# Regulation of Glomerular Filtration

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# Objectives

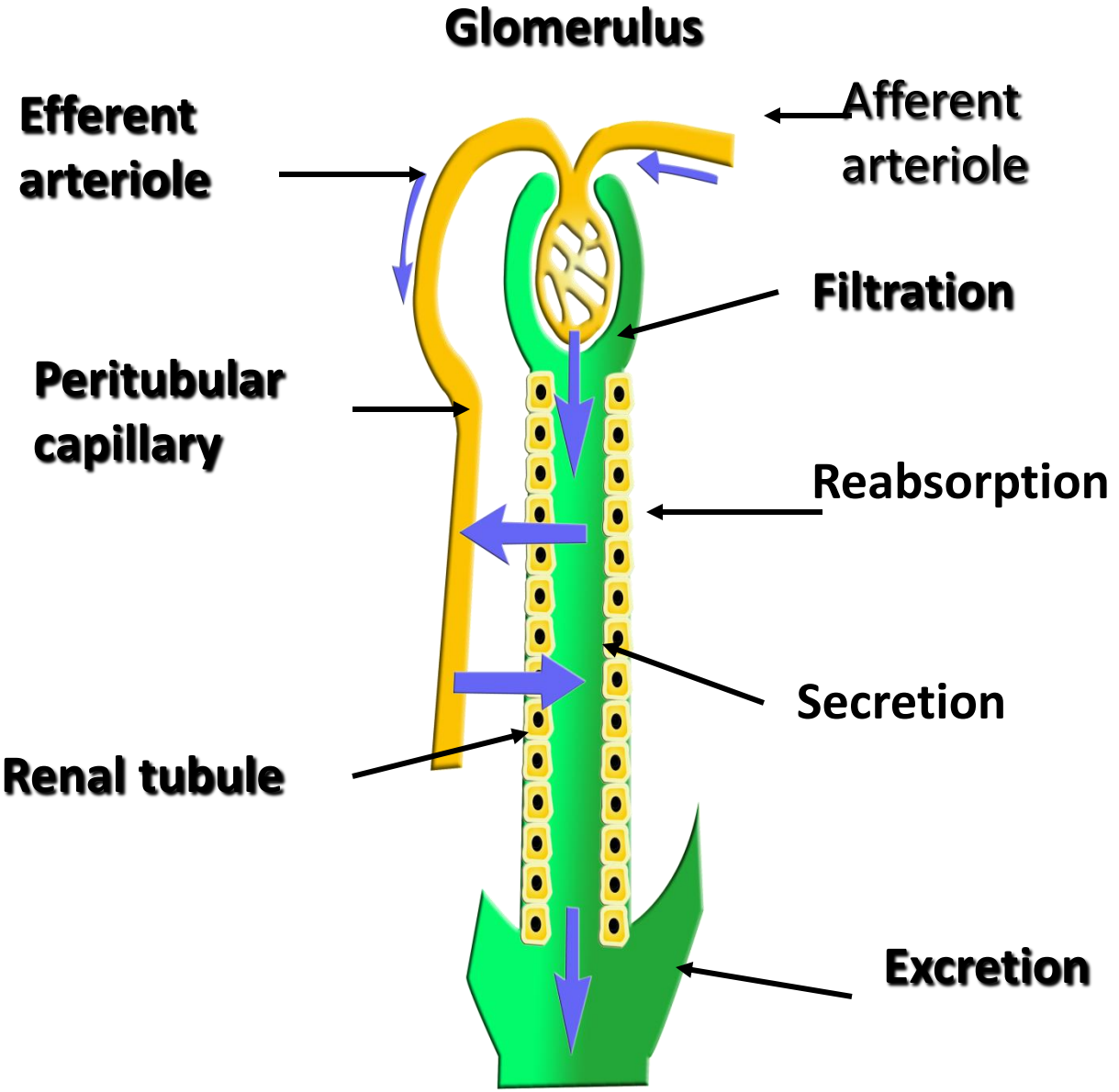
**At the end of this lecture student should be able to describe**

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

# Principal of urine formation

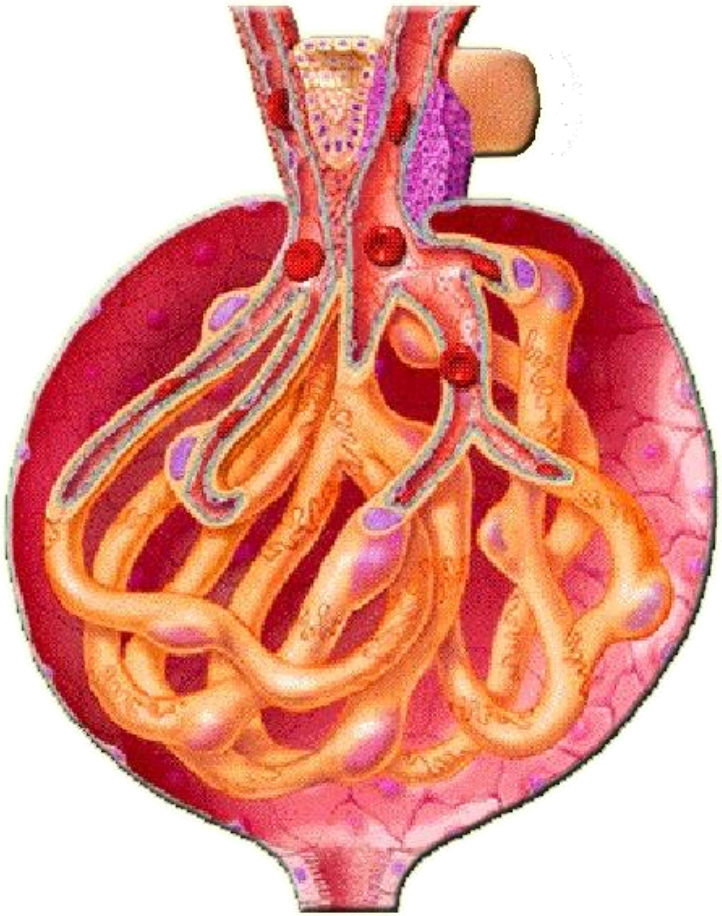
1. Filtration
   glomerulus

2. Absorption
   and secretion
   tubule



# Basic Mechanisms of Urine Formation

1. **Glomerular filtration**
2. **Reabsorption**
3. **Secretion**
4. **Urine concentration**



# Glomerular Filtration

**During filtration, large quantity of water and solutes pass through the filtration membrane from the blood into the glomerular capsule.**

# Glomerular Filtration

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

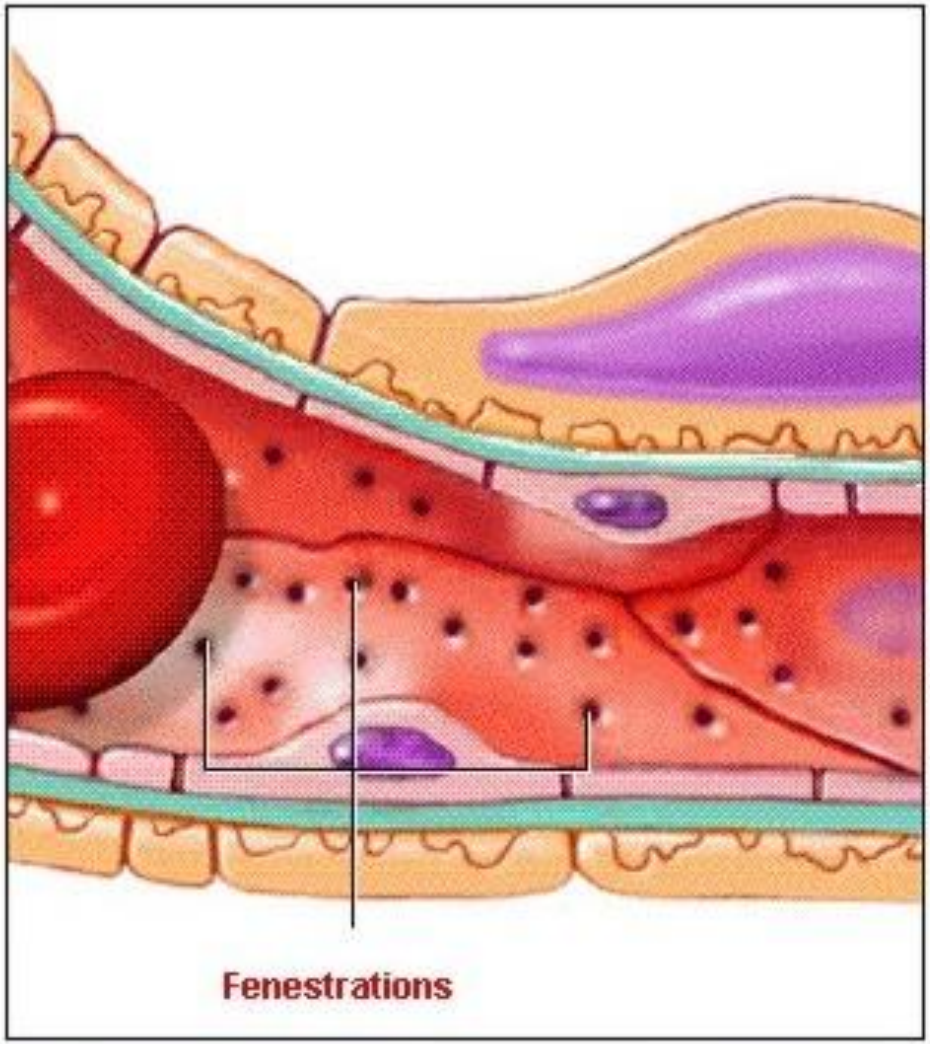
# Filtration membrane

- **Filtration membrane**
  - **Capillary endothelial**
  - **Basement layer (mesengial cell)**
  - **Capsule epithelial layer podocytes**

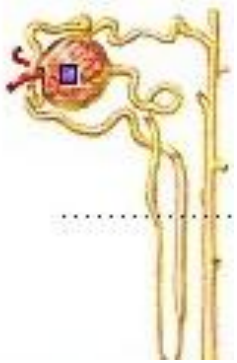
# Characteristic of filtration membrane

- **Endothelial layer**
  - **Fenestration 70-100 nm (pores)**
- **Basement membrane**
  - **Homogenous collagenous fibers with no pores**
  - **-vely charge** (sailoprotein)
  - **Contractile mesengial cells**
- **Epithelial membrane**
  - **Podocytes**
  - **Slit pores** 25-60nm

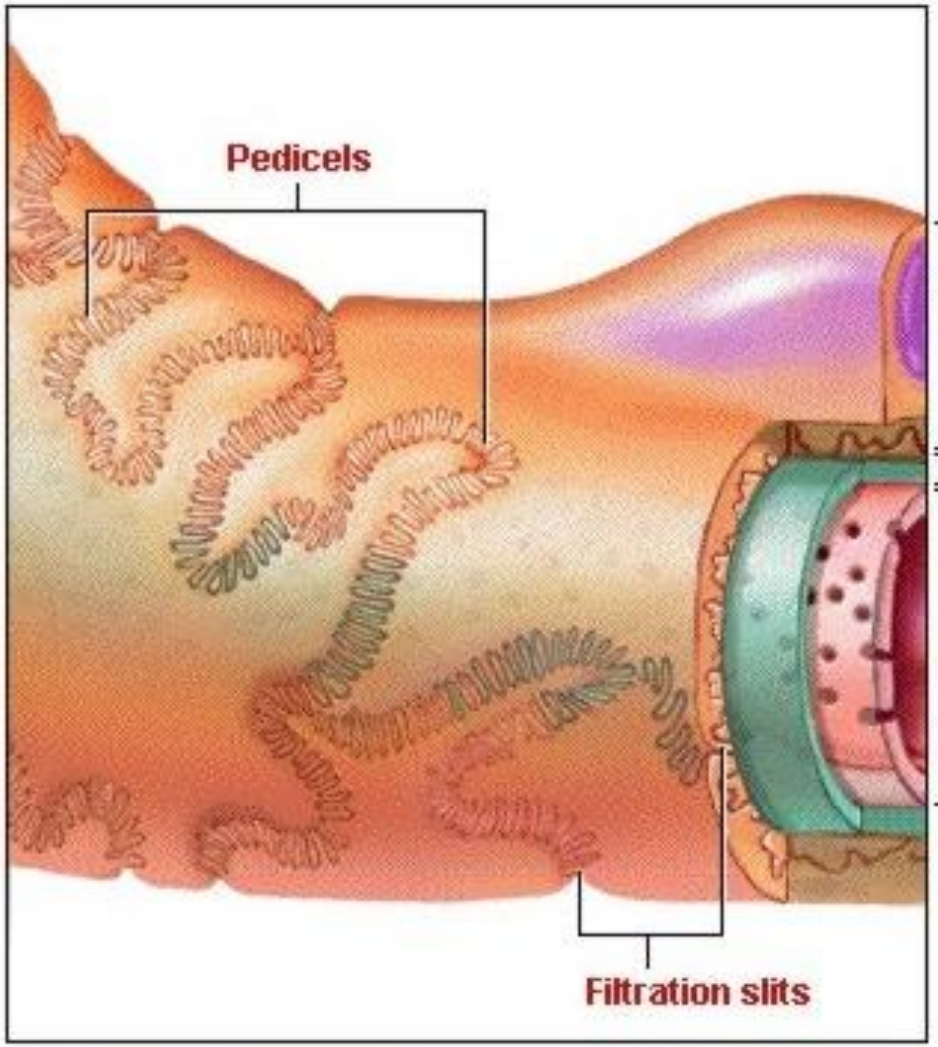
# Cellular Features of the Renal Corpuscle




Here we see a glomerular capillary in longitudinal section.



# Cellular Features of the Renal Corpuscle



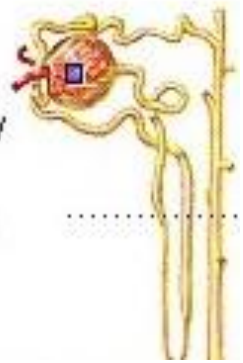

Surrounding the basement membrane is a layer of podocytes.

**Podocyte** cell body with nucleus

**Basement membrane**

Capillary **endothelium**

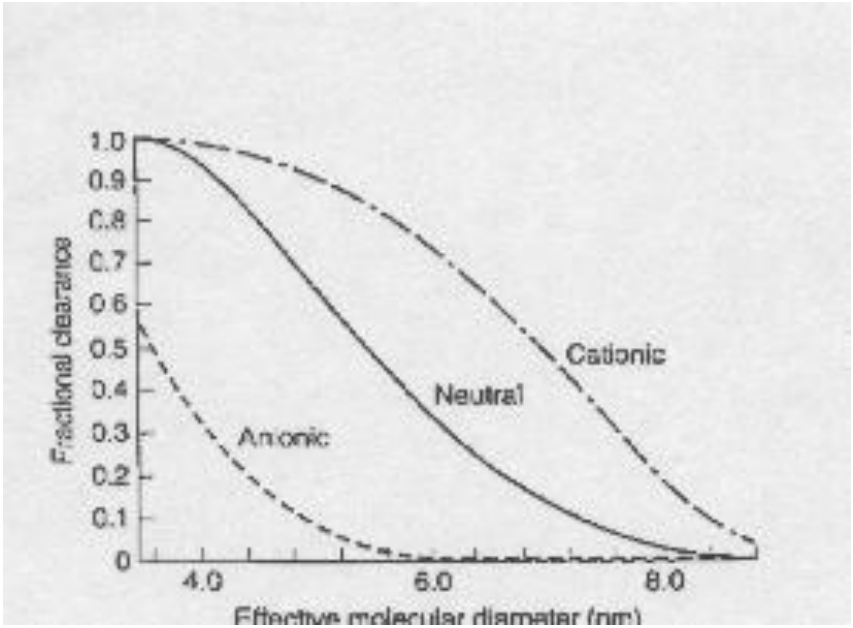
Together, the fenestrated capillary endothelium, basement membrane, and podocytes make up the **filtration membrane**.



# Filtration of Molecules

1. **Molecular size and charge regulate filtration**

- **< 4nm freely filtered**
- **4-8 nm**
  - **–vely charge poorly filtered compared to neutral & +vely charge**
- **> 8 nm not filtered**



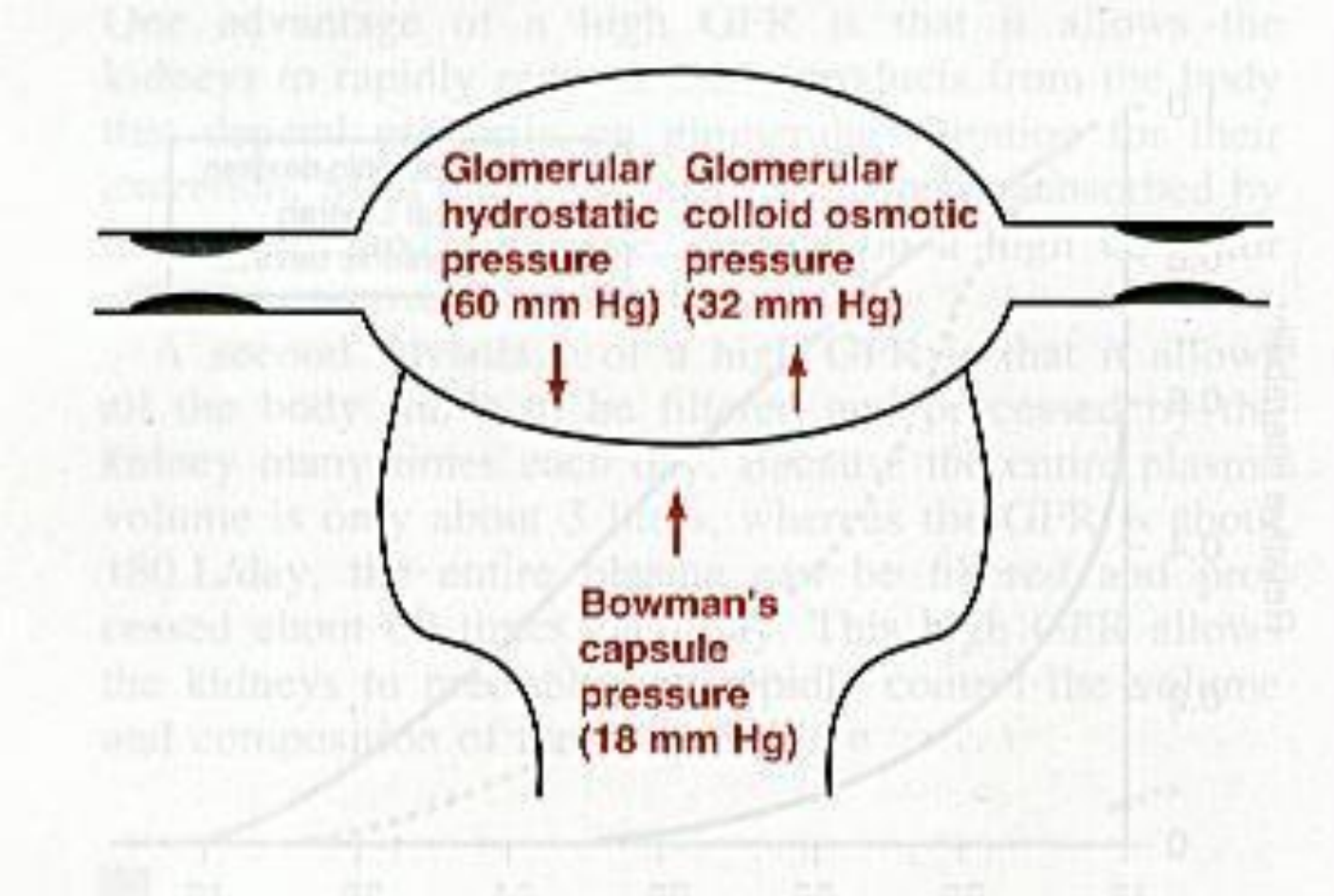
# Filtration pressure

- **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**

# Filtration pressure (starling forces)

1. **Glomerular hydrostatic pressure (PGC)**
2. **Glomerular osmotic pressure ($\pi$GC)**
3. **Bowman hydrostatic pressure (PBS)**
4. **Bowman osmotic pressure ($\pi$BS) = zero**

# Filtration pressure



# Starling forces & filtration

1. **Hydrostatic pressure ($P_{GC}$)**
   - **Favors filtration**
   - **60 mmHg**
   - **Remain constant along the entire glomerular capillary**
2. **Hydrostatic pressure in Bowman space ($P_{BS}$)**
   - **Opposes filtration**
   - **18 mmHg**
   - **Due to filtered fluid in the capsule**

# Starling forces & filtration *cont.*

3. **Colloid osmotic pressure in glomerular capillaries ($\pi_{GC}$)**
   - **Opposes filtration**
   - **32 mmHg**
   - **Caused by plasma protein**
   - **Is not constant**
4. **Colloid osmotic pressure in Bowman capsule ($\pi_{BC}$)**
   - **Zero (no plasma protein)**

# Calculation of net filtration pressure

- **Net filtration pressure**

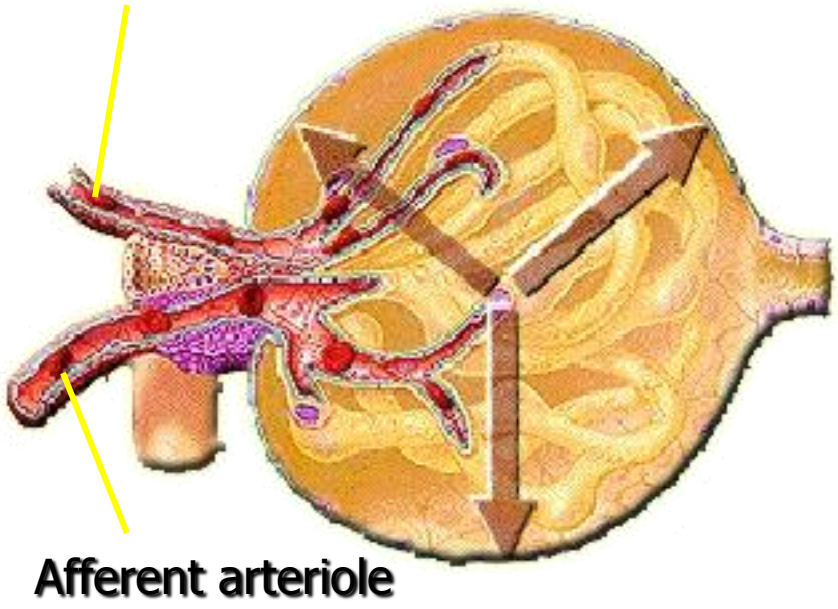
  **= 60-18-32= 10 mmHg**

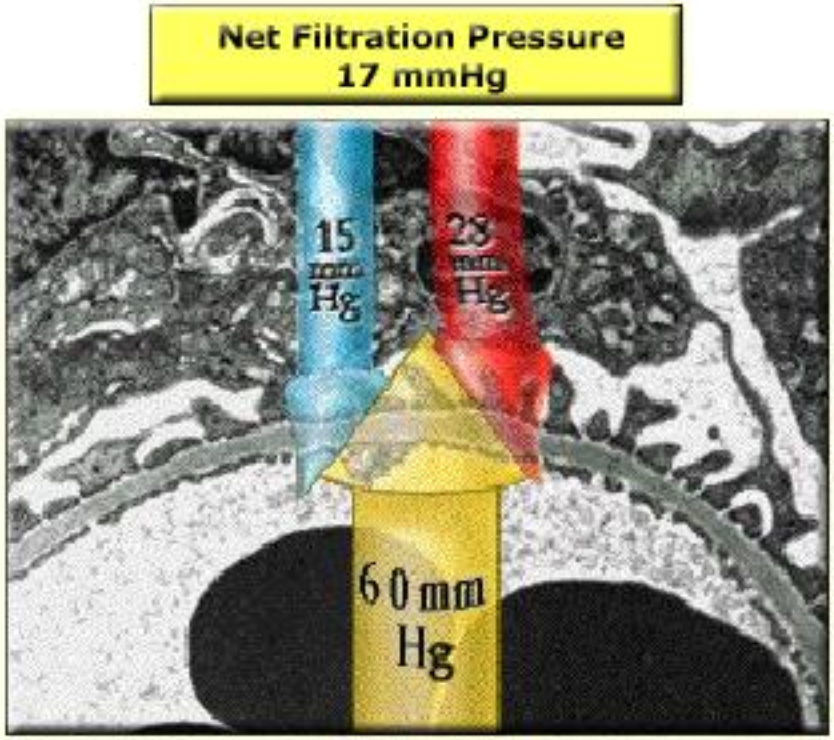
  **= $K_f$ ($P_{GC}$ - $P_{BS}$ ) - ( $\pi_{GC}$ - $\pi_{BS}$)**

- **$K_f$ : Filtration coefficient depend on Filtration membrane**
  - **permeability**
  - **Surface area**
- **Glomerular permeability > 100 x skeletal capillaries permeability**


17

# Net Filtration Pressure (NFP)

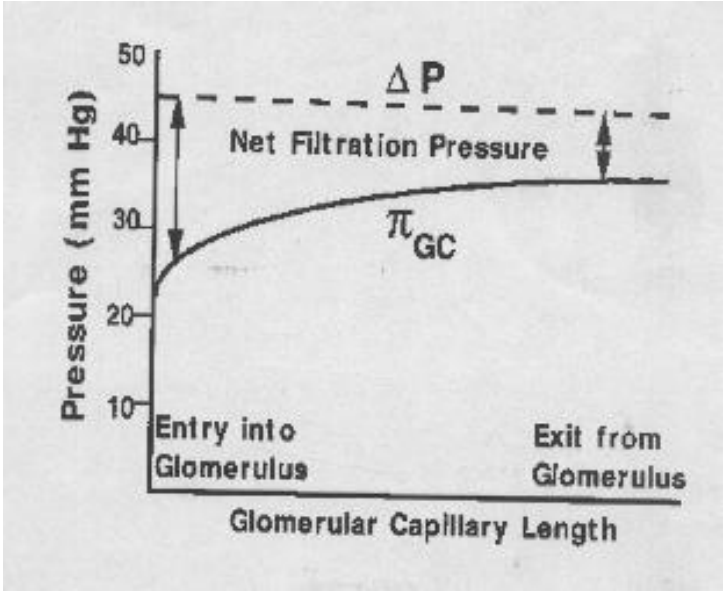


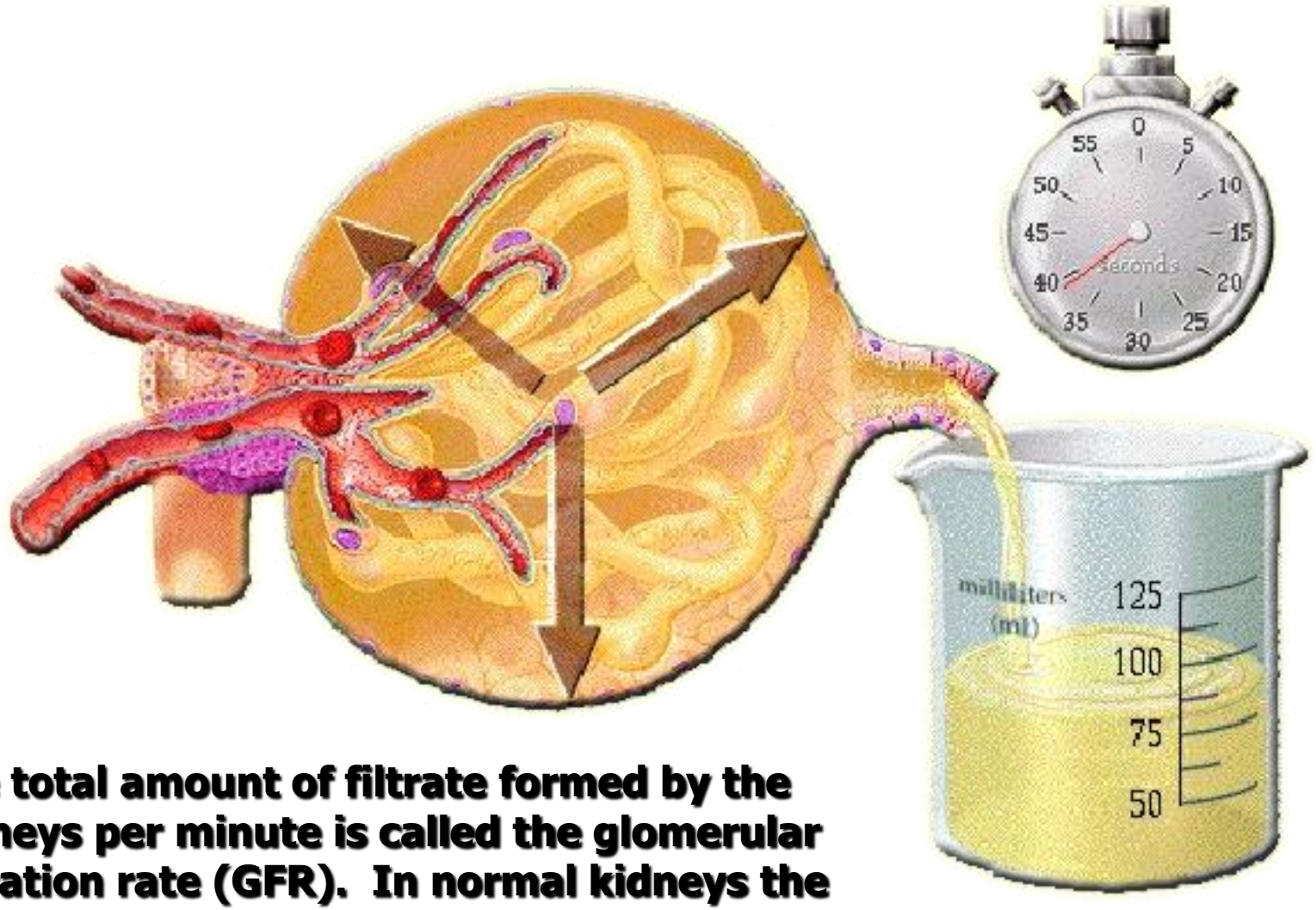

$P_{GC}$ – favors filtration = 60mmHg
$P_T$ – opposes filtration = 15mmHg
$\pi_{GC}$ – opposes filtration = 28mmHg
NFP 60mmHg – (15mmHg + 28mmHg) = 17mmHg

# Net filtration pressure

- **Net filtration pressure decreases as passing along the glomerular capillary**
- **Only plasma is filtrated → ↑ plasma protein conc. → ↑ oncotic pressure → ↓ net filtration pressure**



# Glomerular Filtration Rate (GFR)




**The total amount of filtrate formed by the kidneys per minute is called the glomerular filtration rate (GFR). In normal kidneys the GFR is approximately 125ml per minute.**

# 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

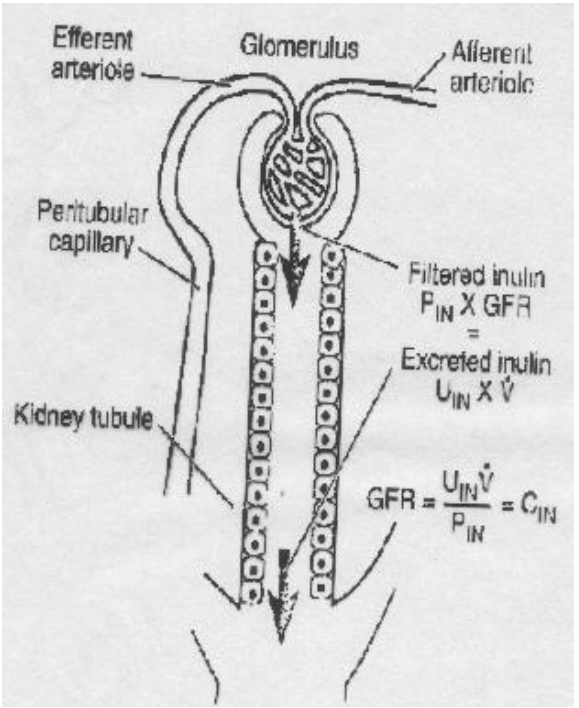
- **Characteristic of substance used**
  - **Freely filtered (not reabsorbed or secreted)**
  - **Not metabolized by the kidney**
  - **Not toxic and stable**
  - **Not bound to plasma protein**
  - **Does not change renal plasma flow**
- **Inulin**

# Measurement of GFR *cont.*

- **Test procedure**
  - **Intravenous loading dose of inulin followed by intravenous infusion of inulin to maintain plasma level constant**
  - **Urine is collected for 15 or 20 min, to measure inulin concentration in urine and urine volume**
  - **Blood sample is taken half way of urine collection to measure inulin concentration**

# Calculation of GFR

- **The amount of inulin excreted = $U_{in}$ x $U_v$**
- **The amount of inulin filtered = Pin x GFR**
- **As inulin is not reabsorbed or excreted both quantity are equal**
- **$P_{in}$ x GFR =$U_{in}$ x $U_v$**
- **GFR = $\frac{U_{in} \times U_v}{P_{in}}$ = ml\min**



# Calculation Of GFR & FF

- **GFR= $K_f$ x net filtration pressure**
- **GFR = 12.5 x 10 = 125 ml/min**
- **$K_f \propto$ GFR (↓ $K_f$ in diabetes - ↓ GFR)**

**Filtration fraction**

- **The fraction of renal plasma flow that is filtered = GFR/RPF**
- **125/ 625= .2= 20%**

# Factors affecting GFR

1. **Changes in $P_{GC}$**
   - **$P_{GC} \propto$ GFR**
   - **Systemic blood pressure**
   - **afferent vasoconstriction - $\downarrow P_{GC}$ -$\downarrow$GFR**
   - **Efferent vasoconstriction $\uparrow P_{GC}$ - $\uparrow$GFR**
2. **Changes in $\pi_{GC}$**
   - **$\pi_{GC}$ $1/\propto$ GFR**
   - **$\uparrow \pi_{GC}$ - $\downarrow$ GFR**
     - **hemo concentration (dehydration) - $\uparrow$ plasma protein concentration $\uparrow \pi_{GC}$**
     - **$\uparrow$ filtration fraction- $\uparrow \pi_{GC}$**

# Factors affecting GFR *cont.*

3. **Changes in $P_{BS}$**
   - **$P_{BC}$ $1/\propto$ GFR**
   - **$\uparrow P_{BC}$ due to obstruction to outflow - $\downarrow$ GFR**
     - **urethral obstruction**
     - **kidney edema**
4. **Changes of filtration coefficient**
   - **glomerular capillary permeability**
   - **Changes in surface area**
5. **Changes in renal blood flow**

# Summary

1. **Filtration membrane**
2. **Molecular filtration**
3. **Filtration pressures**
4. **Net filtration pressure**
5. **GFR**
6. **Measurement of GFR**
7. **Factor affecting GFR**