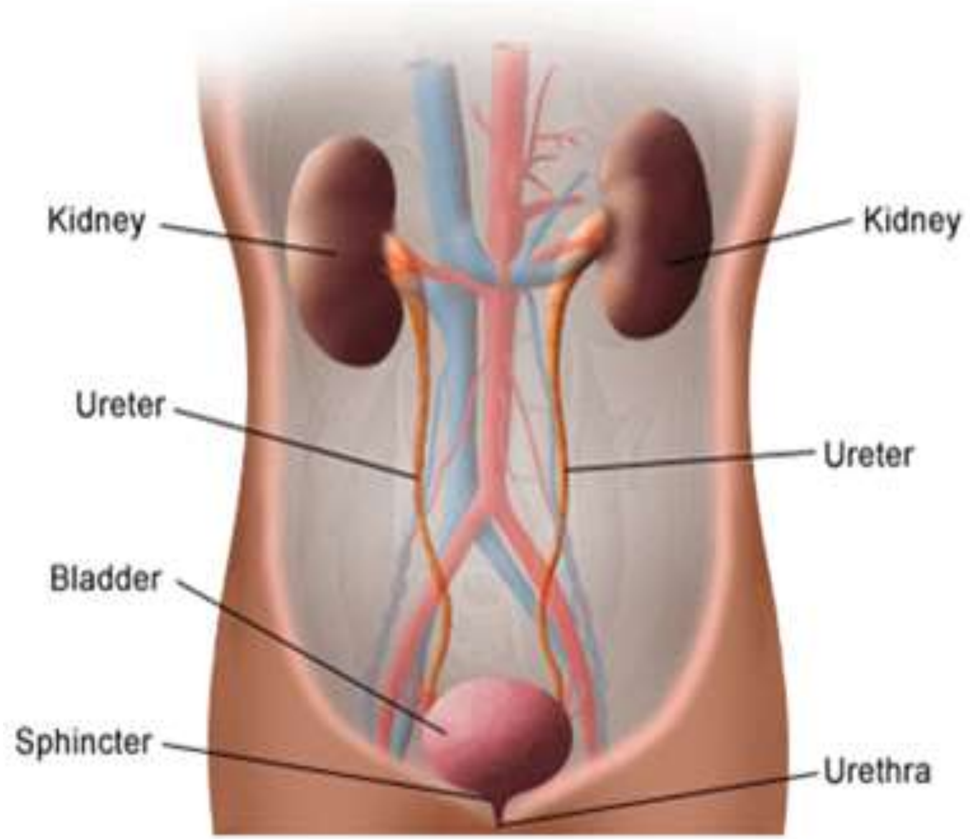
LECTURE NO (2)

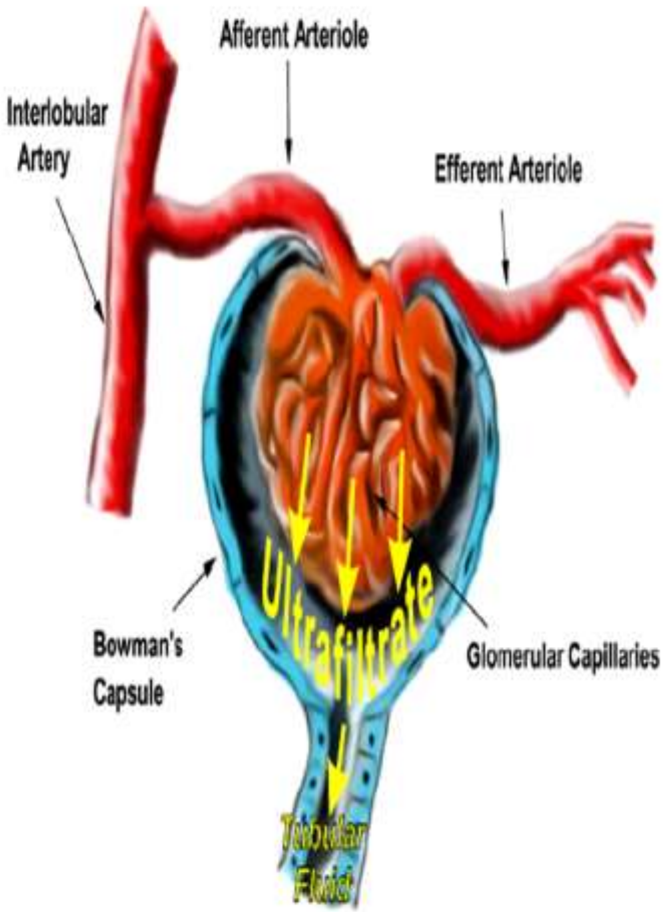
# Renal Physiology

# Glomerular filtration rate (GFR)



# The glomerulus

- Is a tuft of capillaries enclosed within a Bowman capsule.
- It is supplied by an afferent arteriole and drained by an efferent arteriole.
- 200µm in diameter.



# Function of glomeruli

- **Act as ultra filters (fine filters) to plasma.**
- **Allow bulk flow of water & dissolved substances (Na+, K+, glucose, urea ).**
- **Prevent filtration of plasma proteins.**
- **Boman,s capsule fluid is a filtrate of plasma called glomerular filtrate.**

# Glomerular filtration

- ***Definition:-***

  - **It is the transport of fluid and crystalloid from glomerular capillaries to Bowman's space.**

- **The filtrate is similar to plasma. (does not contain proteins)**

# Glomerular filtration rate

- The rate of glomerular filtration is known as the glomerular filtration rate (GFR).
- The GFR is the measurement of the kidneys ability to filter plasma
- Normal GFR= 125ml/min ( 7.5L/h or 180L/d) in average adult male. it is less in females (by about 10%)
- 99% or more of the filtered is normally  reabsorbed

# Mechanism of GF

- ***Factors governing filtration across the glomerular capillaries:***

1. **Surface area of filtration membrane (SA).**
2. **The permeability of the filtration membrane.**
3. **The hydrostatic and osmotic pressure gradients across the capillary wall.**

# The filtration membrane

- **Passive semi-permeable membrane.**
- **Through which plasma is filtered.**
- ***Consist of 3 layers:-***

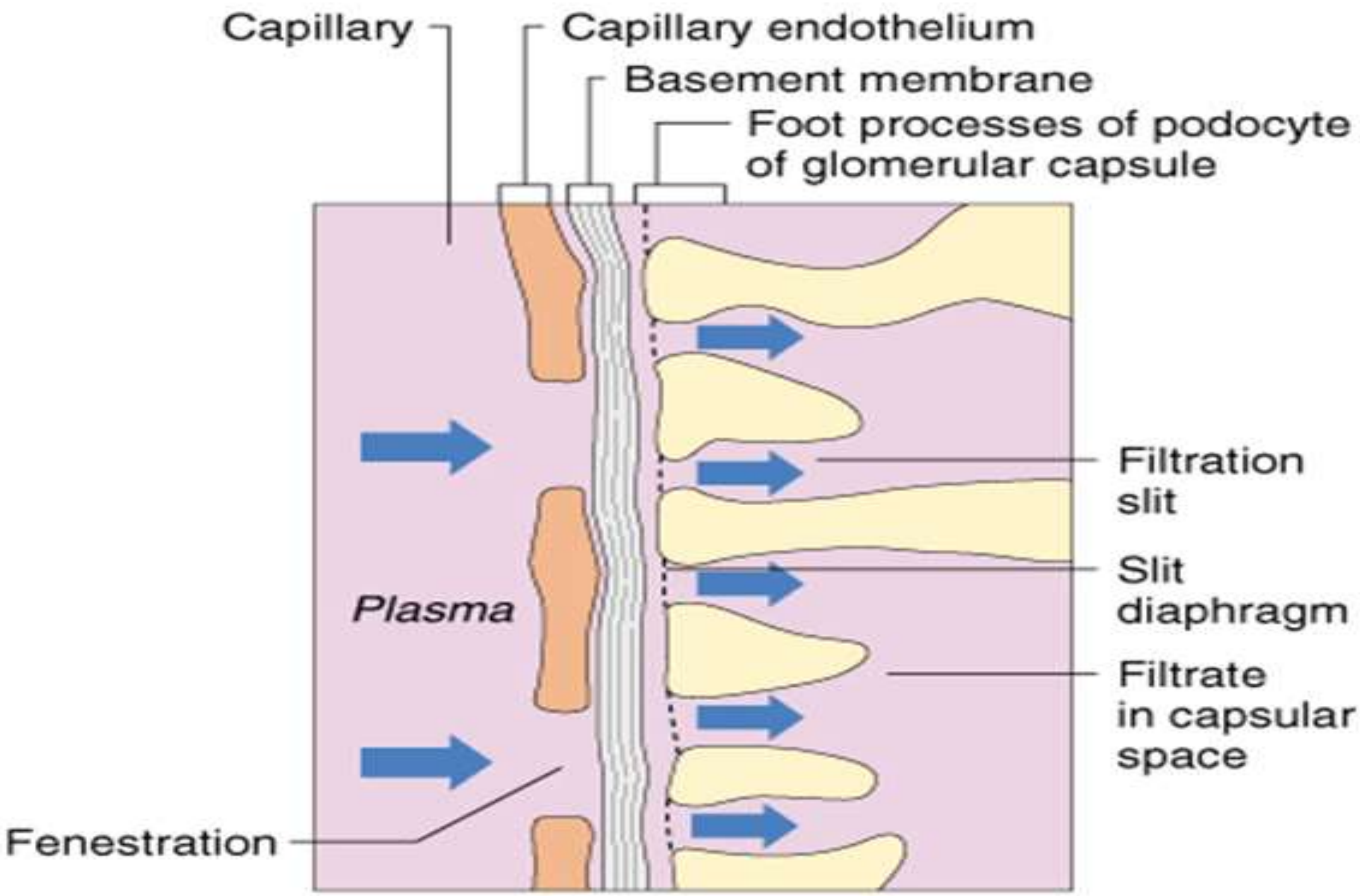
A. **Fenestrated capillary endothelium; its diameter 70-90nm.**

B. **The basement membrane: Negatively charged due to presence of sialoproteins.**

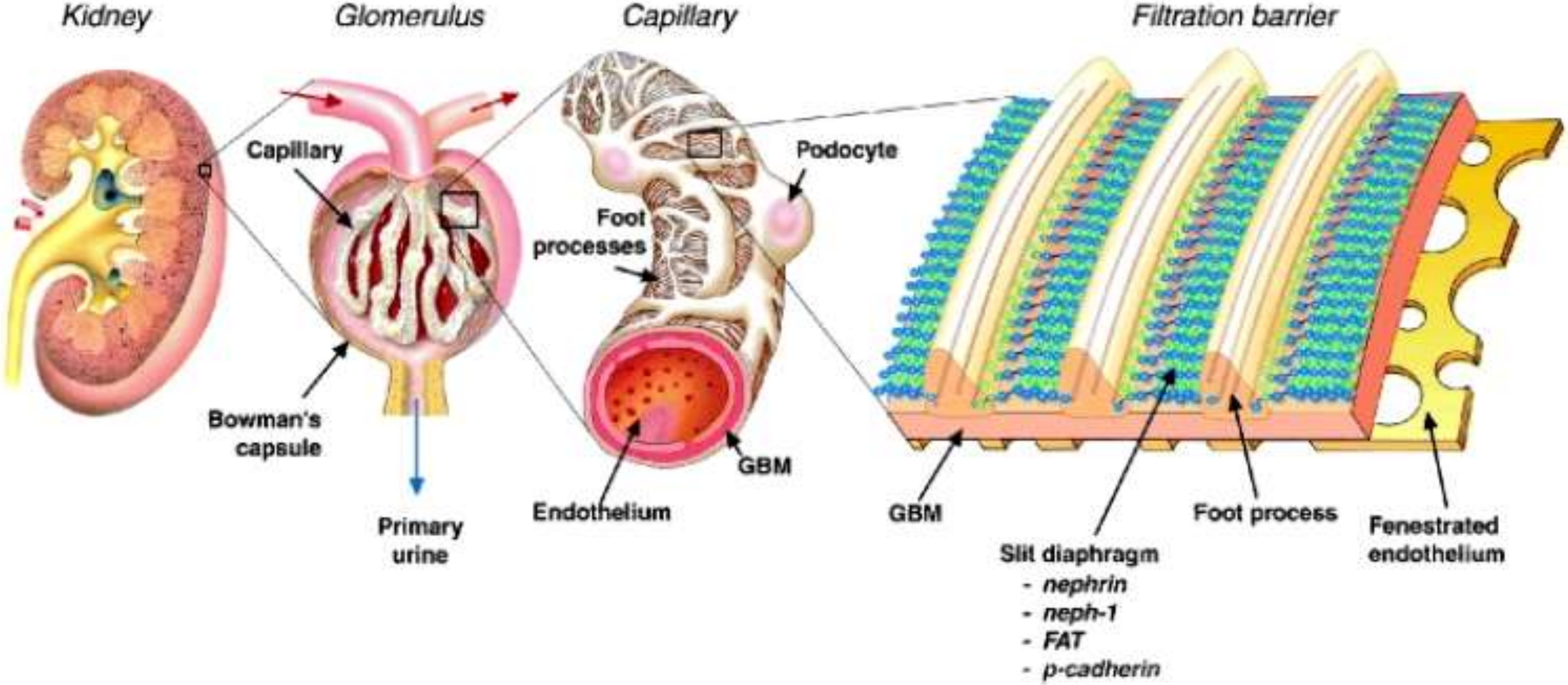
*C. The Boman,s capsule epithelial cells:*

- **Have foot process called podocytes.**
- **Between podocytes there are slits about 25 nm in diameter.**
- **The total surface area across which filtration occurs in humans is a bout 0.8 m2.**

# Triple Filtration Membrane

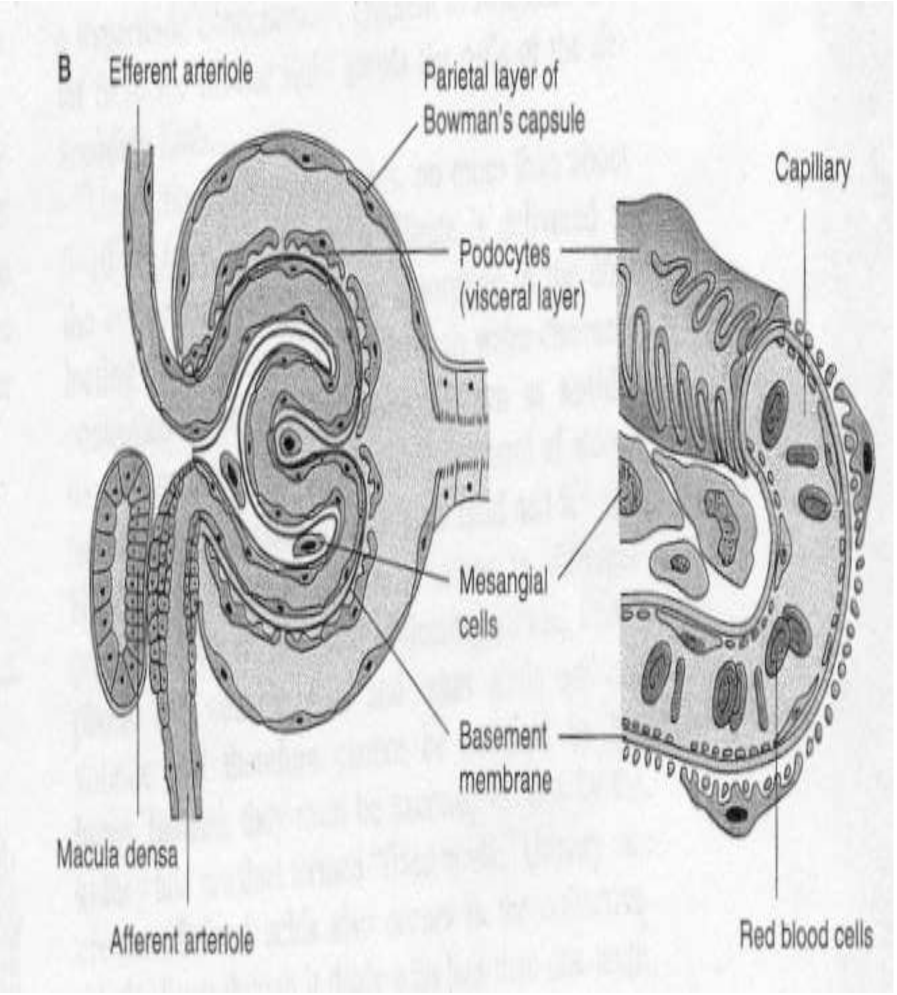


# Structural Components of the Ultrafiltration Barrier



✓ *Mesangial cells*

- ❖ **Are located between the basal lamina and endothelium**
- ❖ **Are contractile cell and play a role in the regulation of glomerular filtration**



# Surface area of glomerular membrane(SA)

- ✓ = 0.8m2
- SA can be altered by the mesangial cells.
- Contraction of these cells producing a decrease in SA (due to reduction in the area available for filtration).
- Contraction of mesangial cells by angiotensin II, endothelin, ADH , histamine, leukotrienes and catecholamine (decrease SA).
- Relaxation by ANP, cAMP and dopamine (increase SA)

# permeability

- The permeability of the glomerular capillaries is about 50 times that of the capillaries in skeletal muscle.
- The permeability of the glomerular capillaries depend on:-

1. *Diameter or Mw of molecule:-*

- Neutral substances with diameter < 4nm freely filtered
- Neutral substances > 8nm excluded (approaches zero)
- Between these values, filtration is inversely proportionate to diameter

- ✓ **Molecule with a molecular weight less than 55.ooo freely filtered.**
- ✓ **With molecular weight more than 70.000 not filtered.**

## *2. Electrical charge of molecule:-*

- **The sialoproteins in the glomerular capillary, have strong negative charges which repel negatively charged substances in blood.**
- **Filtration of cationic substances is greater than that of neutral substances.**
- **This is another cause of the poor filtration of proteins which is negatively charged beside their large size.**

- **The amount of protein in the urine $< 0.30mg/d$ (comes from shed tubular cells).**
- **Urine is normally free of albumin because all the filtered amount is completely reabsorped in the PCT by pinocytosis.**

➢ ***In nephritis:***

- **Albuminuria occur because the negativity charge in the glomerualr wall are disrupted.**
- **There is no ↑in the pores of the glomerular membrane.**

# Hydrostatic & Osmotic pressure

- *For each nephron:*

- **GFR = Kf {(hydrostatic pressure in the glomerular capillaries – hydrostatic pressure in the tubule) – (π the osmotic pressure of the plasma in the glomerular capillaries – π the osmotic pressure of the filtrate in the tubule}**

- ✓ **Kf = the glomerular ultrafiltration coefficient, effective filtration surface area.**

# Hydrostatic & Osmotic pressure

- ***Hydrostatic pressure of glomerular capillaries:***
- **For filtration = 45-60 mmHg**
- **Higher than hydrostatic pressure of systemic capillaries ( 15-35mmHg)**
- **BECAUSE:**
- **The afferent arterioles are short and straight.**
- **The efferent arterioles have a relatively high resistance.**

- ***It is opposed by:***

I. **The hydrostatic pressure in bowman's capsule.**

II. **The osmotic pressure gradient across the glomerular capillaries.**

- ***Osmotic (Oncotic) pressure of glomerular capillaries:***

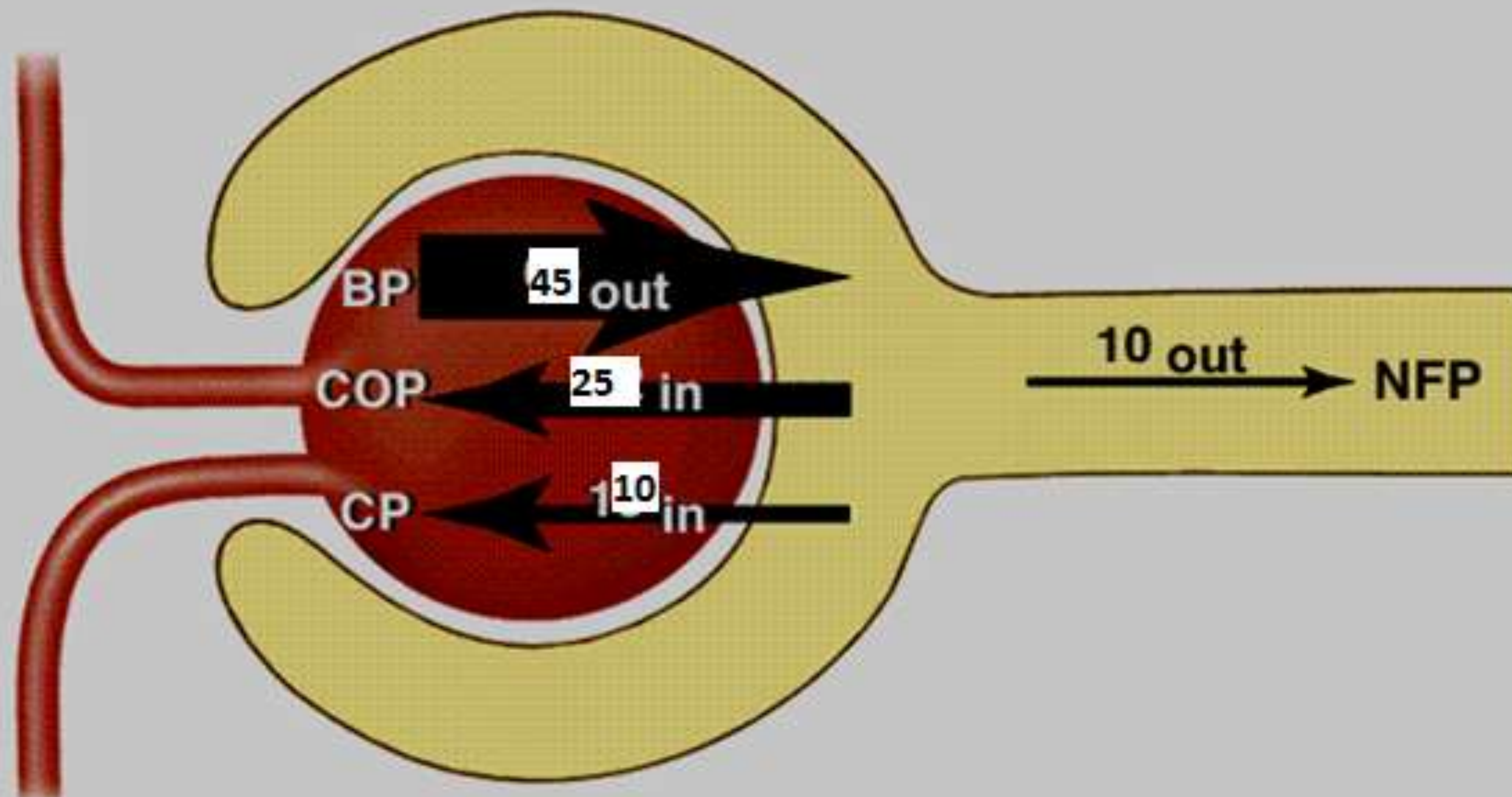
- **It is osmotic pressure of plasma proteins (mainly albumin)**
- **= 20-25 mmHg at the afferent arteriolar end, and increase to 35mmHg at efferent arteriolar (higher concentration of protein after filtration)**

- ***Hydrostatic pressure of Bowman's space:***
  - **= 10mmHg**
- ***Oncotic pressure of Bowman's space:***
  - **= zero ( proteins are not filtered to Bowman's space)**

# Net filtration pressure

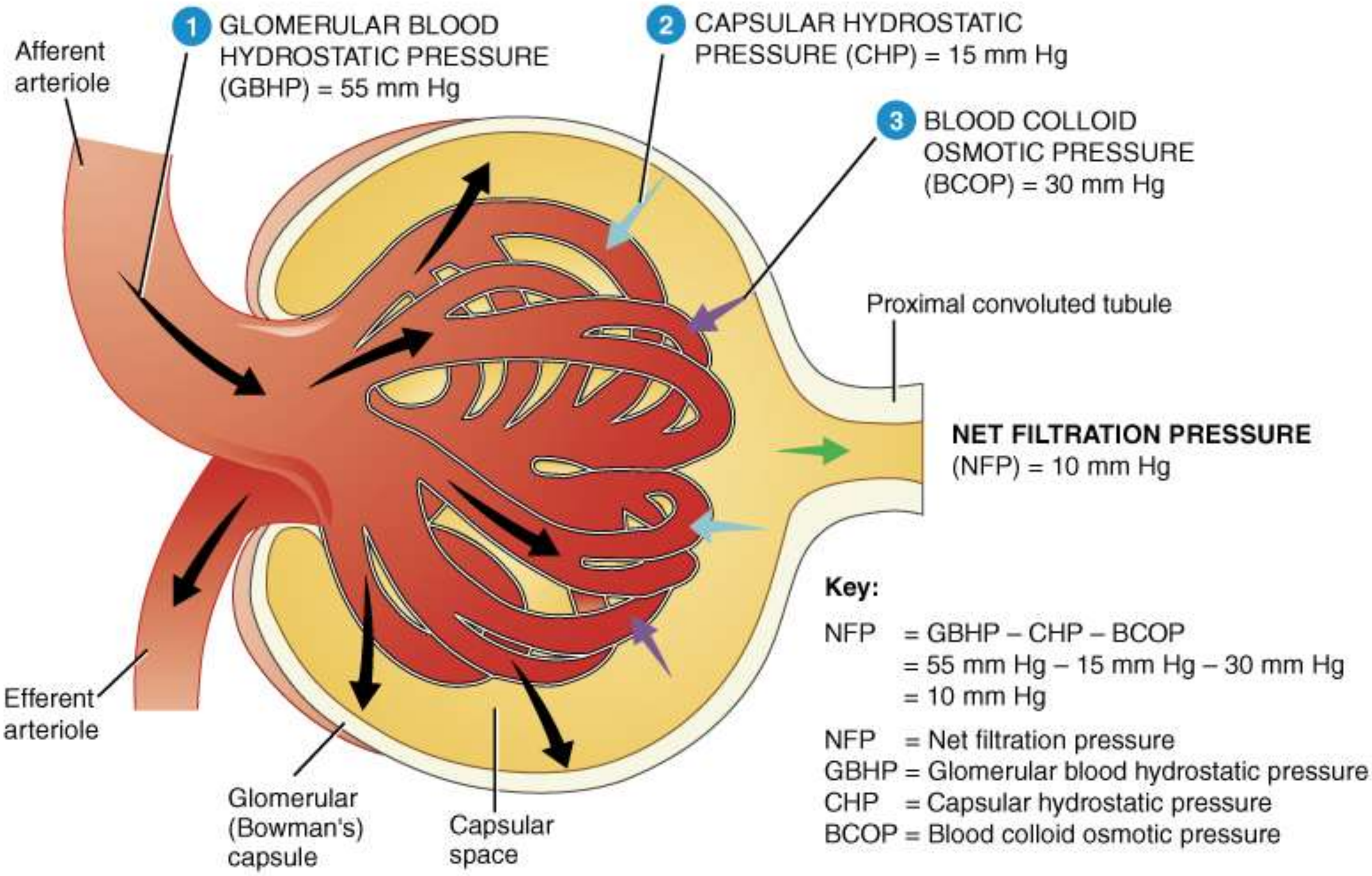
- At the end of the glomerular capillaries near the afferent arterioles:-
- Filtration pressure= 45-(25+10) = 10 mmHg.
- At  the end of efferent arterioles:
- Filtration pressure= 45-(35+10) = 0
- This called filtration equilibrium indicating that filtration normally occur at the first part of glomerular capillaries.
- Because in the efferent arterioles proteins become highly concentrated after filtration of about 1/5 of plasma.

# Glomerular Filtration Forces

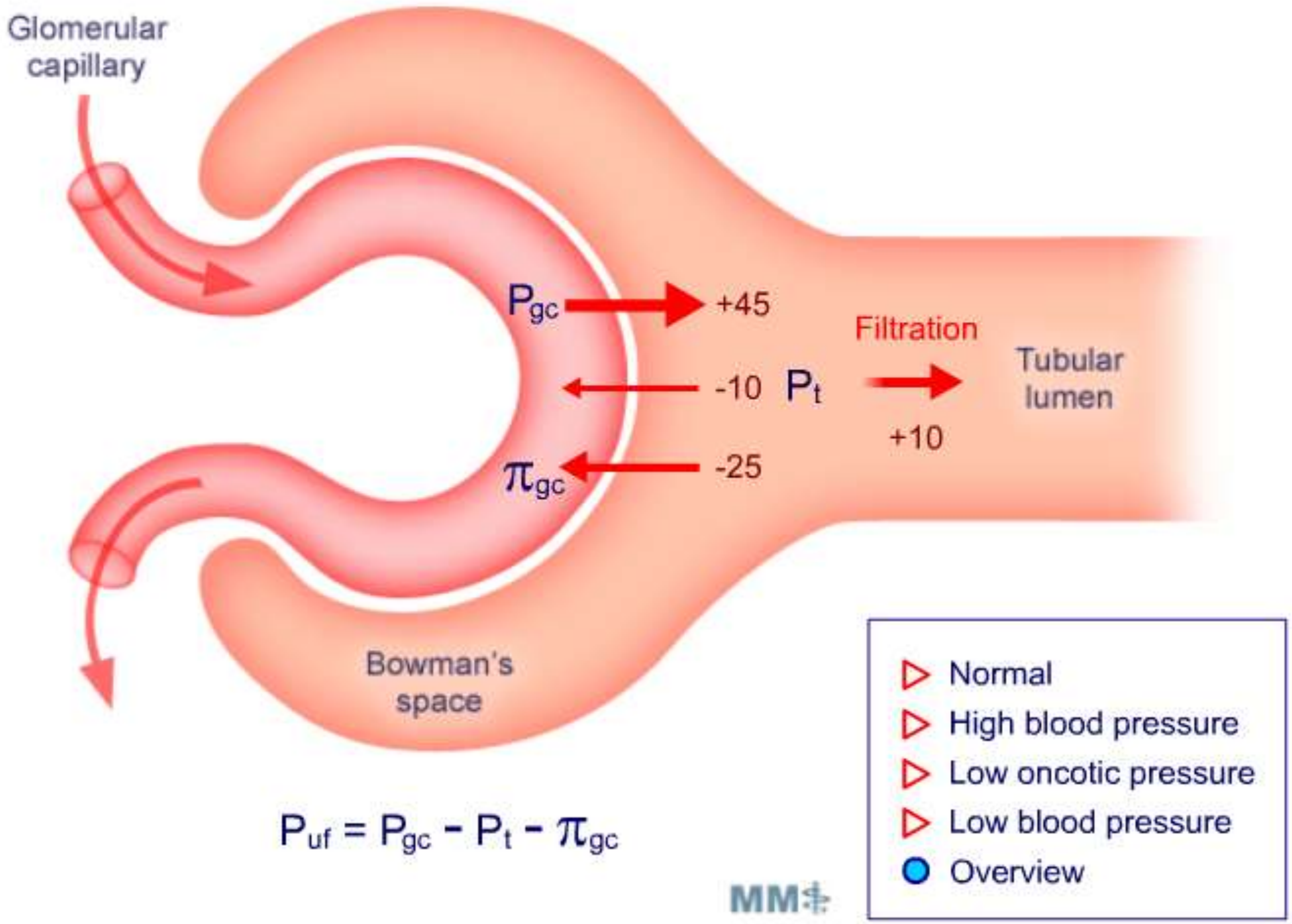



| | |
|---|---|
| Capillary blood pressure (BP) | 45 mmHg out |
| Colloid osmotic pressure (COP) | -25 mmHg in |
| Capsular pressure (CP) | -10 mmHg in |
| Net filtration pressure (NFP) | 10 mmHg out |

# Factors affecting filtration rate in the kidney



## Forces Involved in Glomerular Filtration




$$P_{uf} = P_{gc} - P_t - \pi_{gc}$$

Pt = PBS

# Control of GFR

- Factors affecting the GFR:-

1. *Changes in the PGC :*

- **Changes in blood pressure does not effect the GFR unless the mean pressure is above 160mmHg or below 80mmHg.**
- **Drop of ABP below 80mmHg will stop the GFR leading to anuria.**
- **Marked ↑in ABP above 160mmHg ↑the GFR → ↑urine output (pressure diuresis)**

***2. Changes in πGC :-***

❖ **Hypoproteinemia: ↑ the GFR by ↓ the πGC.**

❖ **Dehydration: ↓ the GFR by ↑ the πGC.**

***3. Changes in the PT :-***

**I. Edema of the kidney:**

- ✓ **Distension of the kidney with in the renal capsule ↑ hydrostatic pressure in the tubules & ↓the GFR.**

**II. Obstruction of the urinary tract:**

- ✓ **↑ PT ↓the GFR.**

**_4. Changes in the surface area:_**

- ✓ **If the glomerualr surface area available for filtration ↓ the GFR will ↓.**

- ➢ **_This occur due to:-_**

**A. A decrease in the number of functional nephrons as that occur in chronic renal failure or after nephectomy.**

**B. Contraction of mesangial cells.**

***5. Changes in permeability:***

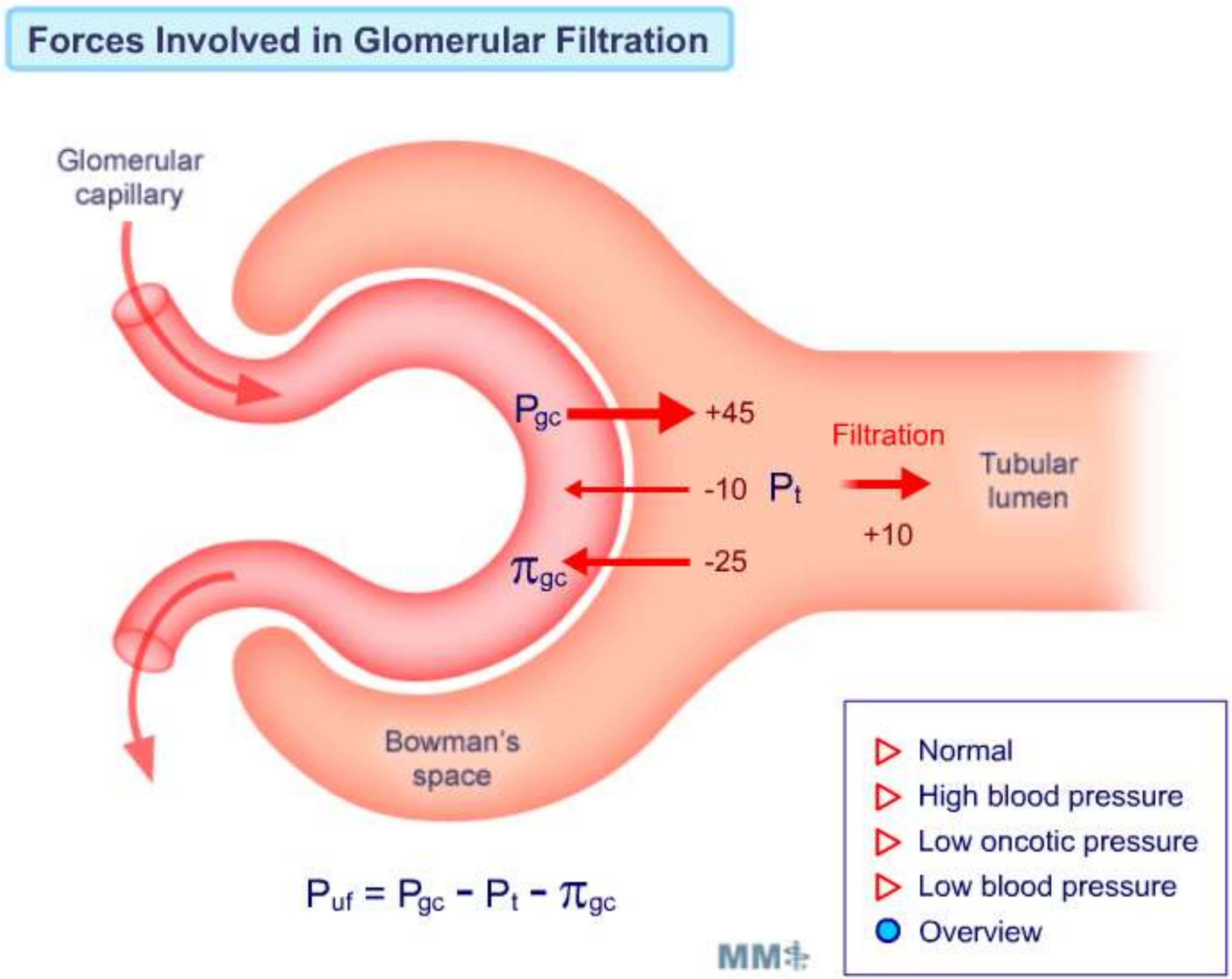
- **The GFR is directly proportional to the glomerular capillary permeability.**
- **In nephritis the permeability increase which ↑ the GFR.**

### *6. Sympathetic stimulation:-*

- **Mild stimulation:**
  - **produces no effect due to autoregulation.**
- **Strong stimulation:**
  - **Causes marked vasoconstriction in glomerular arterioles leading to reduction of both RBF & GFR.**

*7. Tubulo-glomerular feed back:-*

- **When the tubular fluid flow rate ↑ at the distal part of the nephron (ascending LH & DCT).**
- **GFR in the same nephron will ↓ and vice versa.**



Forces Involved in Glomerular Filtration
Glomerular capillary
$P_{gc}$
+45
-10
$P_t$
$\pi_{gc}$
-25
Filtration
+10
Tubular lumen
Bowman's space
$P_{uf} = P_{gc} - P_t - \pi_{gc}$
Normal
High blood pressure
Low oncotic pressure
Low blood pressure
Overview


Pt = PBS

# Mechanism

- ↑ the tubular flow rate → large amount of fluid, sodium and chloride enter the distal tubules.
- $Na^+$ & $CL^-$ enter the macula densa cells.
- ↑ $Na^+$ concentration increased $Na^+$-$K^+$ ATP ase activity.
- As a result of ↑ATP hydrolysis more adenosine is formed.

- Adenosine act via adenosine A1 receptors on the macula densa cells ↑ calcium release.
- Calcium causes contraction of the vascular smooth muscle of the afferent arterioles leading to their constriction & ↓ the GFR.

- **Afferent arteriolar constriction:**
- **↓the GFR by decreasing PGC.**
- **Efferent arteriolar constriction:**
- **Mild constriction ↑ the GFR by ↑ the PGC.**
- **Severe constriction ↓the GFR by decreasing PGC.**

Figure 7

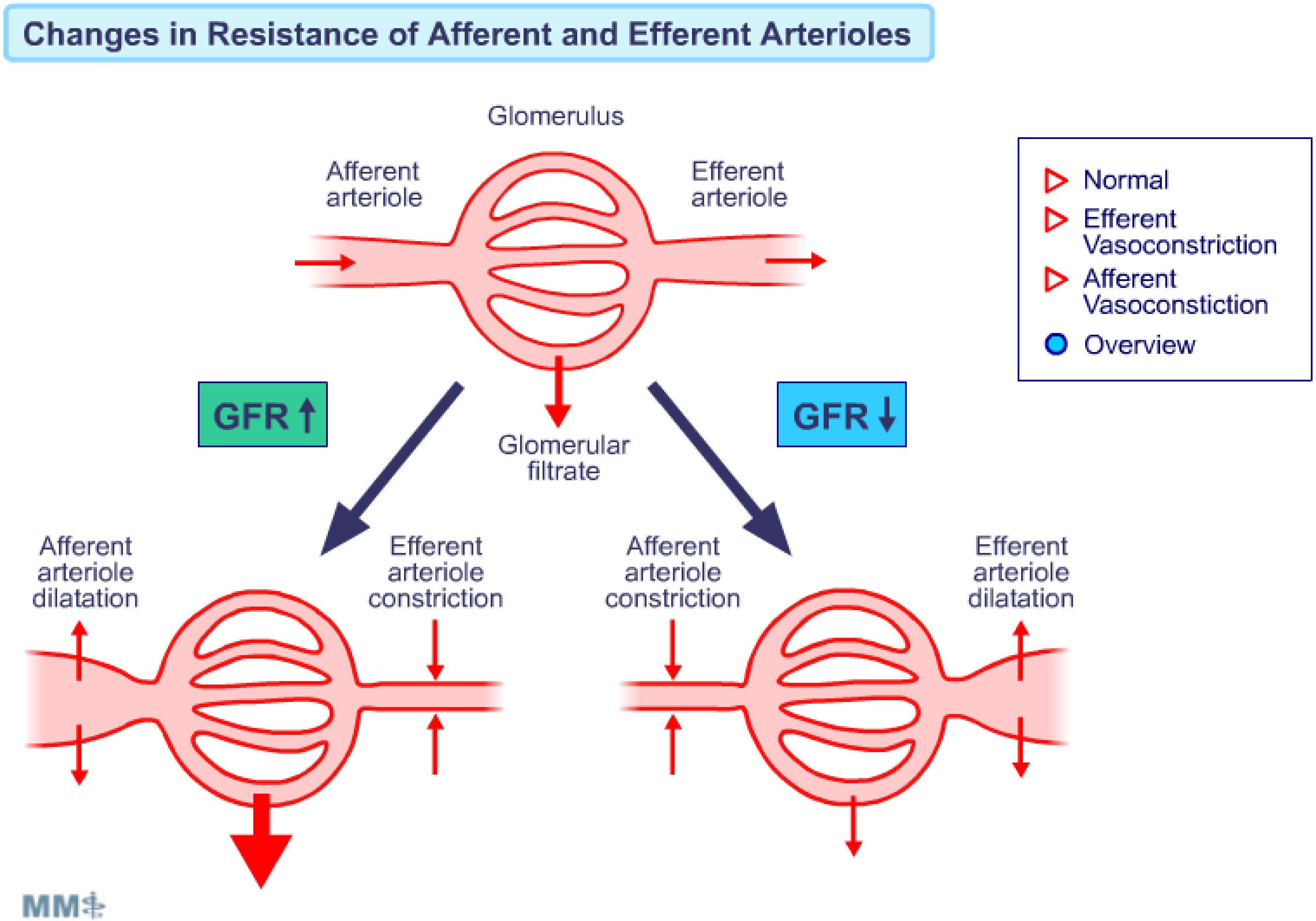
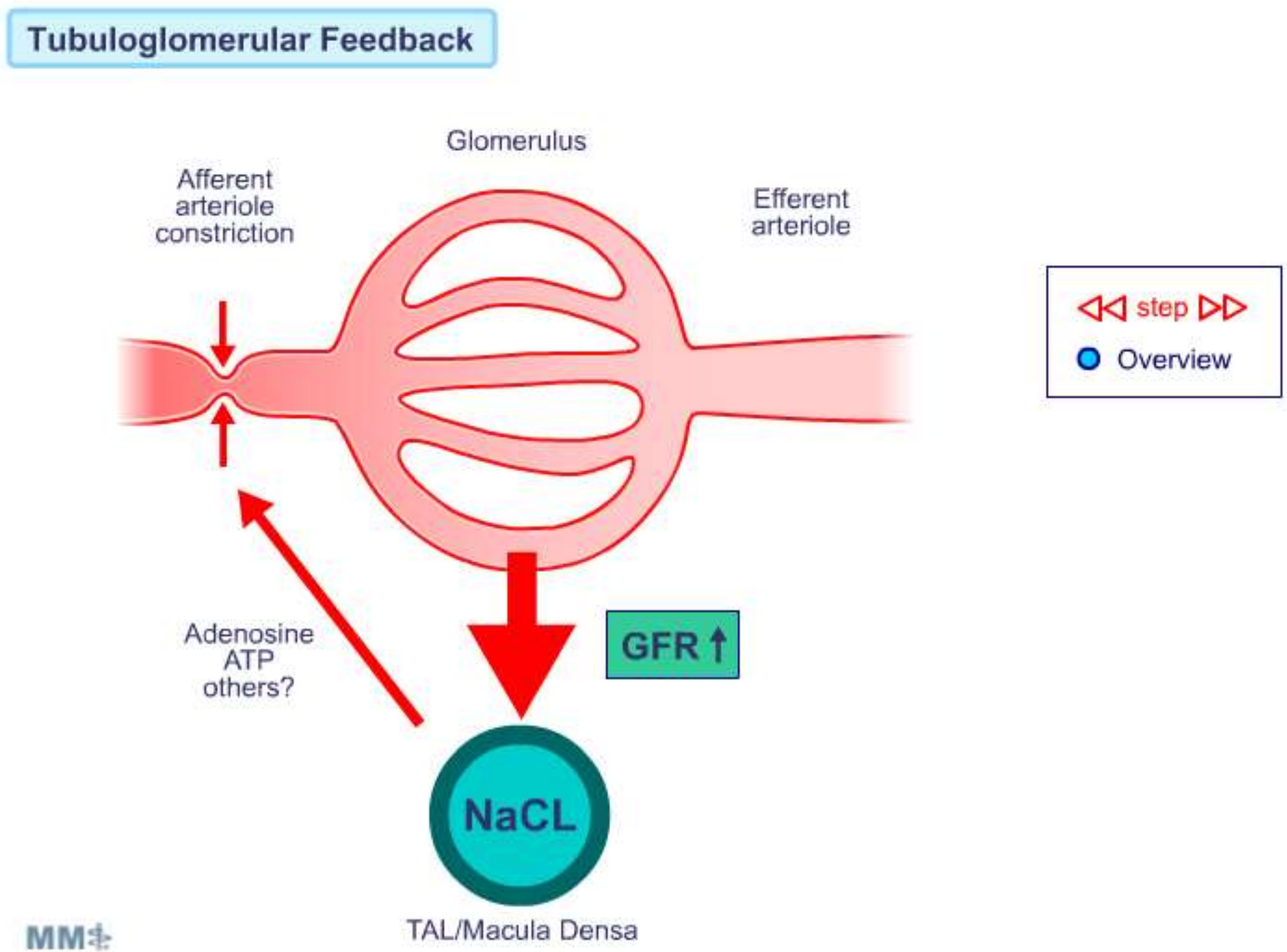
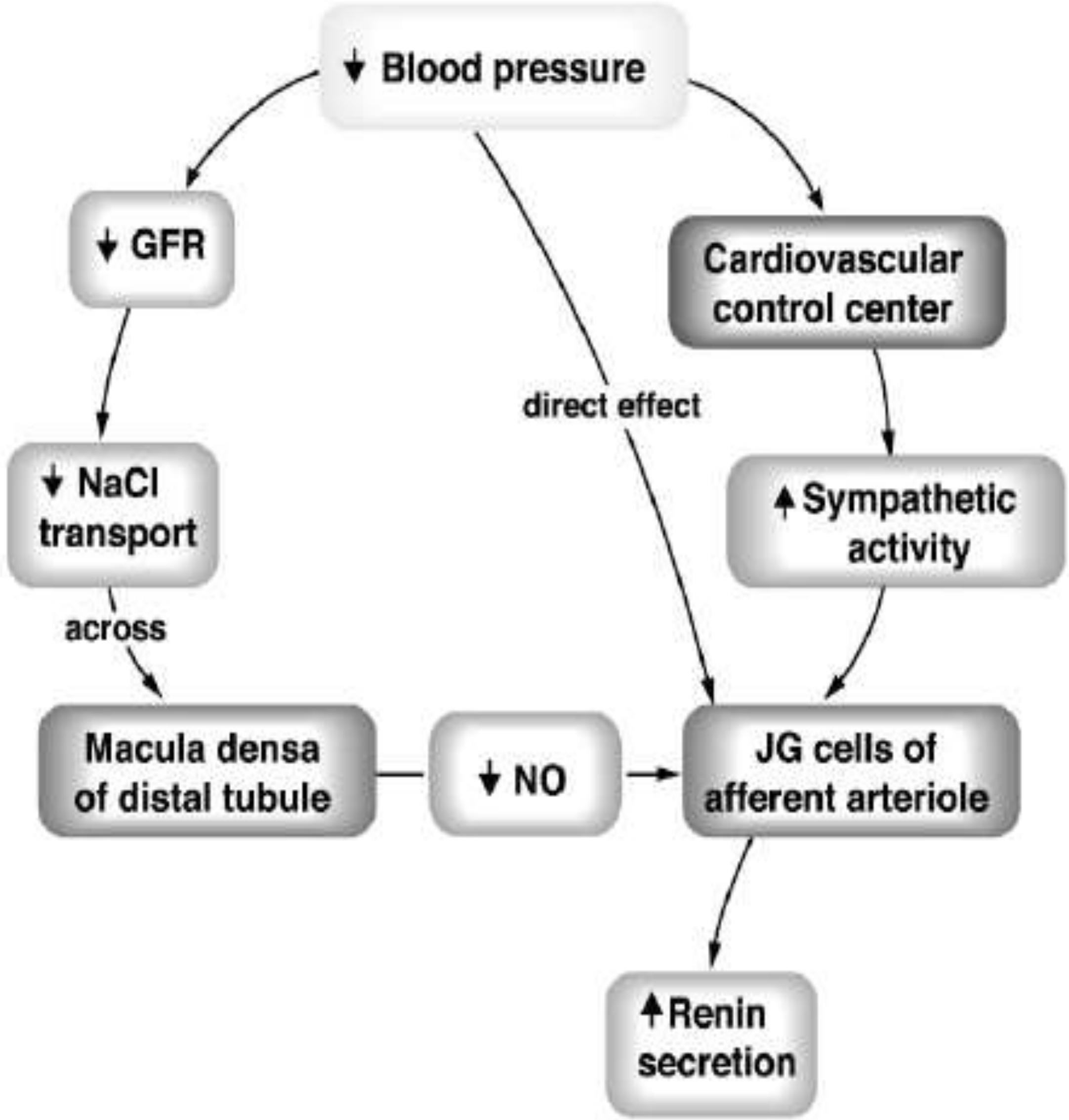
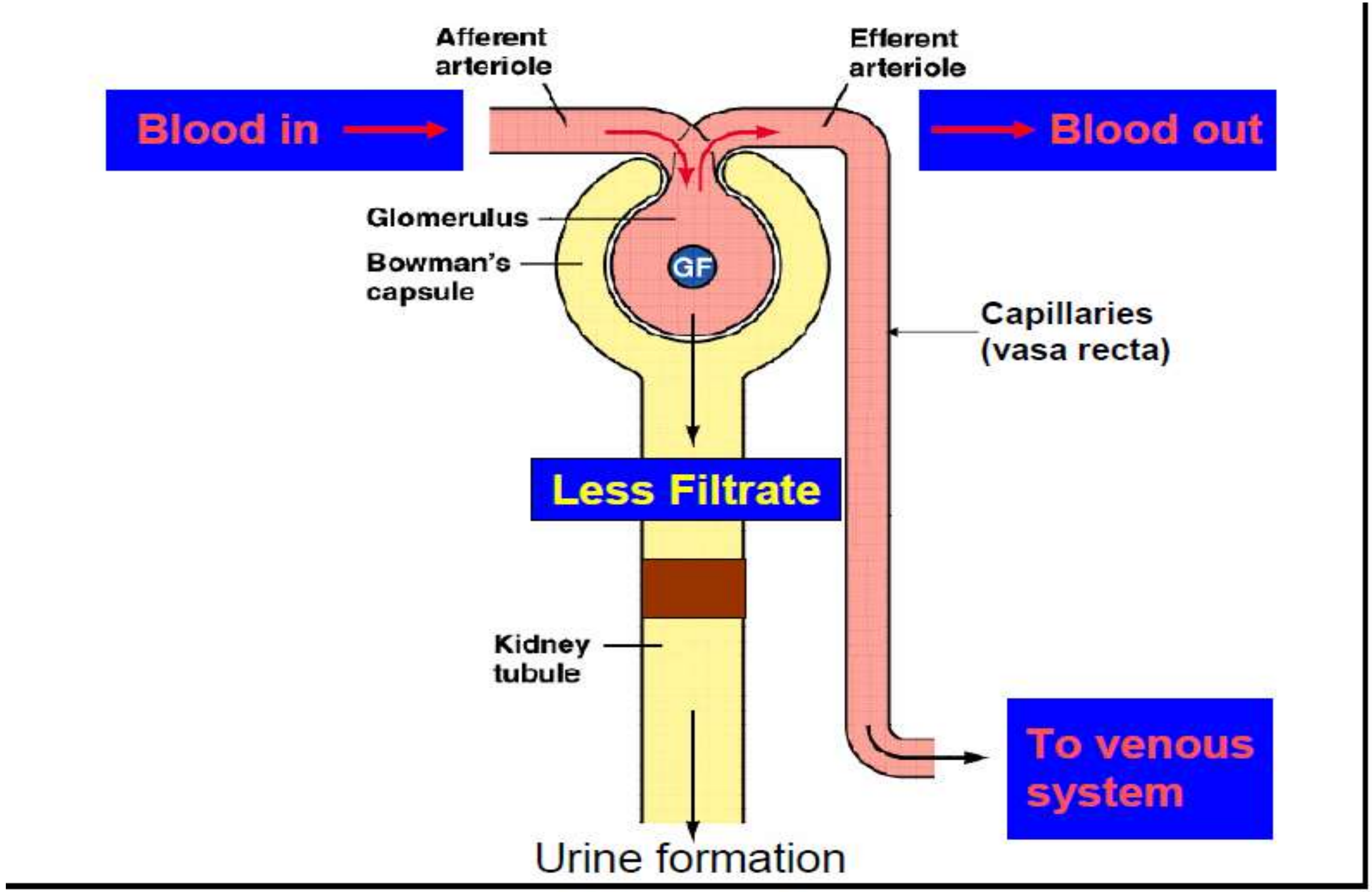

Changes in Resistance of Afferent and Efferent Arterioles
Glomerulus
Afferent arteriole
Efferent arteriole
Normal
Efferent Vasoconstriction
Afferent Vasoconstriction
Overview
GFR
GFR
Glomerular filtrate
Afferent arteriole dilatation
Efferent arteriole constriction
Afferent arteriole constriction
Efferent arteriole dilatation
MM

Figure 9


Tubuloglomerular Feedback
Glomerulus
Afferent
arteriole
constriction
Efferent
arteriole
step
Overview
GFR
Adenosine
ATP
others?
NaCL
MM
TAL/Macula Densa

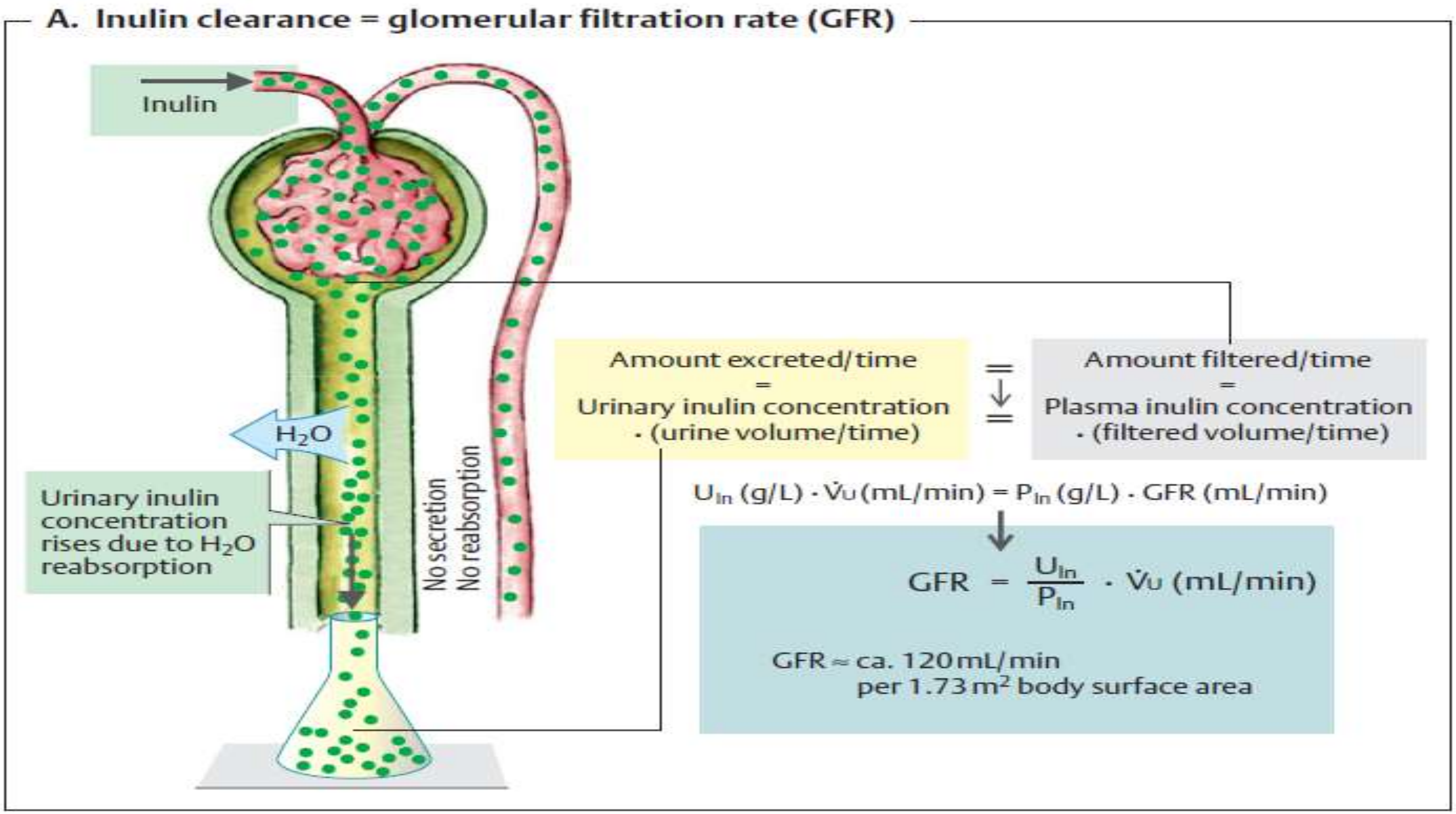

↓ Blood pressure
↓ GFR
Cardiovascular control center
direct effect
↓ NaCl transport
↑ Sympathetic activity
across
Macula densa of distal tubule
↓ NO
JG cells of afferent arteriole
↑ Renin secretion

# Renal obstruction



# Measurements of the GFR

- **Using inulin or creatinine clearance.**



# Mode of handling of inulin

1. Freely filtered in the glomeruli, then the filtered amount is excreted.
2. It is neither reabsorbed nor secreted in the renal tubules i.e. the amount of inulin excreted/min = the amount filtered/min.

- This means that the volume of plasma that is cleared from inulin/min (inulin clearance) is that volume filtered in the glomeruli/min (the GFR).

# Clearance Equation

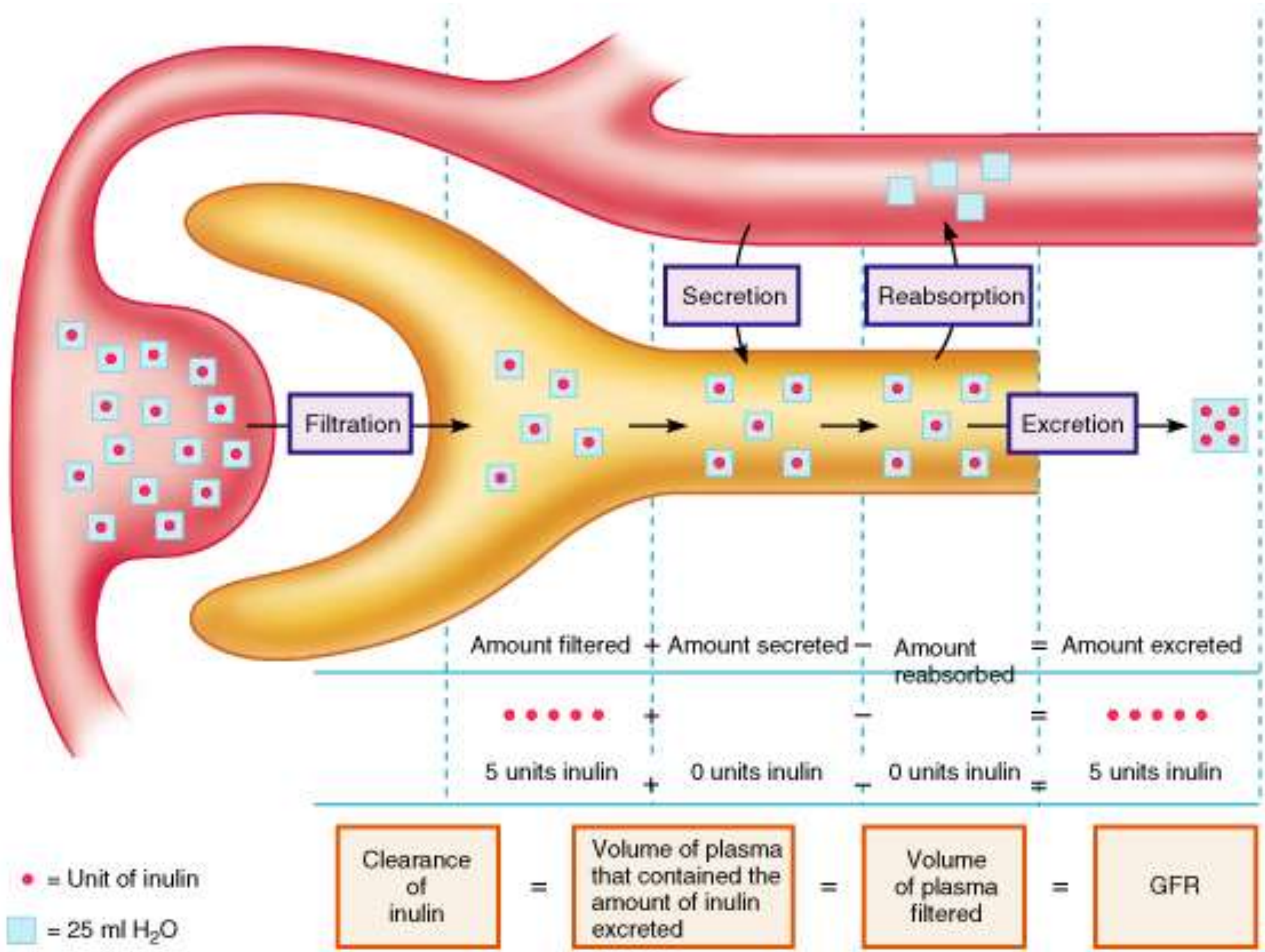
$$Cx = \frac{V \times Ux}{Px}$$

Pin = .25mg/ml

Uin = 35mg/ml

V = .9m/min

GFR= 125ml/min


Secretion
Reabsorption
Filtration
Excretion
Amount filtered + Amount secreted − Amount reabsorbed = Amount excreted
+ − =
5 units inulin + 0 units inulin − 0 units inulin = 5 units inulin
= Unit of inulin
= 25 ml $H_2O$
Clearance of inulin = Volume of plasma that contained the amount of inulin excreted = Volume of plasma filtered = GFR