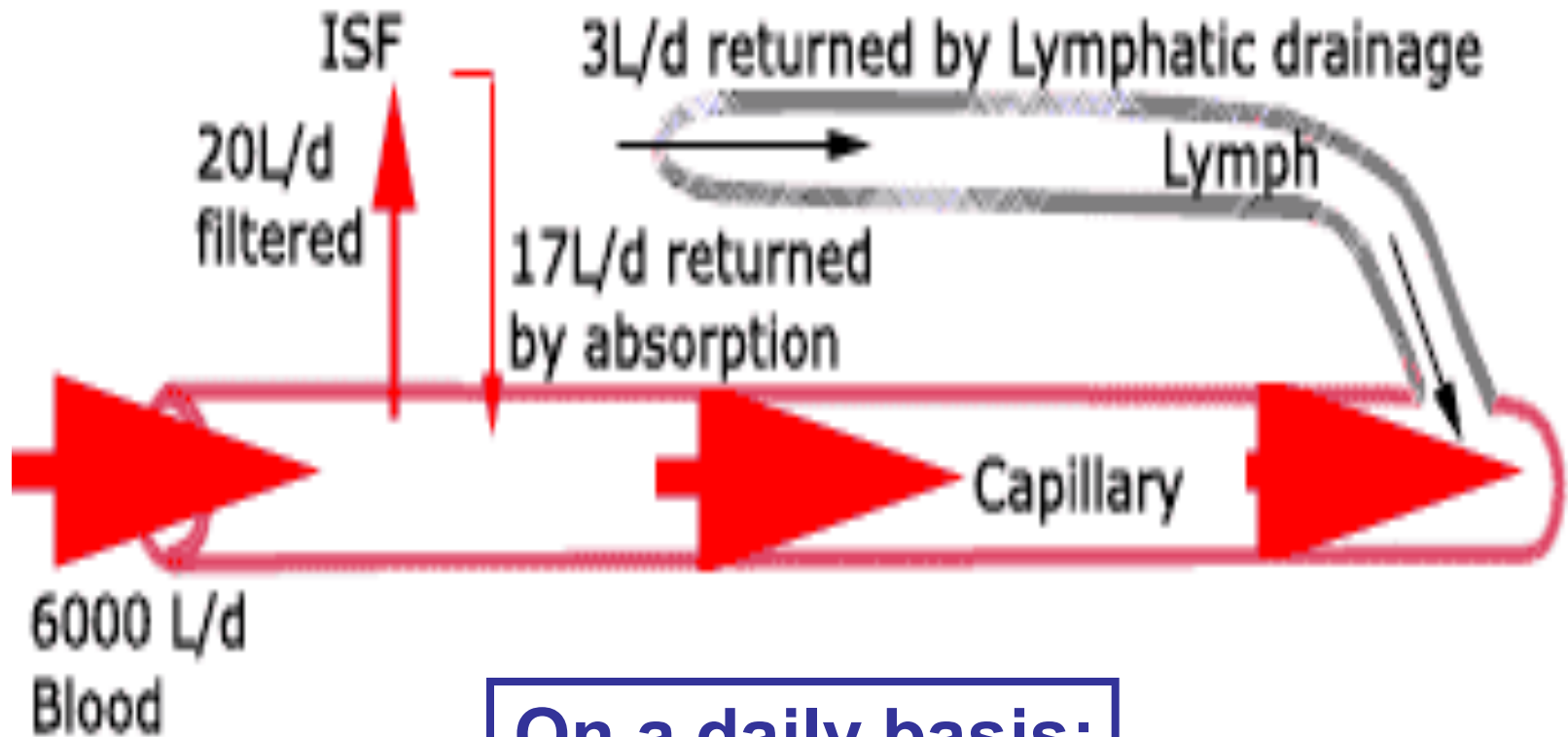
A network of blind-ended terminal tubules,

which coalesce to form larger lymphatic vessels,

which converge to form large lymphatic ducts,

which drain into the large veins in the chest

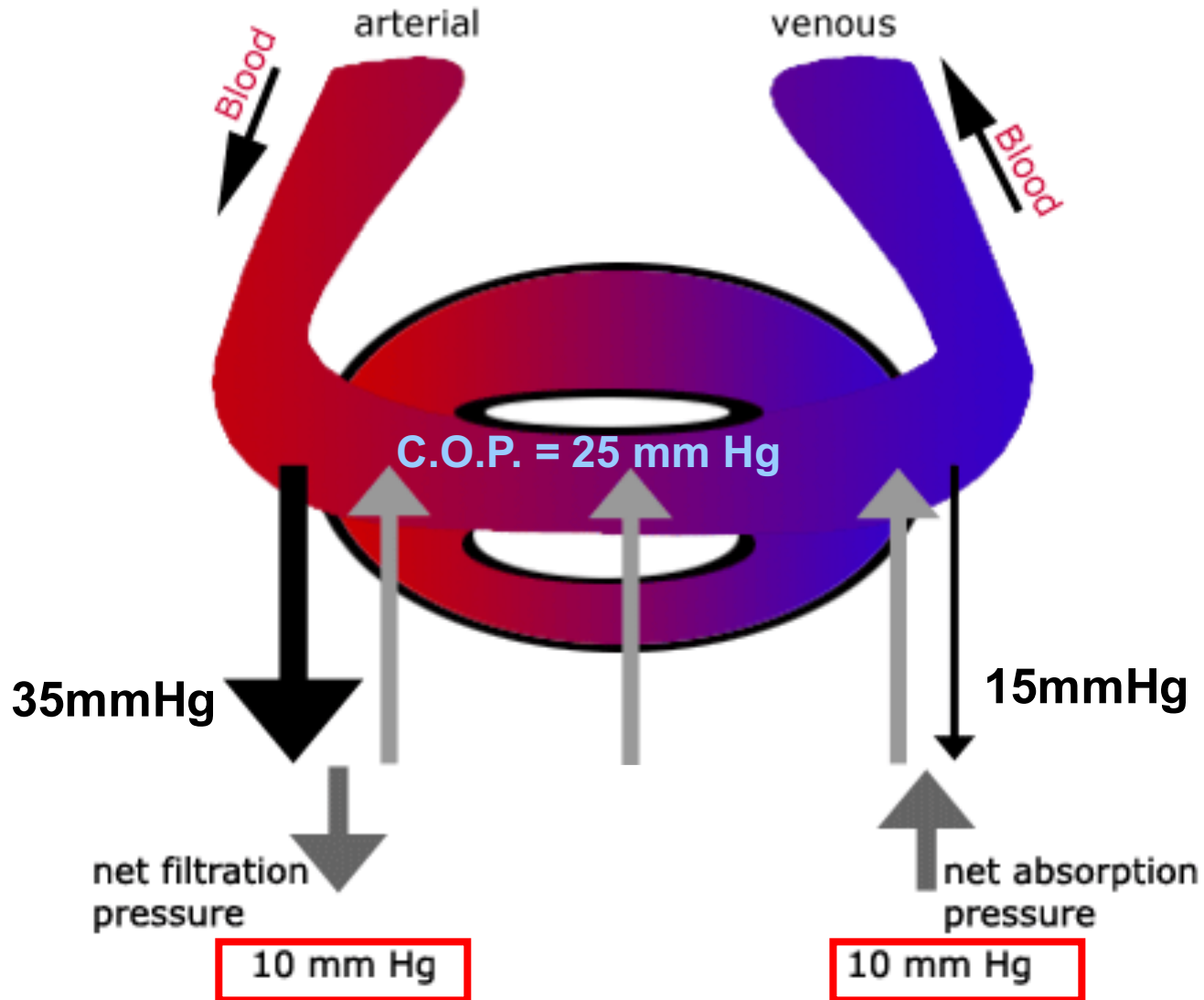
Lymphatic vs Blood Flow Volumes



On a daily basis:

Total Blood Flow	6,000L
Volume filtered into ISF	20L
Volume returned by absorption	17L
Volume returned by lymph drainage	3L

Starling's Transcapillary Dynamics



Read pp 388-392¹² (398-402¹³) Vander

Which proteins contribute the most to c.o.p.?

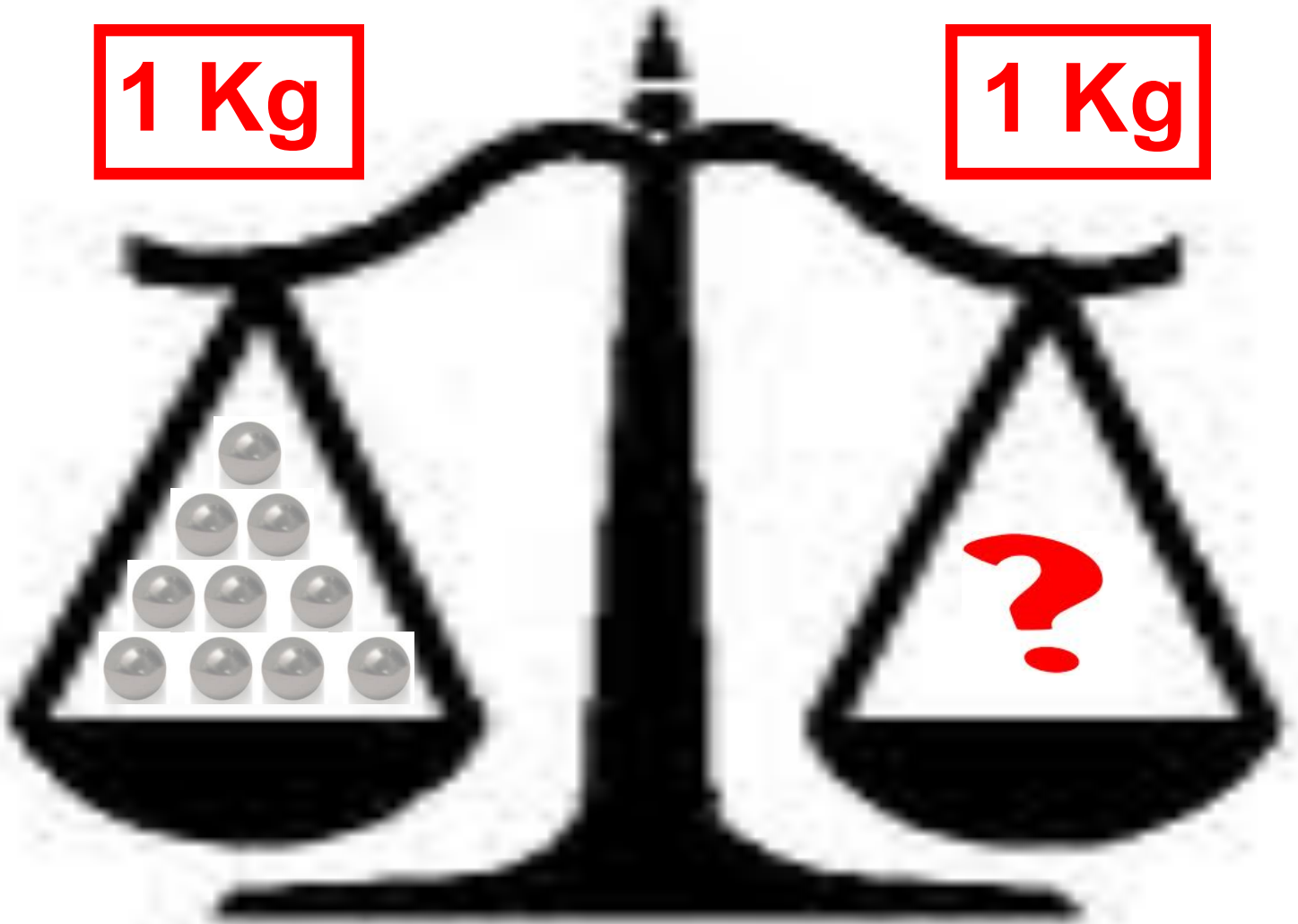
The osmotic pressure of a solution depends on the **NUMBER** of osmotically active particles/unit volume.

Each protein fraction exerts an osmotic pressure which is

- (i) directly related to its **CONCENTRATION** in the plasma
- (ii) inversely related to the **MOLECULAR WEIGHT** of that protein

1 Kg

1 Kg




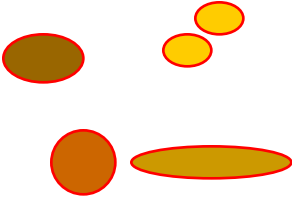
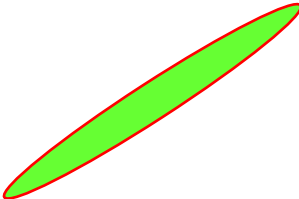
Steel Ball



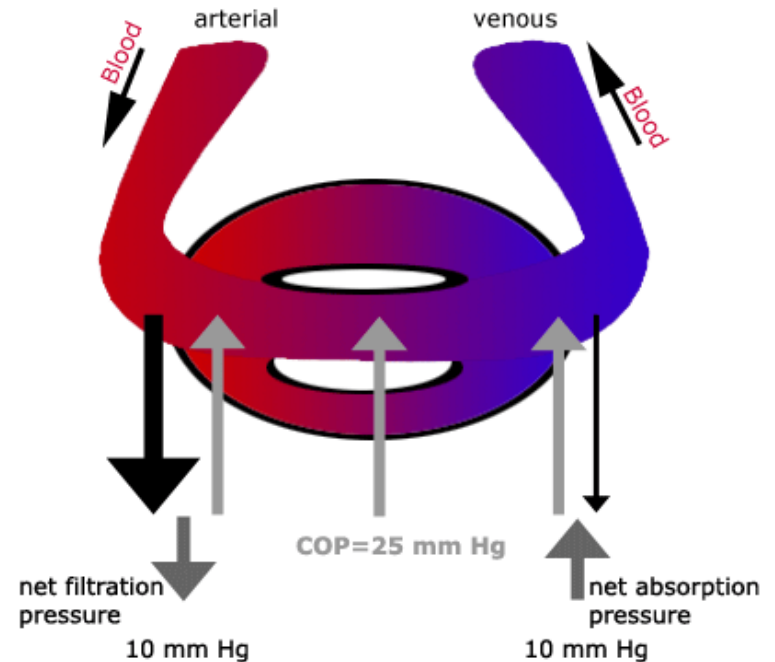
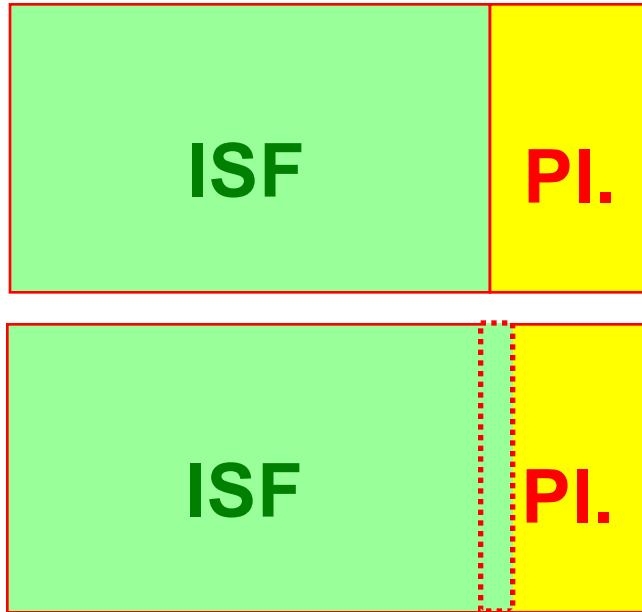
Feather

You need MANY MORE feathers than steel balls!!!

Plasma Protein Properties

Protein	Shape	Molec.Wt (K)	Conc'n (g%)	COP (mm Hg)
Albumin		69	4	~20
Globulins		90-800	2.7	~ 5
Fibrinogen		350	0.3	<1

EDEMA – accumulation of excess fluid in the interstitial spaces



Under which conditions can edema develop?

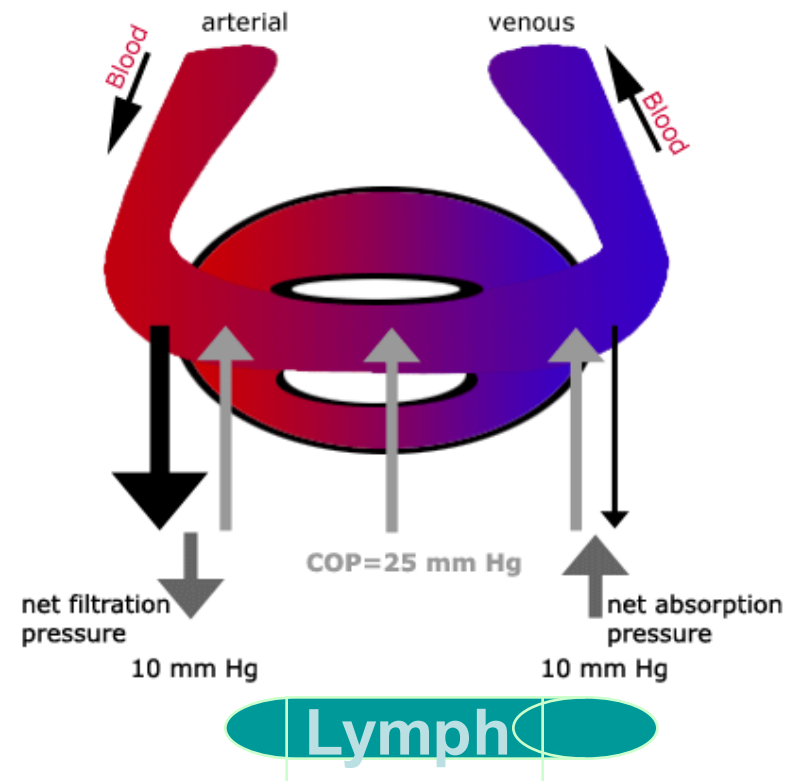
Factors leading to EDEMA

↑ 1. Hydrostatic Pressure

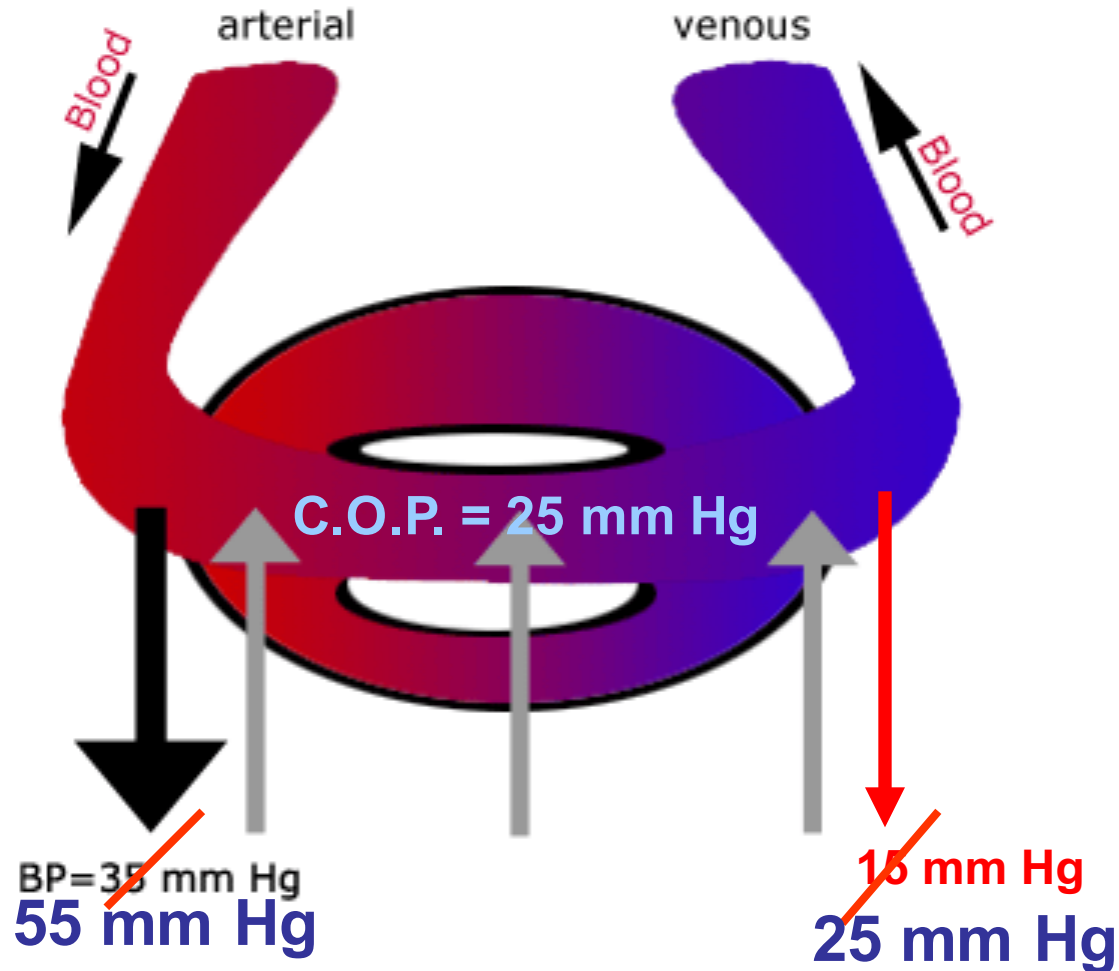
↓ 2. C.O.P.

↑ 3. Capillary Permeability

X 4. Lymphatic Drainage



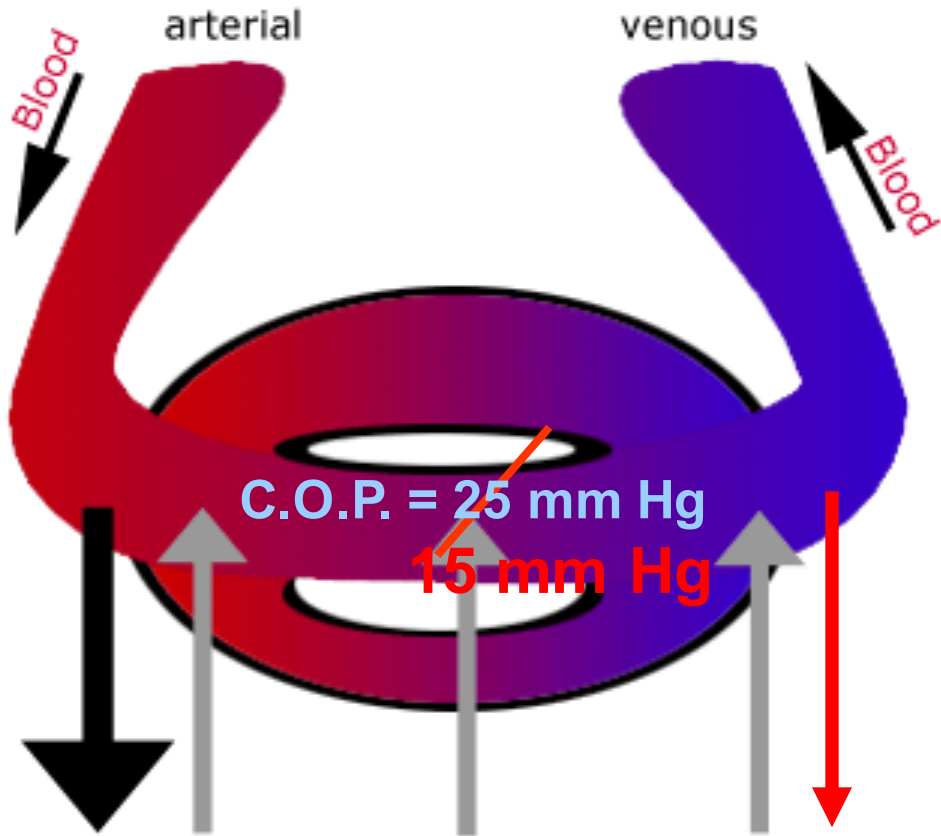
INCREASED HYDROSTATIC PRESSURE



NET FILTRATION
30 mm Hg

NET ABSORPTION
0 mm Hg

DECREASED C.O.P.



BP=35 mm Hg

NET FILTRATION
20 mm Hg

15 mm Hg

NET ABS.
0 mm
Hg

DECREASED C.O.P.



KWASHIORKOR

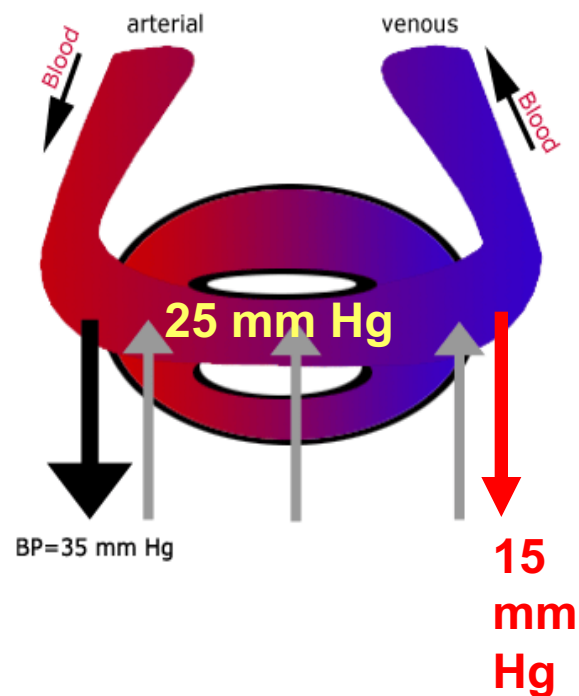
[Severe Protein Malnutrition]

Increased Capillary permeability

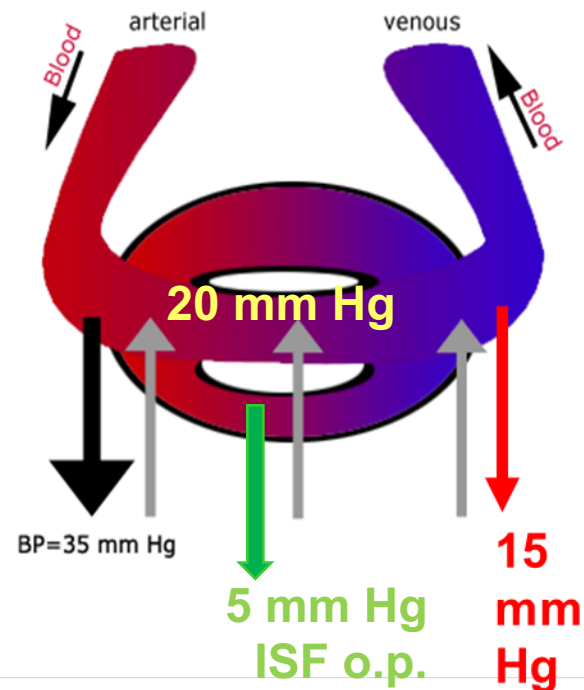
Normally, there is very little protein in the ISF

If the capillary wall becomes more permeable, some of the plasma proteins escape into the ISF where they can exert an oncotic effect

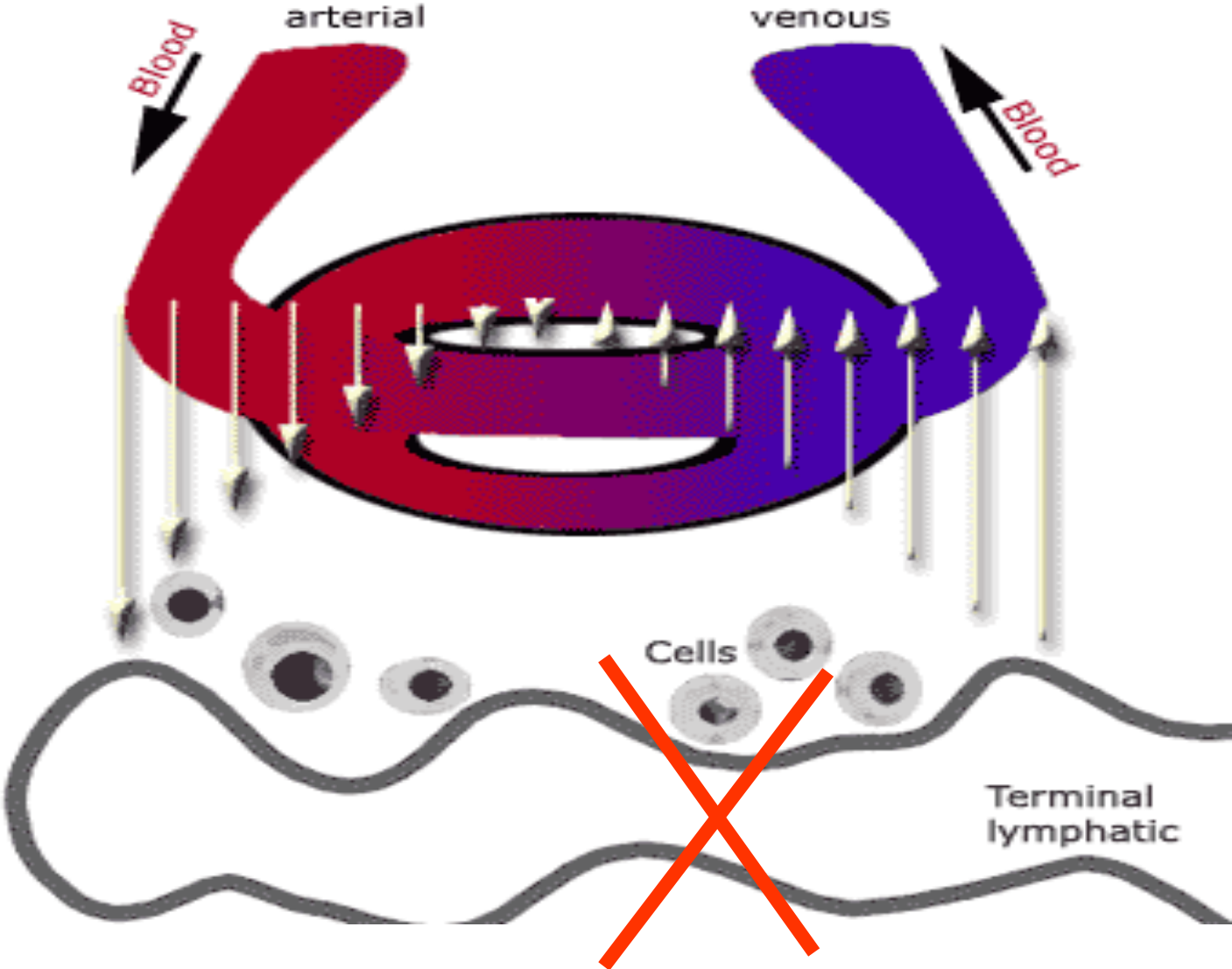
Normal permeability?



Abnormal permeability?



Obstruction of Lymphatic Drainage



OBSTRUCTED LYMPHATIC DRAINAGE



ELEPHANTIASIS

[blockage of lymphatic drainage resulting from parasite (*Filaria nematode*) infestation]

Role of Plasma Proteins

1. Major role in determining **distribution** of fluid between the **plasma** and the **ISF** compartments by controlling **transcapillary dynamics**

2. Contribute to the **viscosity** of **plasma**

(Viscosity is a contributing factor to the maintenance of blood pressure)

3. Contribute to the **buffering** power of **plasma**

Normal pH range ~7.4

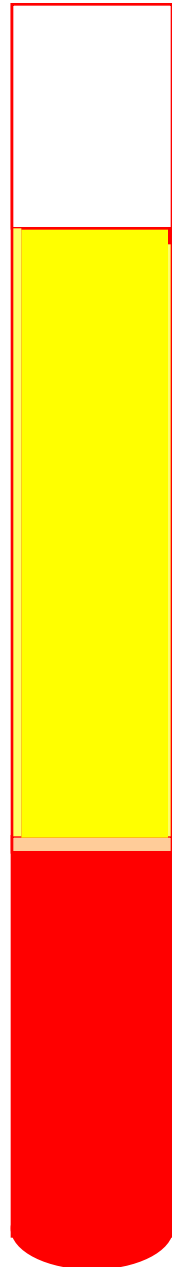
SPECIFIC PLASMA PROTEIN FUNCTIONS

- (i) **Fibrinogen** and **some globulins** are essential to clotting
- (ii) **γ - globulins** (Immunoglobulins) provide specific resistance to infection
- (iii) **Albumin** and **some globulins** act as carriers for lipids, minerals, hormones

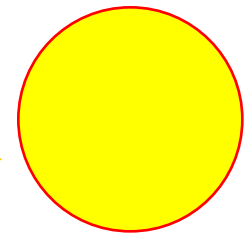
Whole
Blood



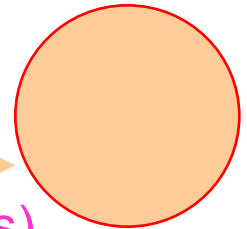
Centrifuged
Blood



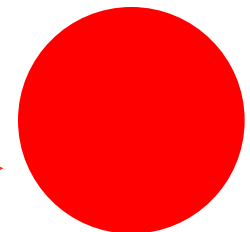
Plasma



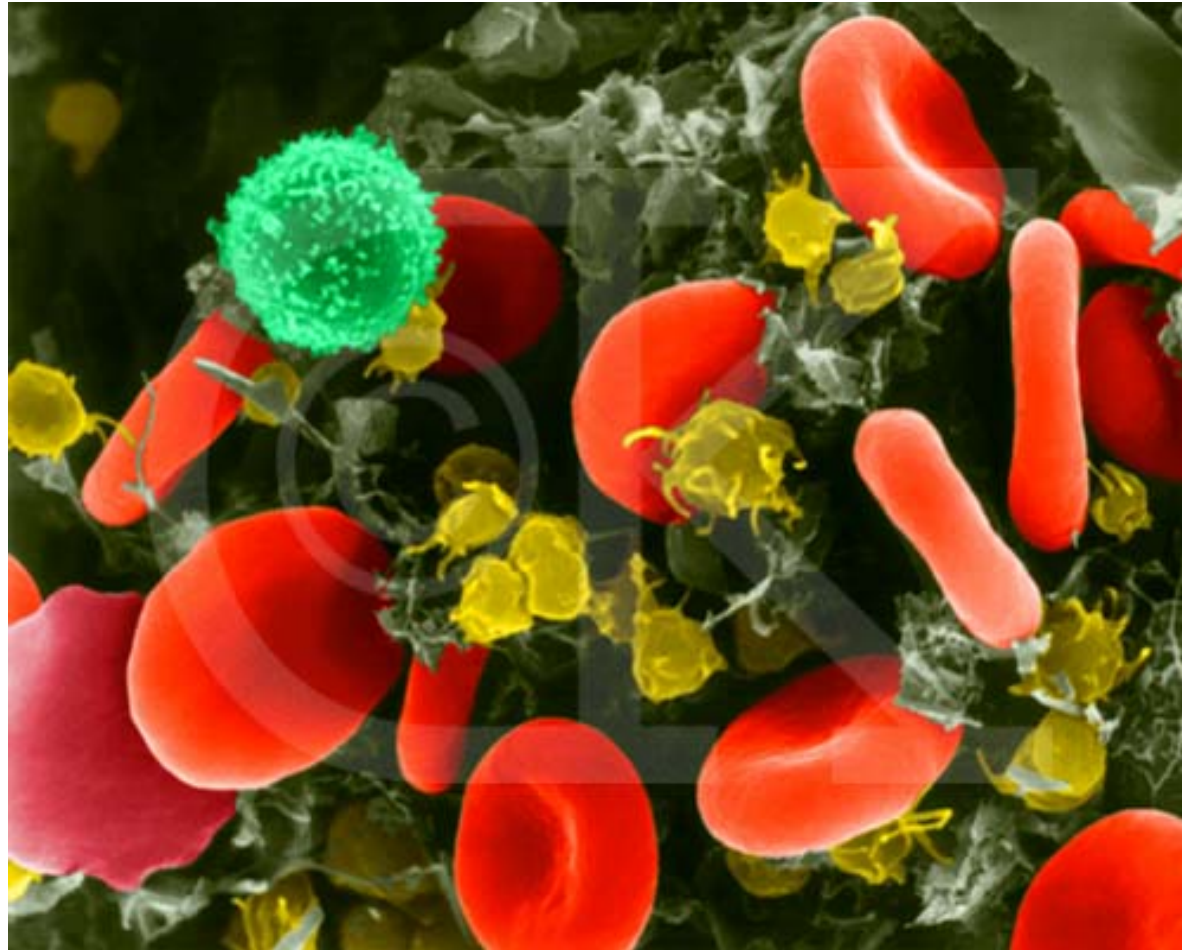
Buffy Layer
(WBCs, Platelets)



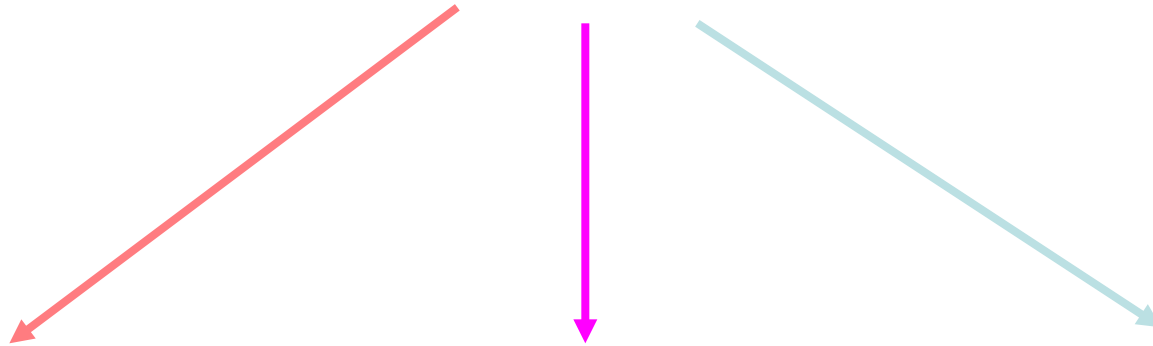
RBCs



BLOOD CELLS



BLOOD CELLS

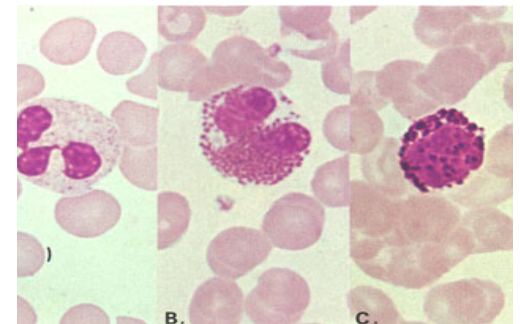
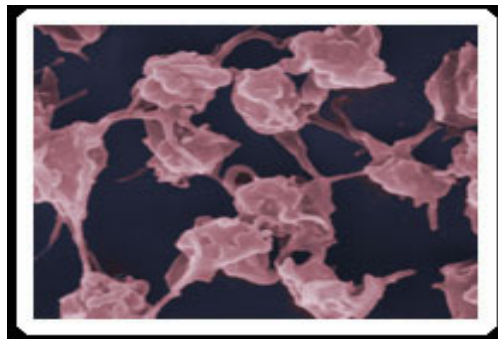
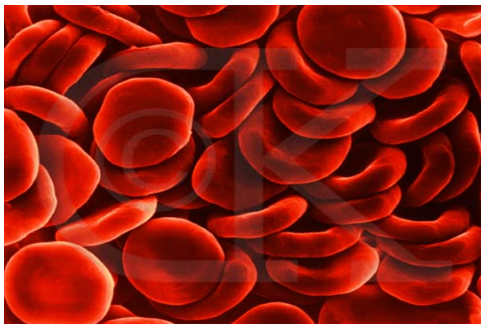


Red Blood Cells
Erythrocytes
 $5 \times 10^6/\mu\text{L}$

Platelets

$250,000-400,000/\mu\text{L}$

White Blood Cells
Leukocytes
 $8,000-10,000/\mu\text{L}$



7.2 μ

2-3 μ

10-18 μ

120 d

7-8 d

hrs-yrs

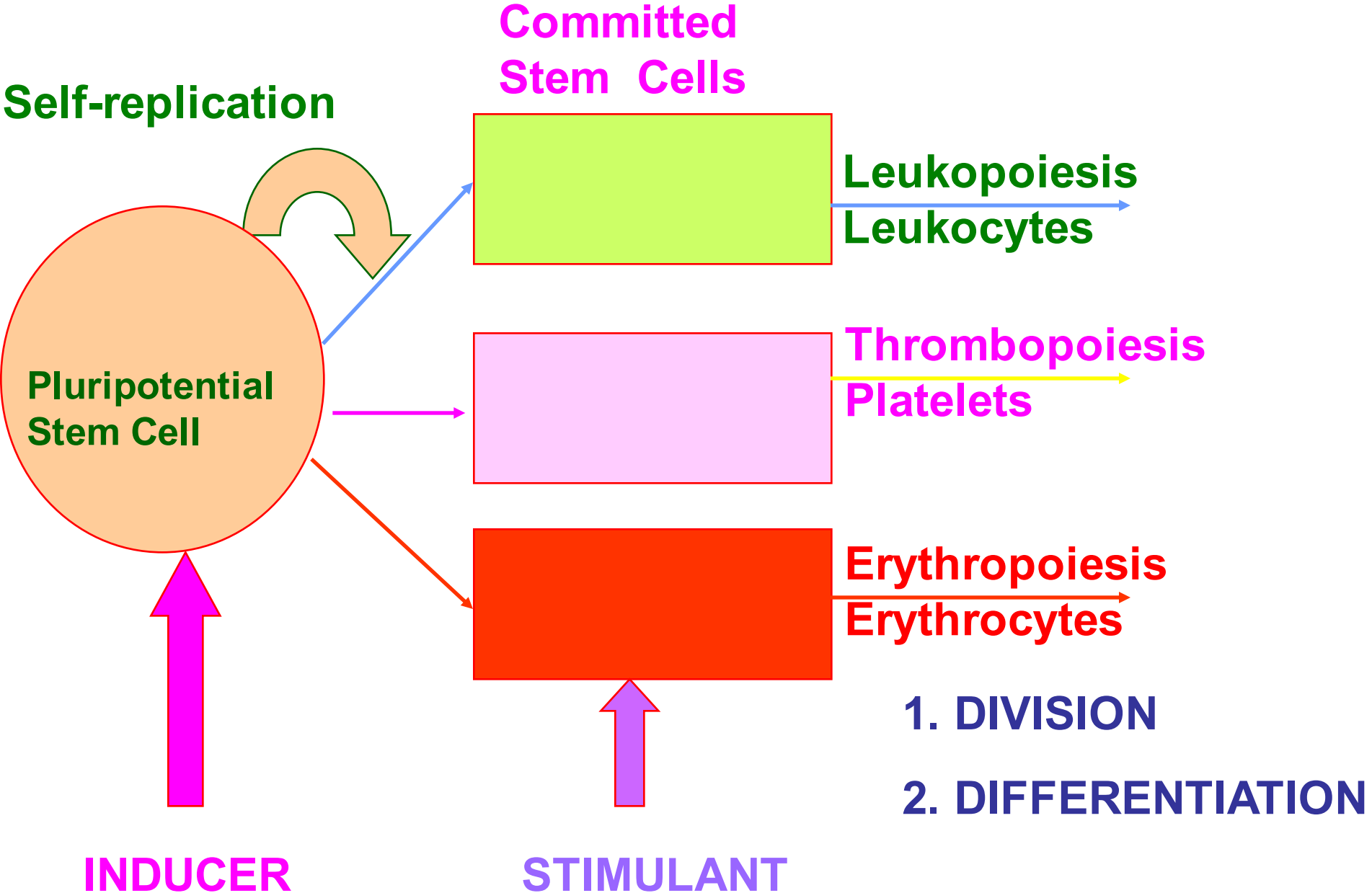
HEMATOPOIESIS = Production of Blood Cells

ERYTHROPOIESIS = Production of Red Blood Cells

THROMBOPOIESIS = Production of Platelets

LEUKOPOIESIS = Production of White Blood Cells

HEMATOPOIESIS (GENERAL PATTERN)

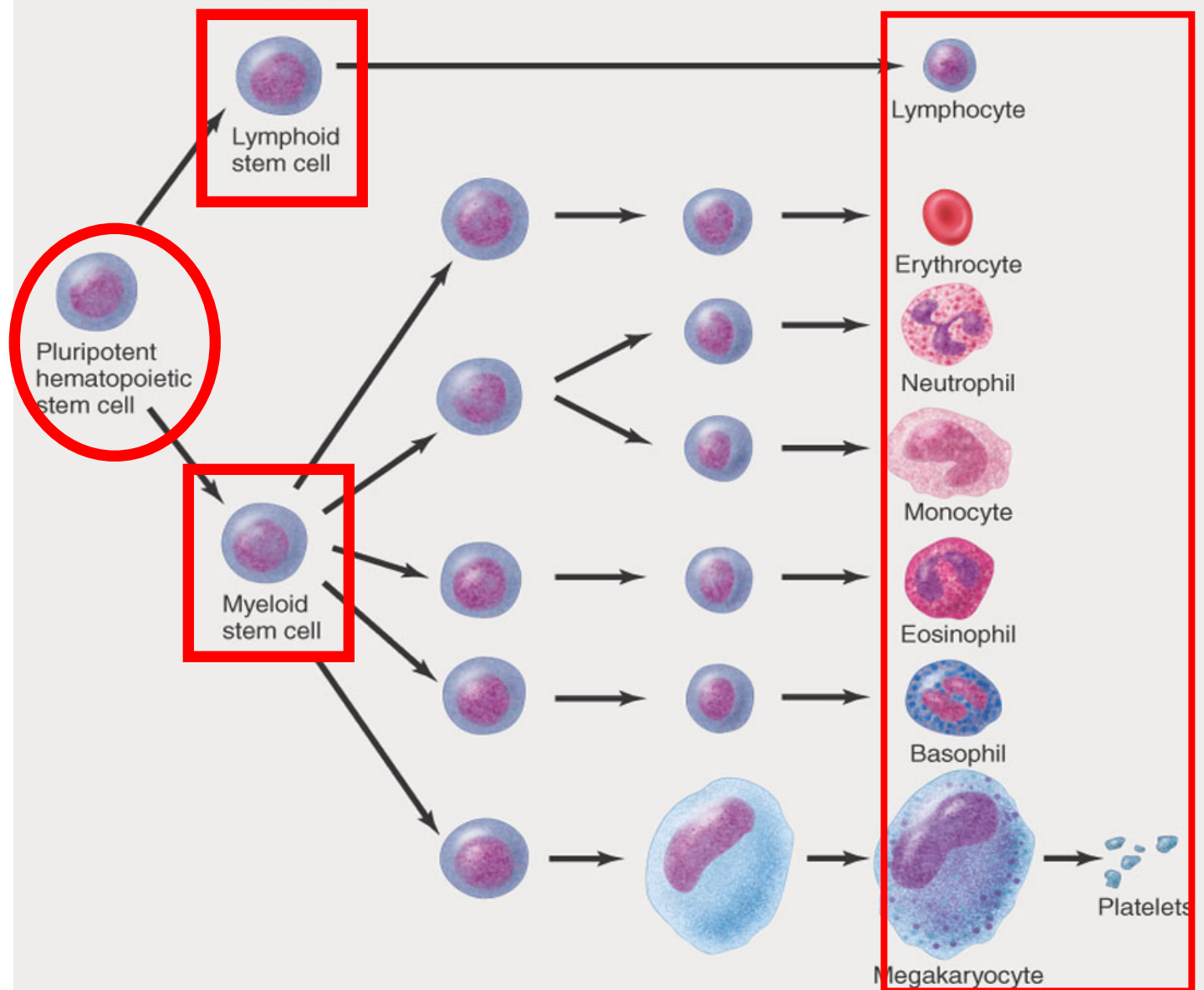


CYTOKINES – substances
(proteins or peptides) which are
released by one cell and affect the
growth, development, and activity
of another cell

The cytokines influencing the proliferation and differentiation of blood cell precursors are known as **Hematopoietic Growth Factors (HGFs)**

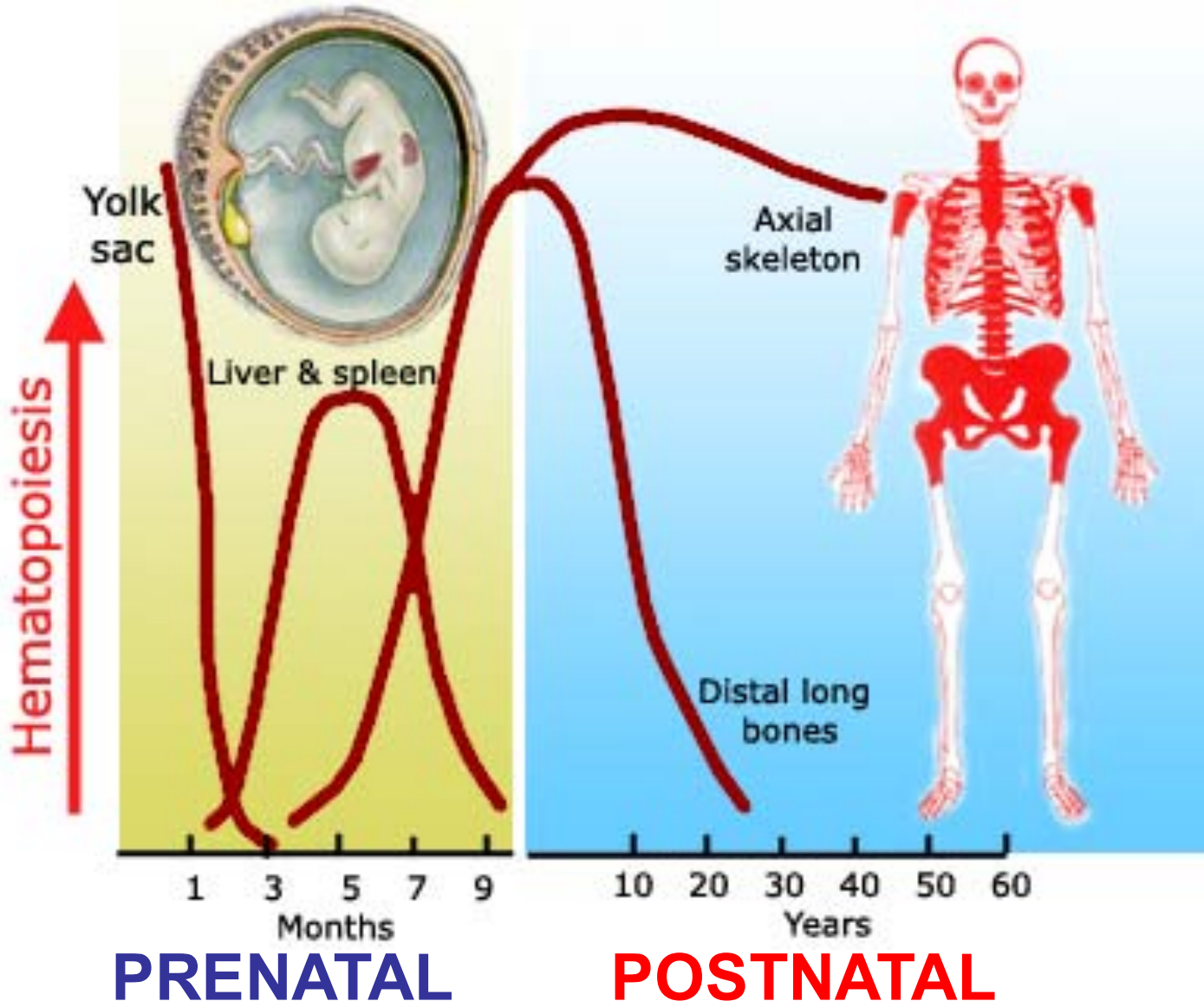
HEMATOPOIESIS—pp 421- 422¹² (428- 429)¹³Vander

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



**Injection of
Bone Marrow
Stem cells
can
reconstitute
ALL
hematopoietic
Cell Types**

SITES of HEMATOPOIESIS



Flat bones of skull, shoulder blades, pelvis, vertebrae, sternum, ribs, proximal epiphyses of long bones

FEMUR

