PHYSIOLOGY TEAM 432

LECTURE : 2

Regulation of Glomerular Filtration

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OBJECTIVES

At the end of this lecture you should be able to describe :-

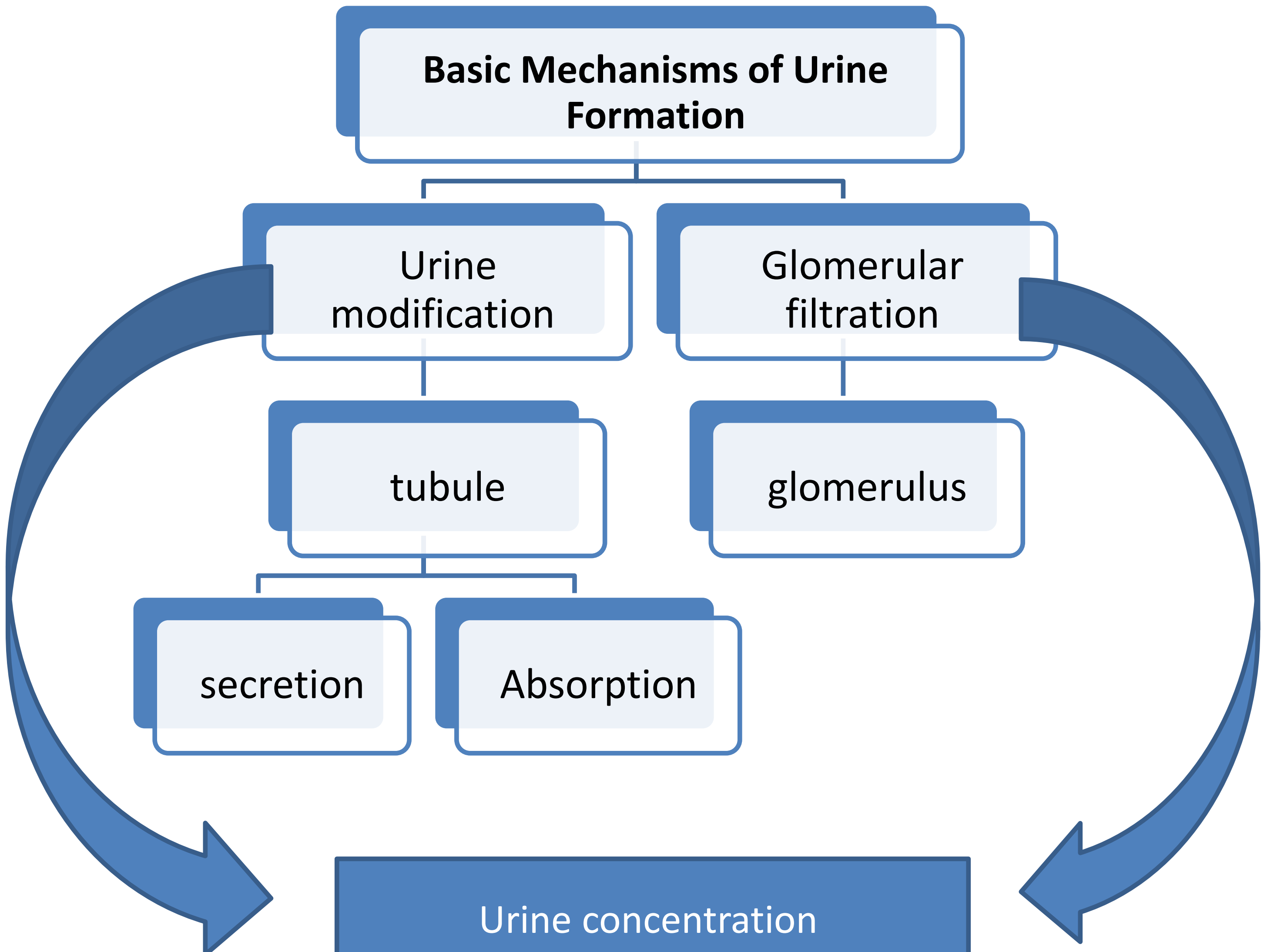
- Mechanisms of urine formation
- Composition of filtrate
- Filtration Membrane
- Filtration pressures
- Calculation of GFR, FF
- Factors affecting GFR

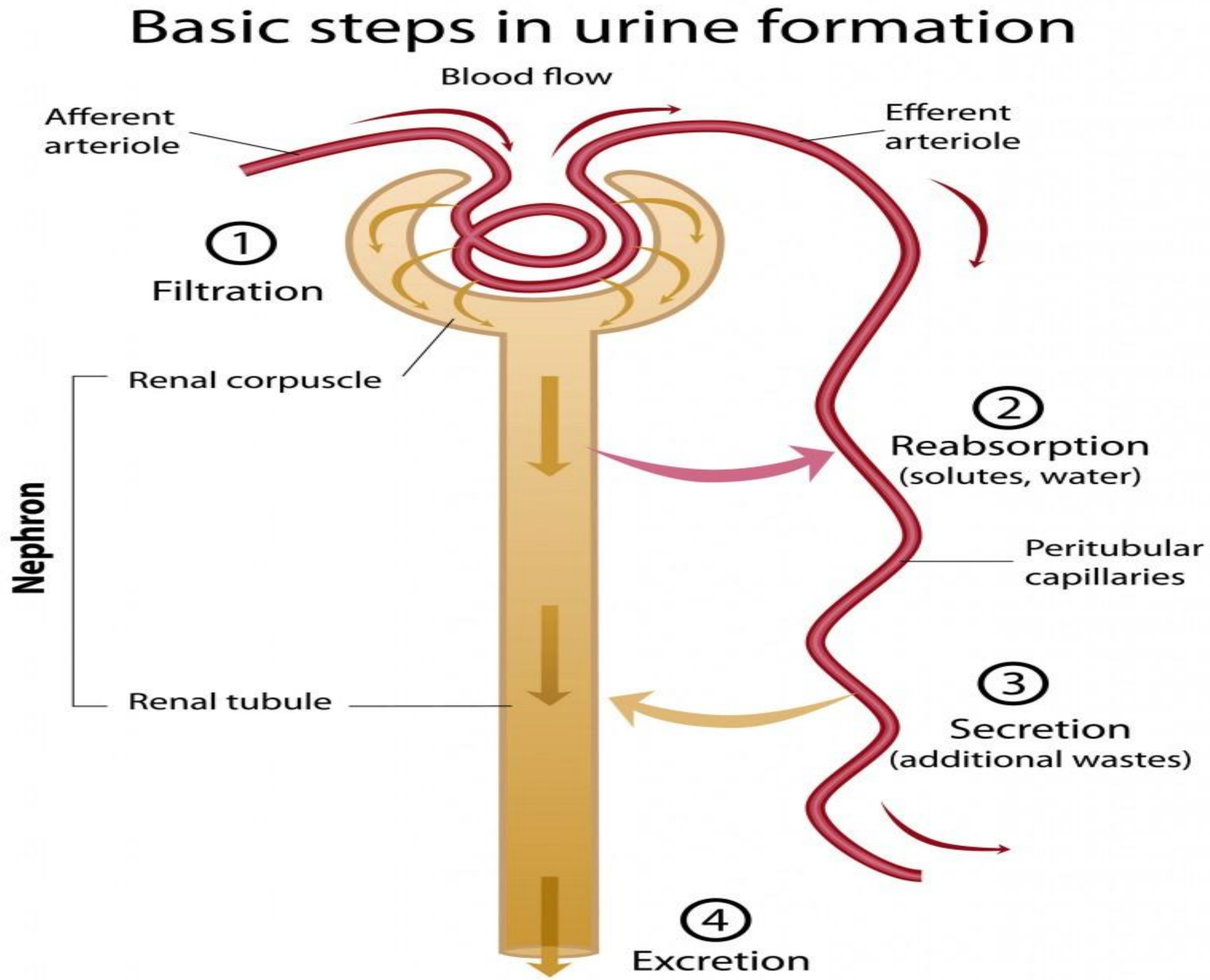
This square means for more explanation ☺

MIND MAP

- **Urine formation**
  - Glomerular filtration
  - Tubular reabsorption
  - Tubular secretion
  - Urine concentration
- **Composition of filtrate**
  - Same as plasma except for portions
- **Filtration Membrane**
  - 1) Endothelial layer.
  - 2) Basement membrane.(contain sailoprotein → -ve charge)
  - 3) Epithelial membrane
- **Filtration pressures**
  - Glomerular hydrostatic pressure (PGC) = 60 mmHg
  - Glomerular osmotic pressure (∏GC)= 28-36 (32) mmHg
  - Bowman hydrostatic pressure (PBS) = 18 mmHg
  - Bowman osmotic pressure (∏BS) = zero
- **Calculation of GFR, FF**
- **Factors affecting GFR**

↑ PGC	↑ GFR
↑ ∏GC	↓ GFR
↑ PBS	↓ GFR
↓ Kf	↓ GFR

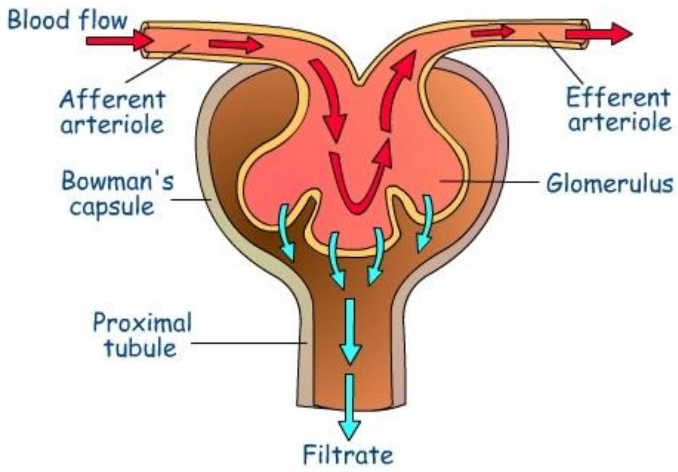

Basic Mechanisms of Urine Formation
Urine modification
Glomerular filtration
tubule
glomerulus
secretion
Absorption
Urine concentration



Basic steps in urine formation
Blood flow
Afferent arteriole
Efferent arteriole
1
Filtration
Renal corpuscle
Nephron
2
Reabsorption
(solutes, water)
Peritubular capillaries
3
Secretion
(additional wastes)
Renal tubule
4
Excretion

Glomerular Filtration:-

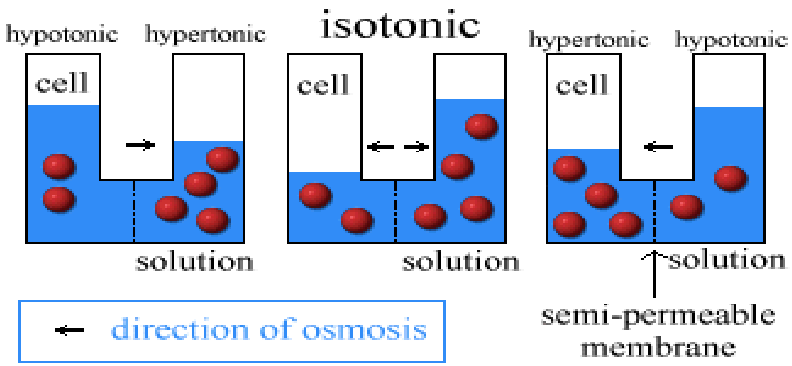
During filtration, large quantity of water and solutes pass through the filtration membrane from the blood into the glomerular capsule (Bowman's capsule)



Filtrate properties:-

- **Isotonic (~300 mosmo/l)**
- **Plasma ultrafiltration (small molecules)**
- **Composition of filtrate (same as plasma except plasma protein) :**
  - **Water**
  - **Electrolytes**
  - **Glucose**
  - **Urea**
  - **Creatinine**

Isotonic solution:
A solution that has the same salt concentration as cells and blood.



filtration membrane:-

3 layers:

1)Endothelial layer :

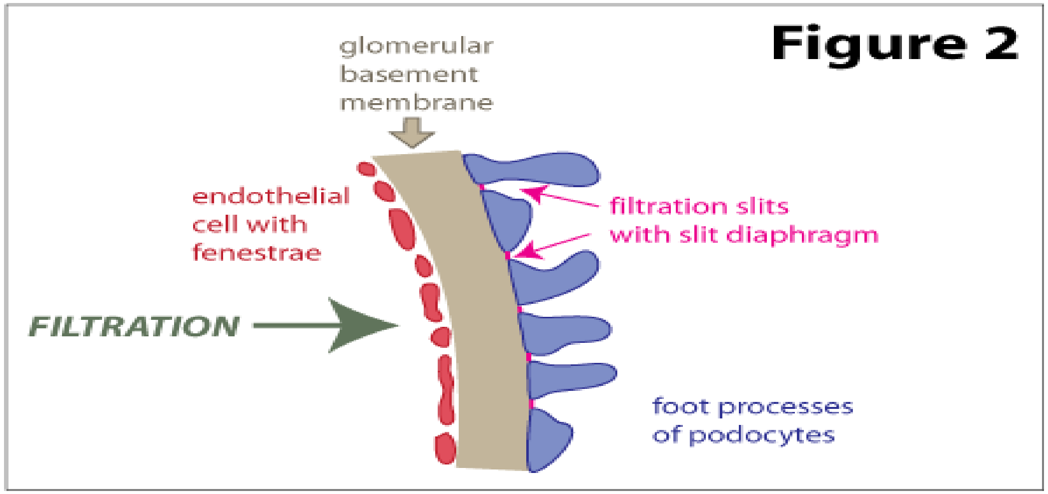
- Fenestration (pores) without diaphragm → 70-100 nm

2)Basement membrane:

- Homogenous collagenous fibers with no pores
- Negative charge ,due to → presence of negative charge protein along the membrane such as (sailoprotein)
- Contractile mesengial cells

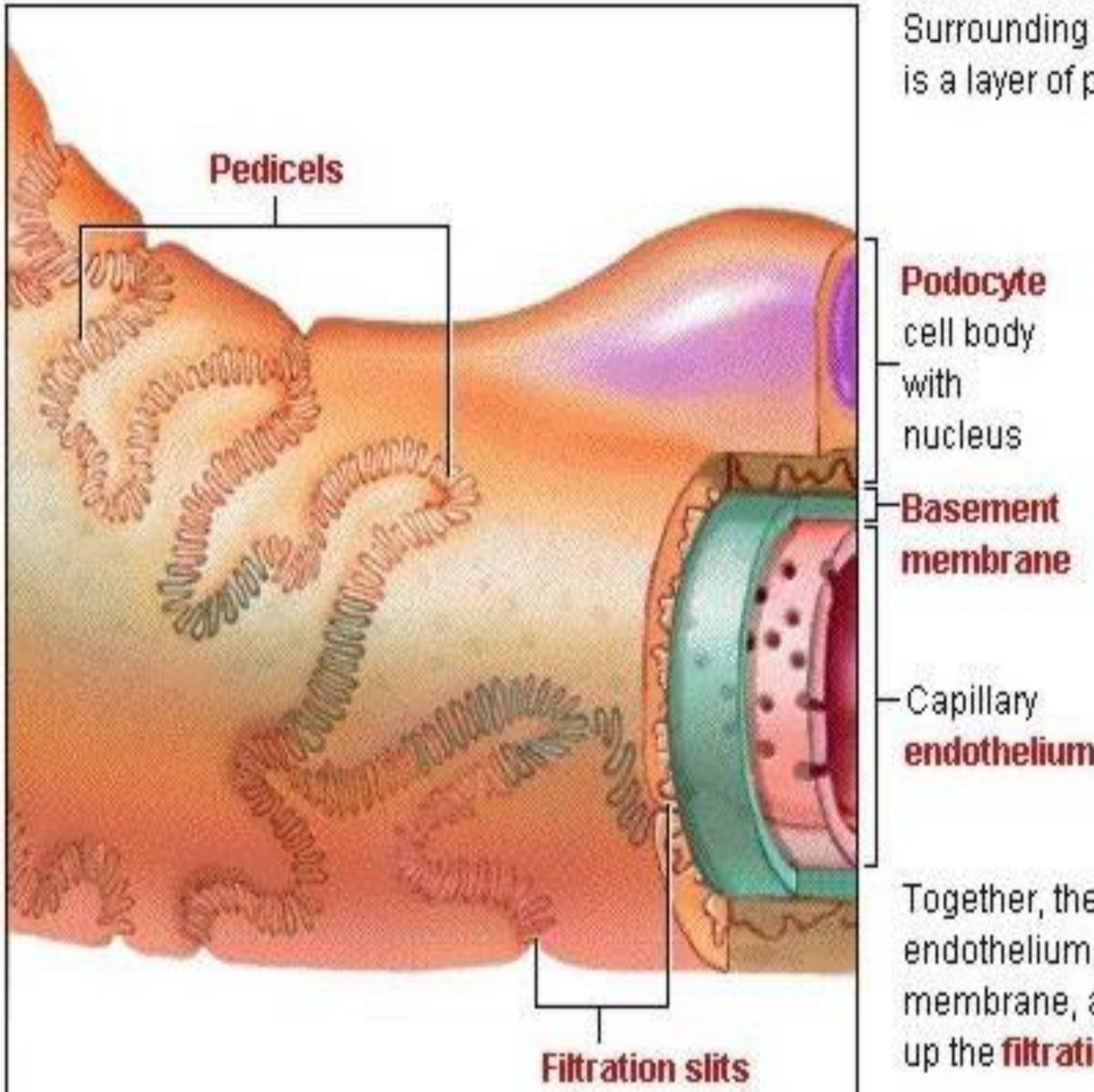
3)Epithelial membrane :

Podocytes and between each podocyte there is a slit → 25-60nm

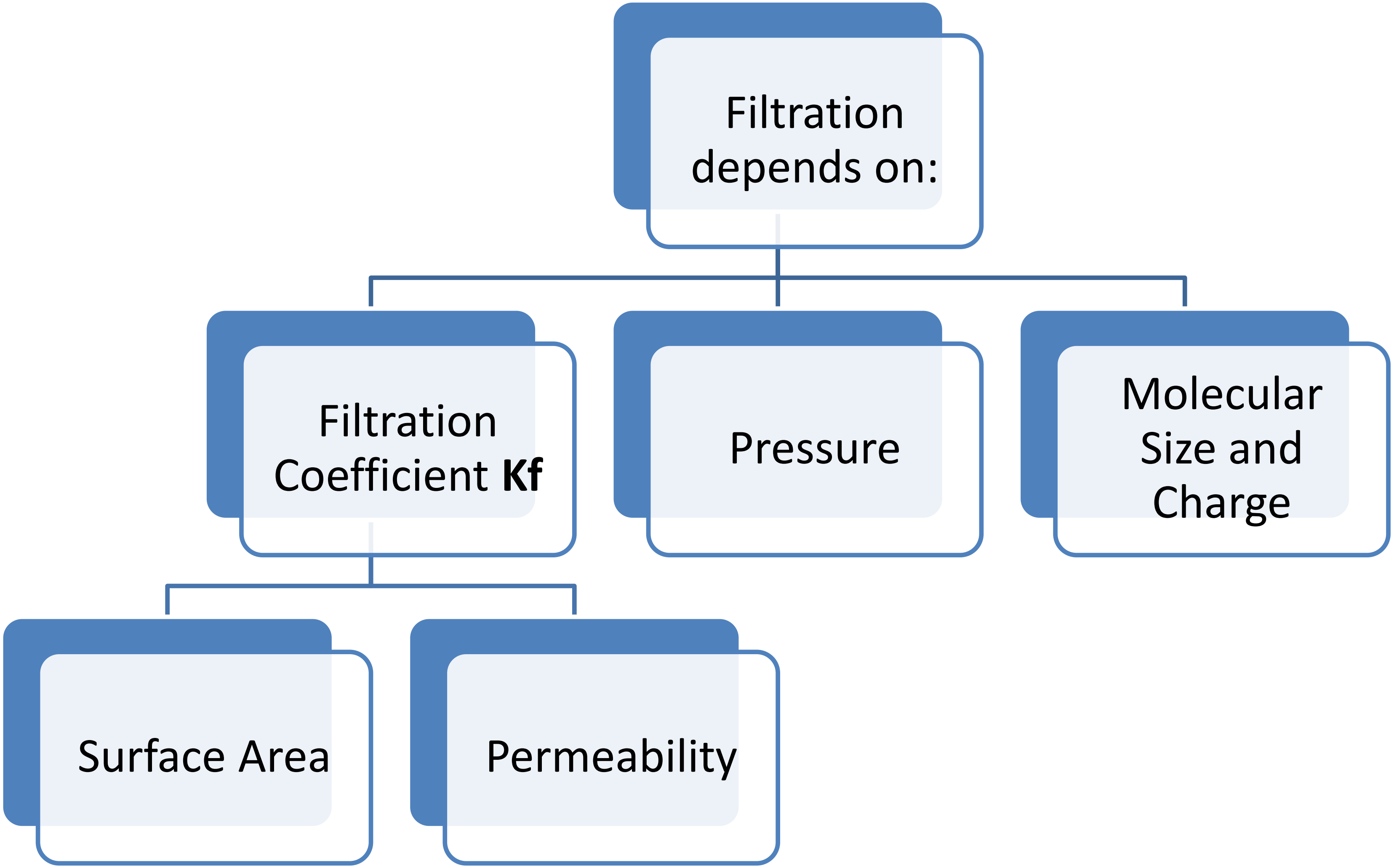


CELLULAR FEATURES OF THE RENAL CORPUSCLE

Surrounding the basement membrane is a layer of podocytes.



Together, the fenestrated capillary endothelium, basement membrane, and podocytes make up the **filtration membrane**.



Filtration depends on:
Filtration Coefficient **Kf**
Pressure
Molecular Size and Charge
Surface Area
Permeability

Filtration of Molecules:-

<u>Molecular size and charge</u> regulate filtration:

- The Molecular size is < 4nm — **<u>freely filtered</u>**
- The Molecular size is 4-8 nm — **<u>depends on the charge</u>**
  - Positive will be more filtered
  - Negative will be poorly “less” filtered
- The Molecular size is > 8 nm — **<u>not filtered</u>**

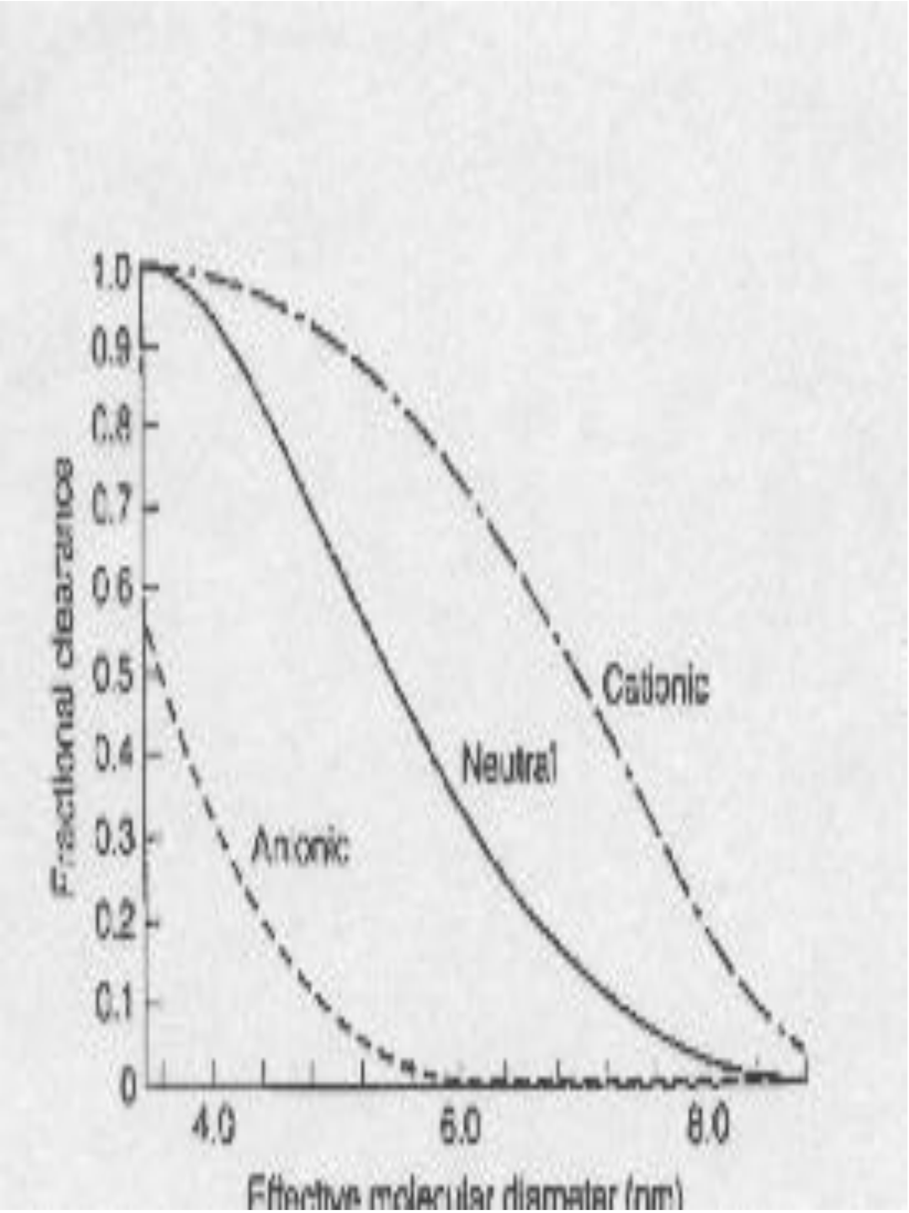
For example :-

The albumin size is 6 nm → should be filtered , but it can't be filtered because of it's negative charge

But WHY ??

Because the membrane also have a negative charge (basement membrane)

So there won't be an attractive force between them → no filtration



Filtration pressure:-

- Pressure that moves plasma out of the glomerulus capillary into the Bowman capsule space
- Four different pressures affect filtration
- The algebraic sum of these pressures is the driving pressure for filtration

These different pressures are :-

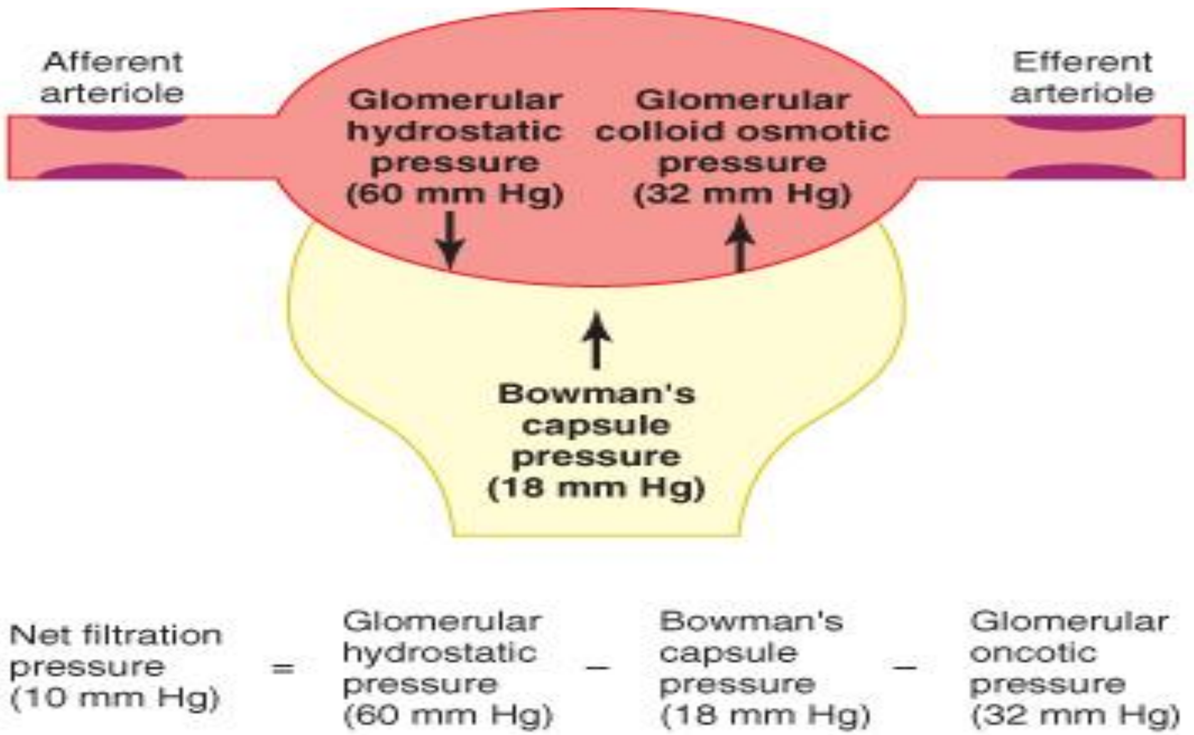
Glomerular hydrostatic pressure (PGC)	Bowman hydrostatic pressure (PBS)	Glomerular osmotic pressure (∏GC)	Bowman osmotic pressure (∏BS)
Favors filtration	Opposes filtration	Opposes filtration	No effect
60 mmHg	18 mmHg	(28 – 36 mmHg) Average : 32 mmHg	Zero
Due to blood in the capillary "systemic pressure"	Due to filtered fluid in the capsule	Due to plasma protein in the capillary	Due to absent of plasma protein in the capsule
Remain constant	Remain constant	Is not constant	Remain constant

Calculation of net filtration :-

1) net filtration : Kf × (PGC -PBS) - (∏GC-∏BS) = 60-18-32= 10 mmHg

2) Kf: Filtration coefficient depend on Filtration membrane
- Surface area
- Permeability

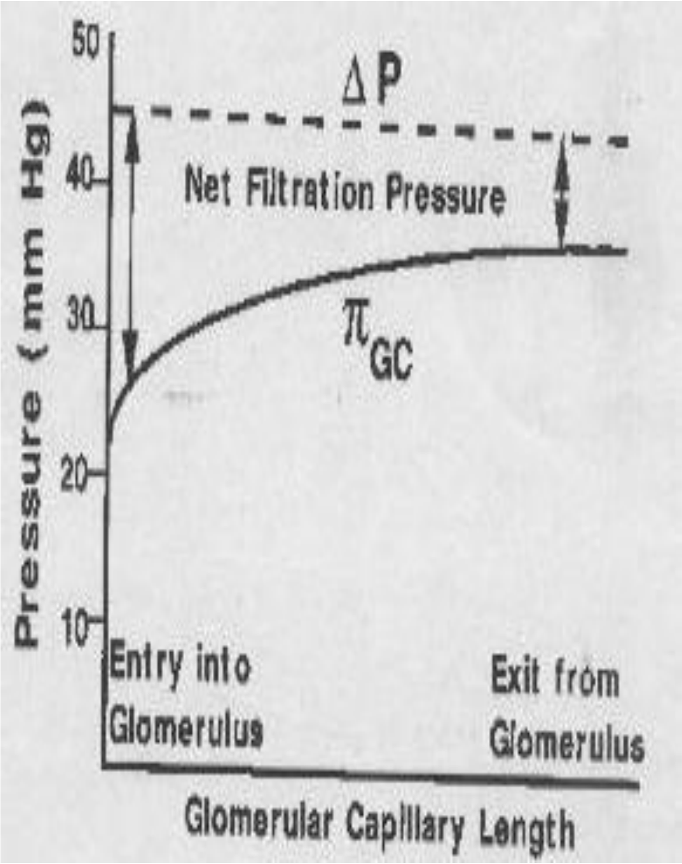
3) Glomerular permeability >> 100 x skeletal capillaries permeability



Net filtration pressure decreases as passing along the glomerular Capillary

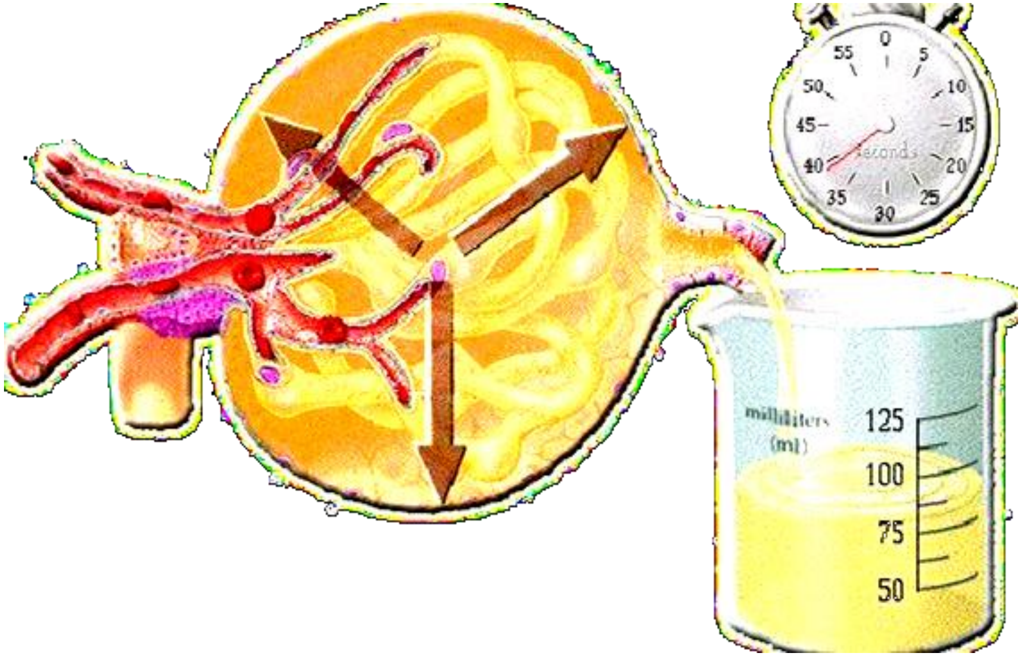
Why??

Only plasma is filtrated → increase plasma protein conc. → high oncotic pressure → decrease net filtration pressure



:Glomerular filtration rate:

- Amount of plasma filtered by all nephrons in both kidneys/unit time
- 125 ml/min
- Kidney function test
- Variation in GFR between different species depend on numbers of nephrons



Measurement of GFR:

■ Test procedure :

- Intravenous loading dose of (X substance ☺) followed by intravenous infusion of (X substance ☺) to maintain plasma level constant
- Urine is collected for 15 or 20 min, to measure (X substance ☺) concentration in urine and urine volume
- Blood sample is taken half way of urine collection to measure (X substance ☺) concentration

Not important

■ Characteristic of substance used (X substance ☺) :

- Freely filtered (not reabsorbed or secreted)
- Not metabolized by the kidney
- Not toxic and stable
- Not bound to plasma protein
- Does not change renal plasma flow

(X substance ☺)= **Inulin**

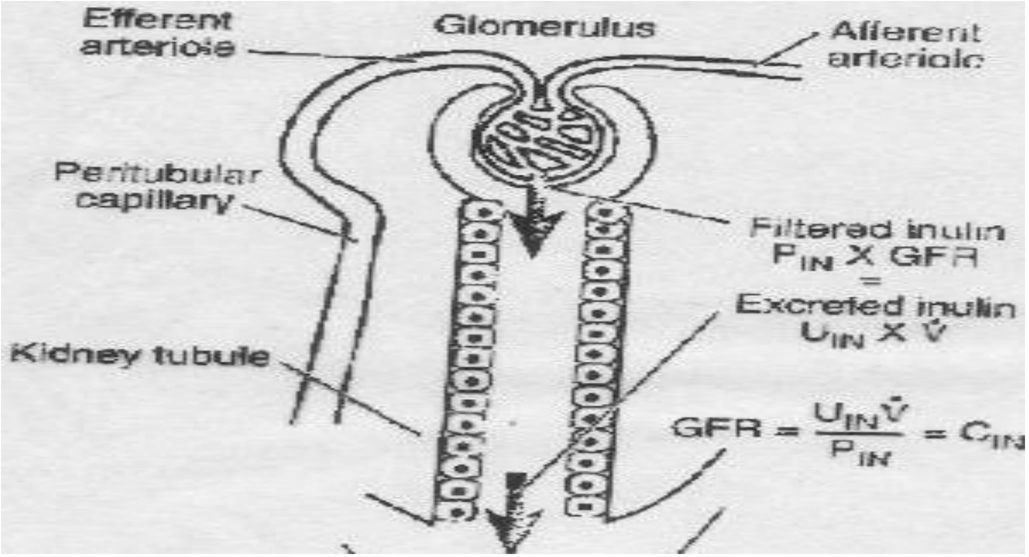
Calculation of GFR:-

The amount of inulin excreted = Uin X Uv

The amount of inulin filtered = Pin X GFR

As inulin is not reabsorbed or excreted both quantity are equal → Pin X GFR =Uin X Uv

So…. **GFR** = $\frac{\text{Uin x Uv}}{\text{Pin}}$ **ml/mil**



Uin: Inulin conc. in Urine.
Uv: Urine Volume
Pin: Inulin conc. in Plasma

Other calculation Of GFR:-

GFR= Kf $\times$ net filtration pressure

- GFR = 12.5 x 10 = 125 ml/min
- Kf α GFR (low Kf " in diabetes" → low GFR)

Filtration fraction:-

The fraction of renal plasma flow that is filtered

$$\frac{GFR}{RPF} = \frac{125}{625} = 0.2 \times 100 = 20\%$$

$$Kf = \frac{GFR}{net\ filtration.P}$$

$$12.5 = Kf = \frac{125}{10}$$

Filtration fraction:-
The portion of blood plasma that enters the kidney and filters through the renal glomerular membranes

Factors affecting GFR:-

Changes in PGC	PGC ∝ GFR	Systemic blood pressure
		afferent vasoconstriction → ↓ PGC → ↓ GFR
		Efferent vasoconstriction → ↑ PGC → ↑ GFR
Changes in ∏GC	∏GC 1/∝ GFR	hemoconcentration (dehydration) → ↑ plasma protein concentration → ↑ ∏GC → ↓ GFR
		High filtration fraction → ↑ ∏GC → ↓ GFR
Changes in PBS	PBC 1/∝ GFR	due to obstruction to outflow → ↑ PBS → ↓GFR 1-urethral obstruction 2- kidney edema 3- stone
Changes of filtration coefficient	Kf ∝ GFR	↑ glomerular capillary permeability → ↑ *GFR*
		↑ in surface area → ↑ GFR
Changes in renal blood flow	↑ *RBF* into Glomerulus → ↑ GFR ↓ *RBF* into Glomerulus → ↓ GFR	

SUMMARY

- Mechanisms of Urine Formation: Glomular filtration, tubular secretion&absorbotion and urine concentration.
- Glomular filtrate is isotonic solution same as Plasma except portions (it has negative charge).
- Filtration membrane : endothelial membrane (inner layer), basement membrane (has sailoprotein → -ve charge and epithelial membrane (outer layer).
- Molecular size and charge regulate filtration .
- Net filtration pressure = Kf (PGC -PBS) - (∏GC-∏BS) = 60-18-32= 10 mmHg
- GFR is a function test and it's measures by several mechanisms:

  1- inulin clearance = Uin x Uv / Pin

  2- GFR= Kf × net filtration pressure.
- Filtration fraction : The portion of blood plasma that enters the kidney and filters through the renal glomerular membranes $= \frac{GFR}{RPF} = \frac{125}{625} = 0.2 \times 100 = 20\%$
- Factores affecting GFR are in the previous slide. (see GUYTON page 314, 315).

Some Questions

Q1: Which of the following events would NOT be expected to decrease glomerular filtration rate?

a) Urinary tract obstruction by renal stones.
b) Hyperalbuminemia (i.e., higher than normal serum albumin concentration).
c) Decreased filtration coefficient (Kf) secondary to glomerular disease
d) Increased activity of the renal sympathetic nerves.
e) Volume expansion with an accompanying increase in arterial blood pressure.

Q2: If the glomerular filtration was zero, how would the kidneys be affected?

a) Kidney function would be unaffected.
b) The kidneys would redirect filtrate flow through the vasa recta.
c) The kidneys would not function.
d) The afferent arteriole would flow blood directly into the proximal convoluted tubule.

Some Questions

Q3 :What are ways the body could increase glomerular filtration rates in a human kidney? Choose all that apply.

a) By dilating the afferent arteriole.
b) By constricting the efferent arteriole
c) By dilating the efferent arteriole.
d) By constricting the afferent arteriole.

Q4:What is the best substance used for measurement of GFR ?

A) Glucose
B) Urea
C) Albumin
D) Inulin

Some Questions

Q5: Whish one of the following pressures is not constant (in physiological conditions)?

A) Glomerular hydrostatic pressure (PGC)
B) Glomerular osmotic pressure (∏GC)
C) Bowman hydrostatic pressure (PBS)
D) Bowman osmotic pressure (∏BS)

The answers :

Q1: E
Q2: C
Q3: A,B
Q4: D
Q5: B

THE END

If there are any problems or suggestions
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THANK YOU