Regulation of Glomerular Filtration

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Objectives

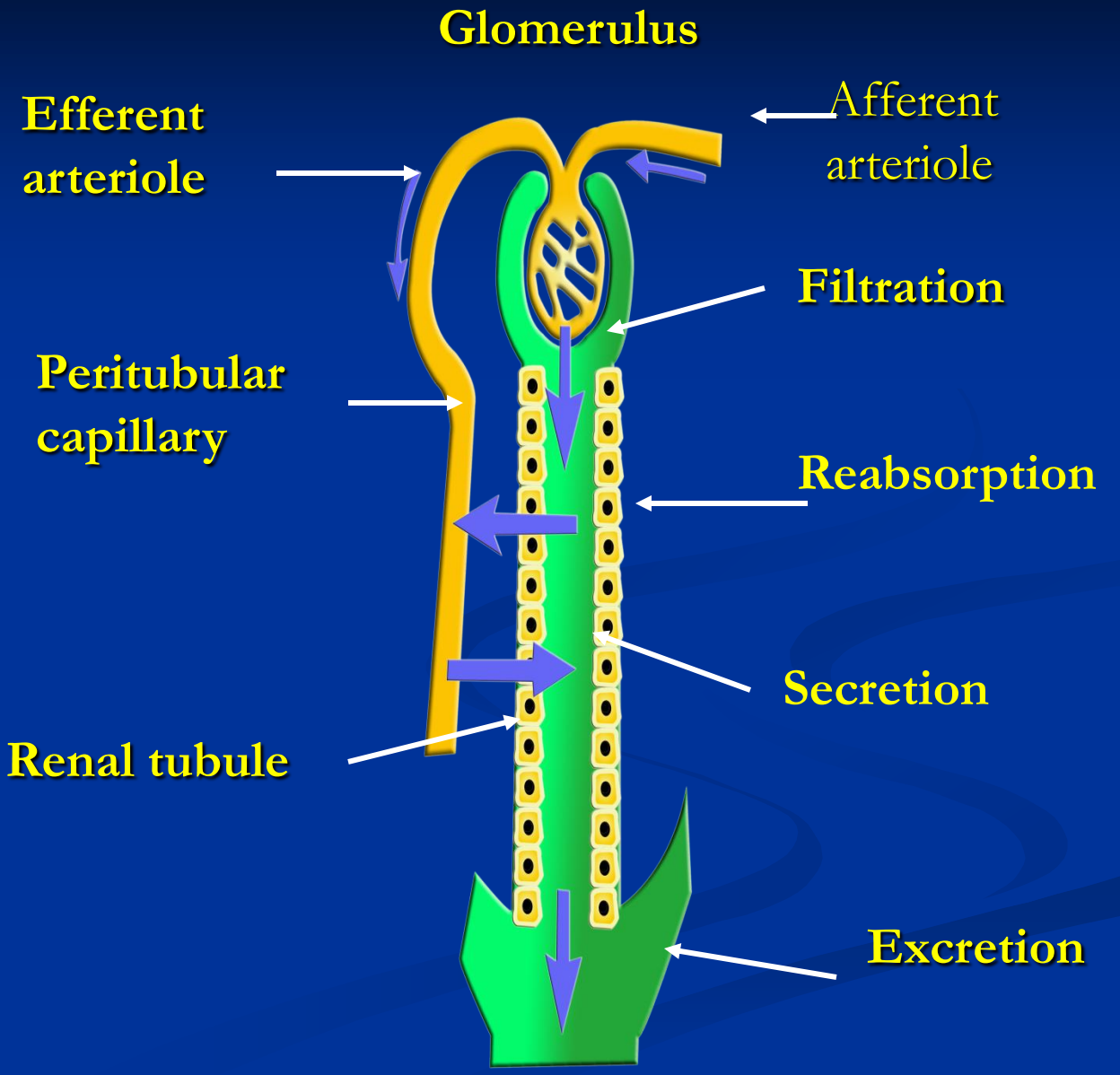
At the end of this lecture student should be able to describe

- **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

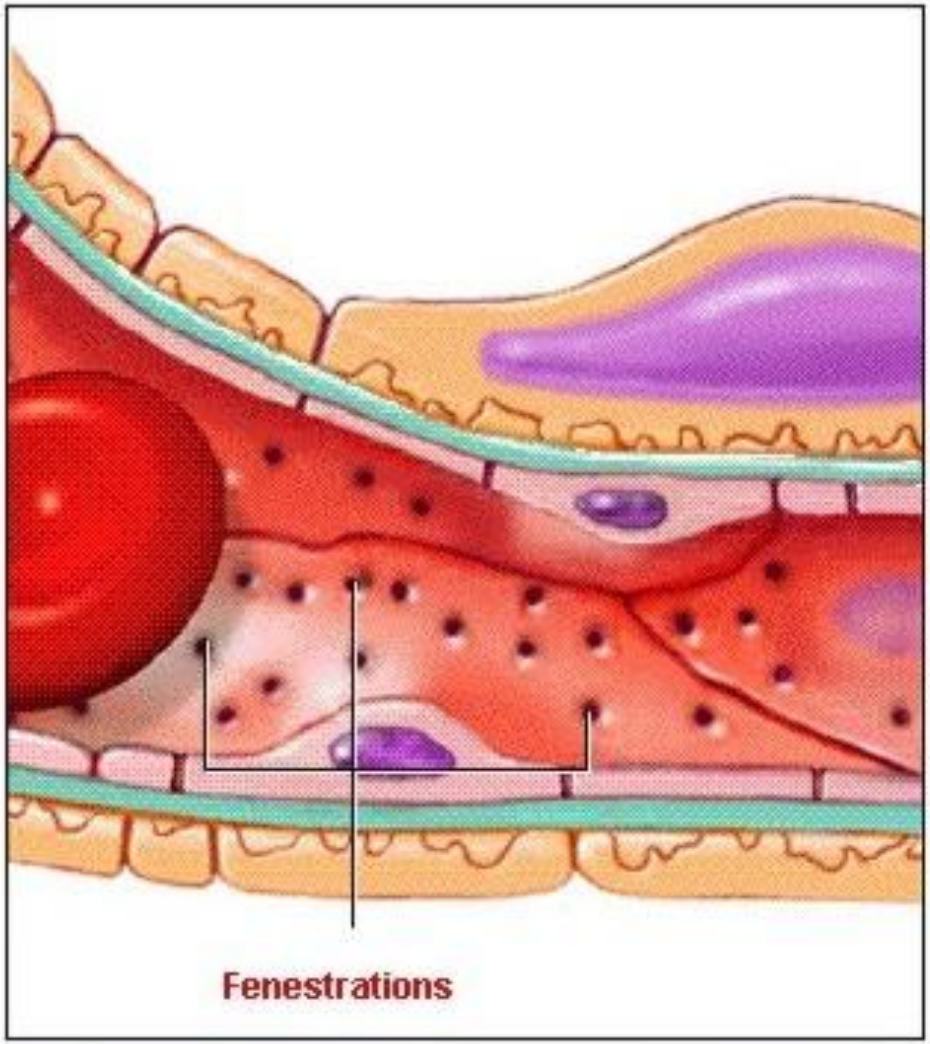
Filtration membrane

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

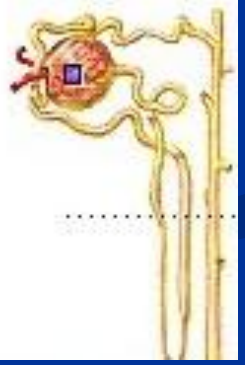
Characteristic of filtration membrane

- 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

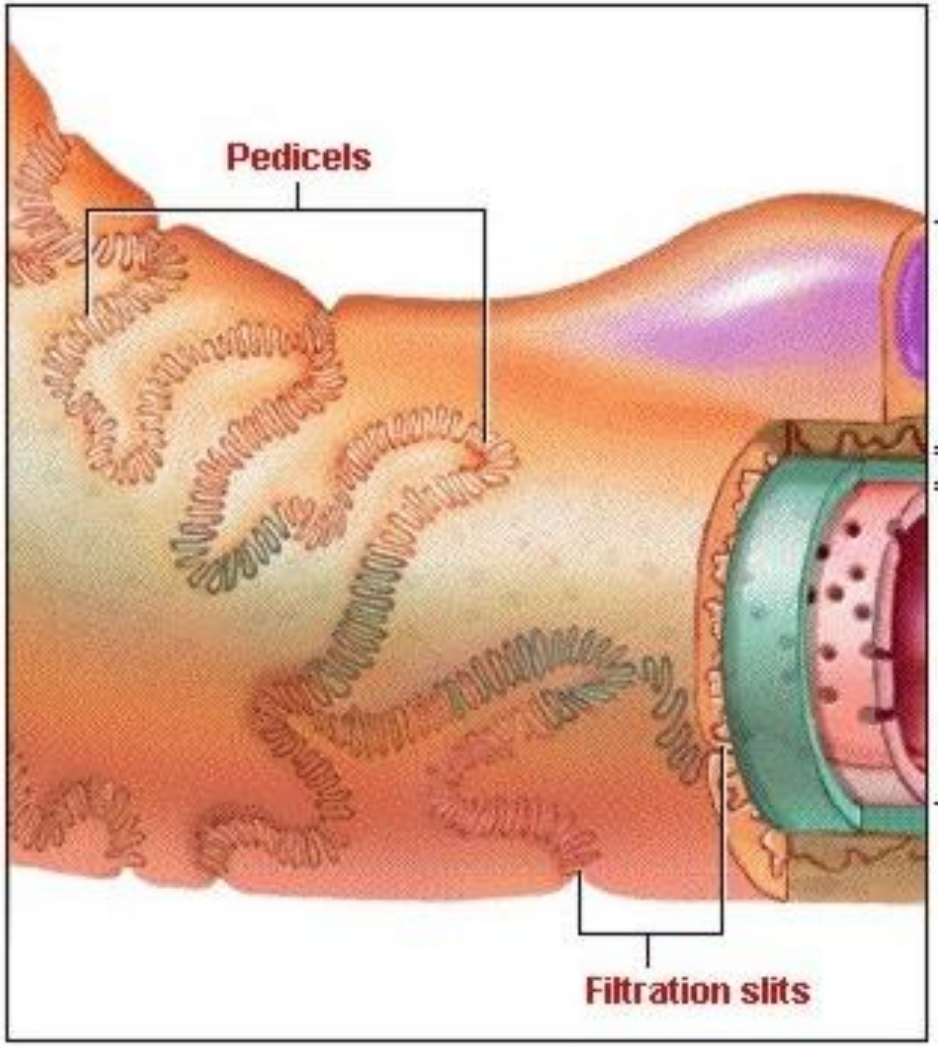
Cellular Features of the Renal Corpuscle



Here we see a glomerular capillary in longitudinal section.



Cellular Features of the Renal Corpuscle



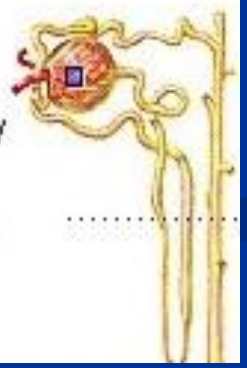
Surrounding the basement membrane is a layer of podocytes.

Podocyte cell body with nucleus

Basement membrane

Capillary **endothelium**

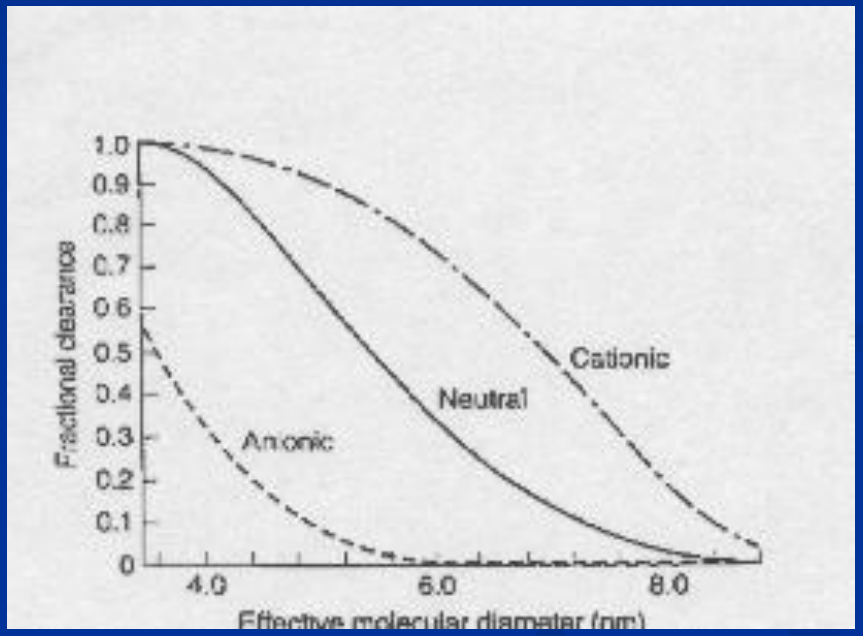
Together, the fenestrated capillary endothelium, basement membrane, and podocytes make up the **filtration membrane**.



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



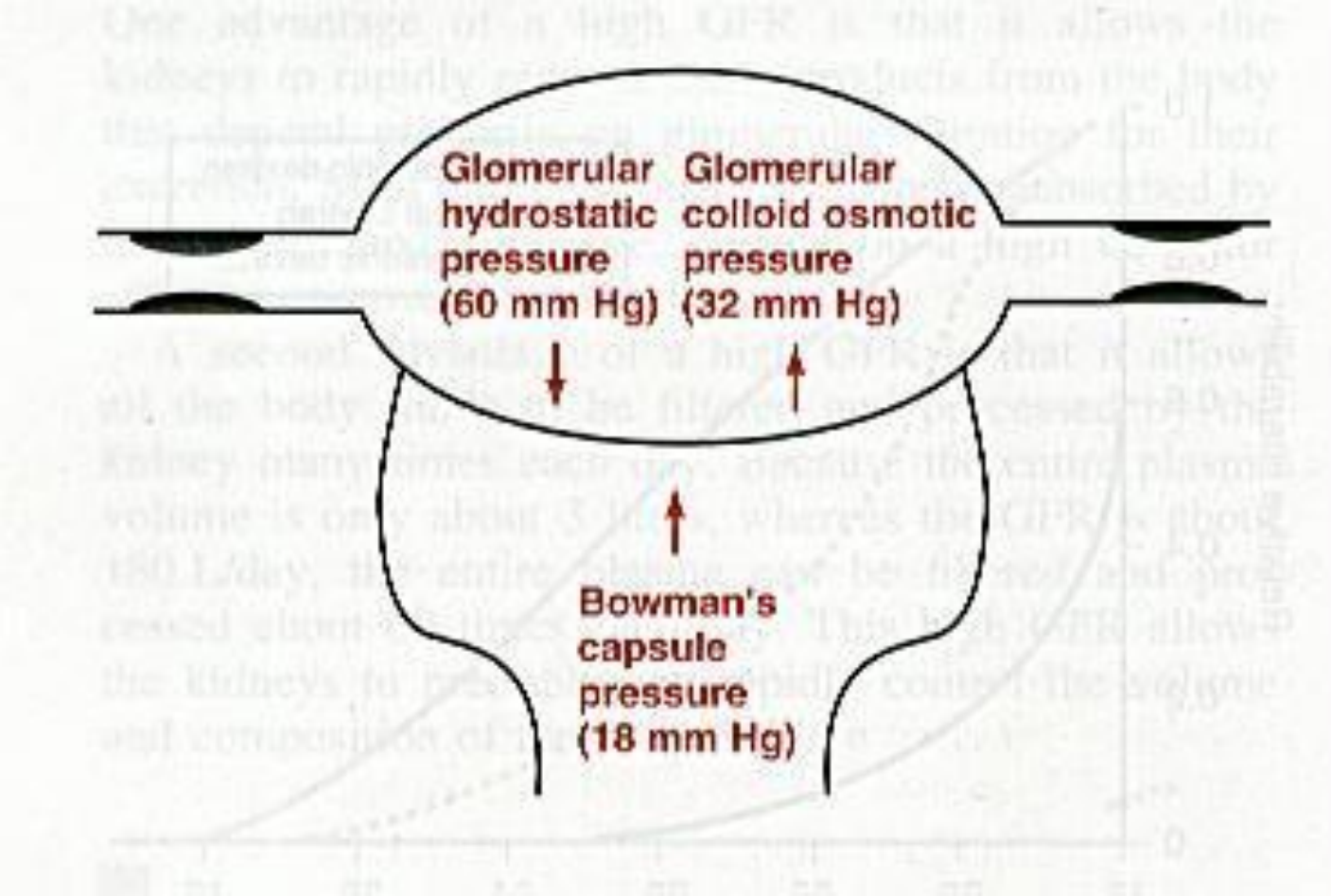
Filtration pressure

- 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 (πGC)
3. Bowman hydrostatic pressure (PBS)
4. Bowman osmotic pressure (πBS) = 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 (π_{GC})
   - Opposes filtration
   - 32 mmHg
   - Caused by plasma protein
   - Is not constant
4. Colloid osmotic pressure in Bowman capsule (π_{BC})
   - Zero (no plasma protein)

Calculation of net filtration pressure

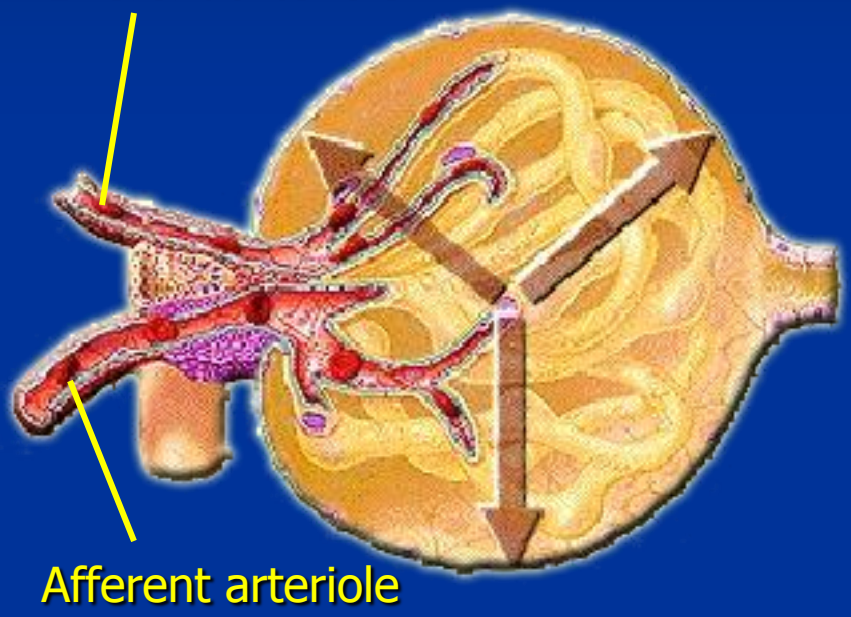
- Net filtration pressure

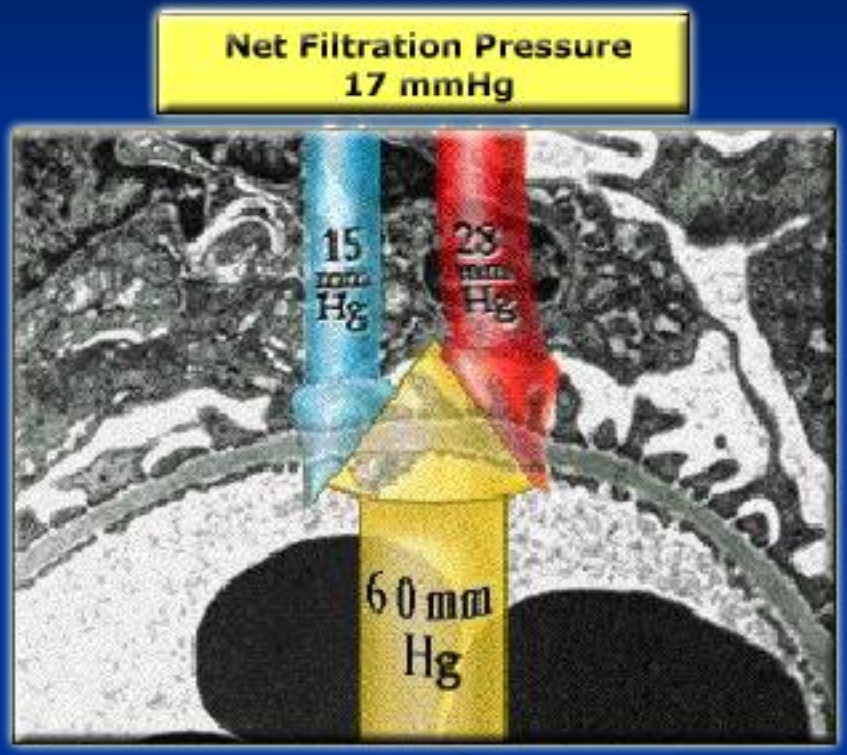
  = 60-18-32= 10 mmHg

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

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

Net Filtration Pressure (NFP)

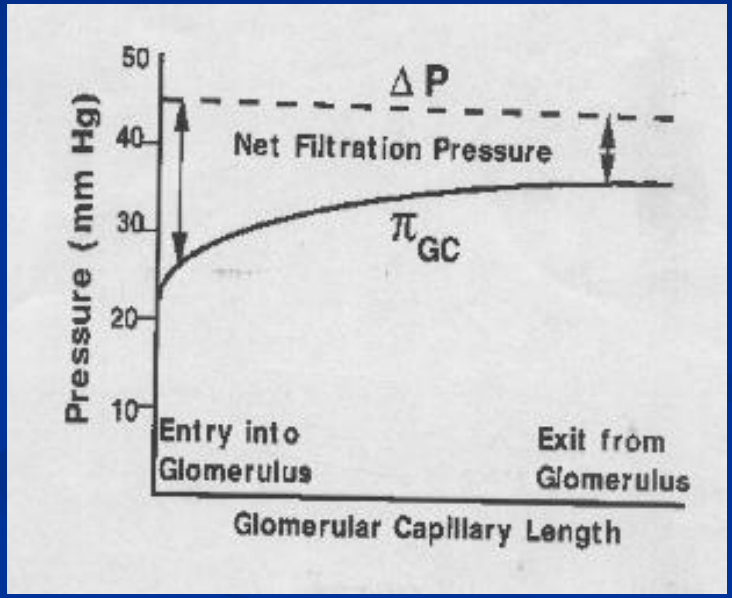




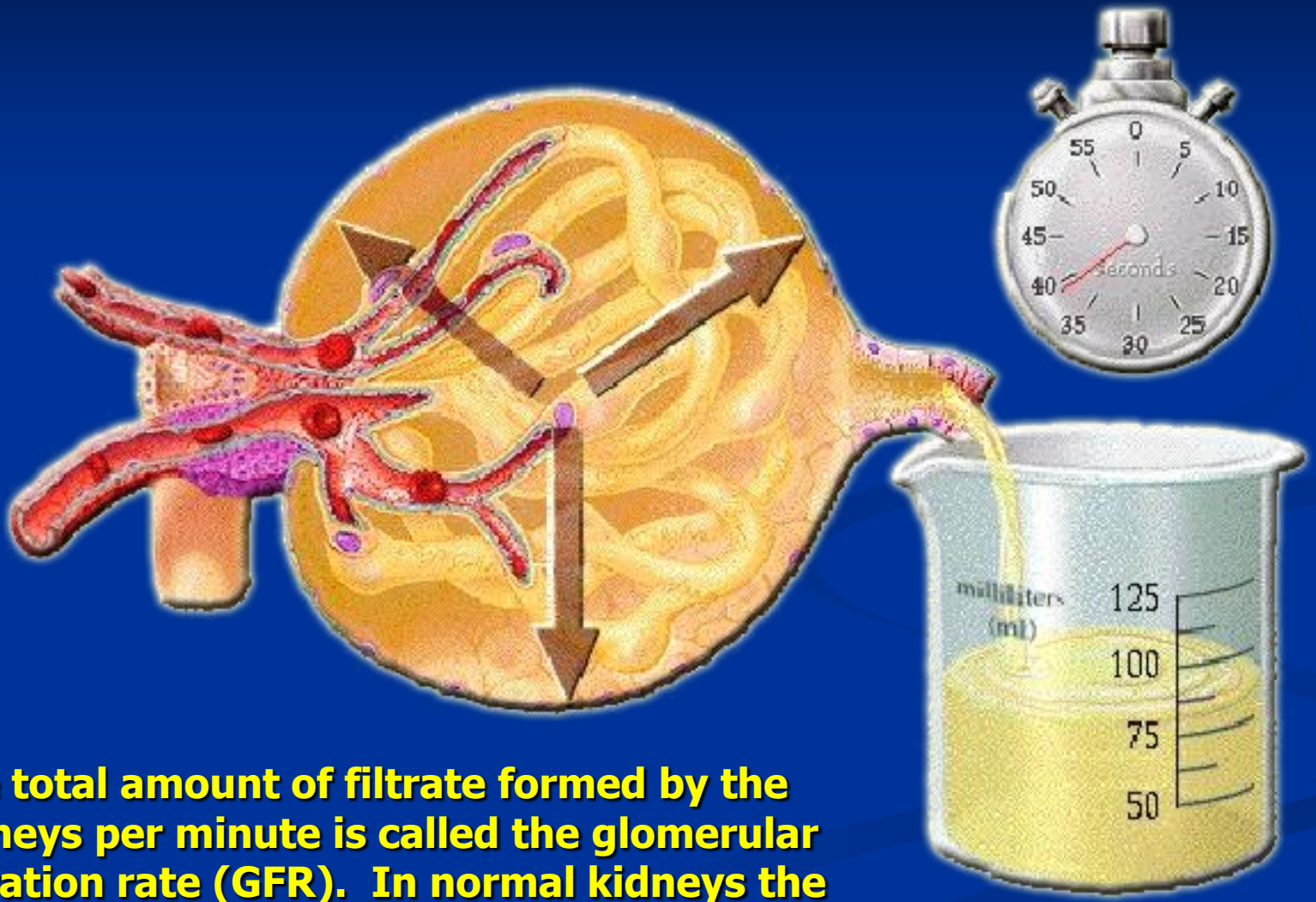
P_{GC} – favors filtration = 60mmHg
P_T – opposes filtration = 15mmHg
π_{GC} – opposes filtration = 28mmHg
NFP 60mmHg – (15mmHg + 28mmHg) = 17mmHg

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.

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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

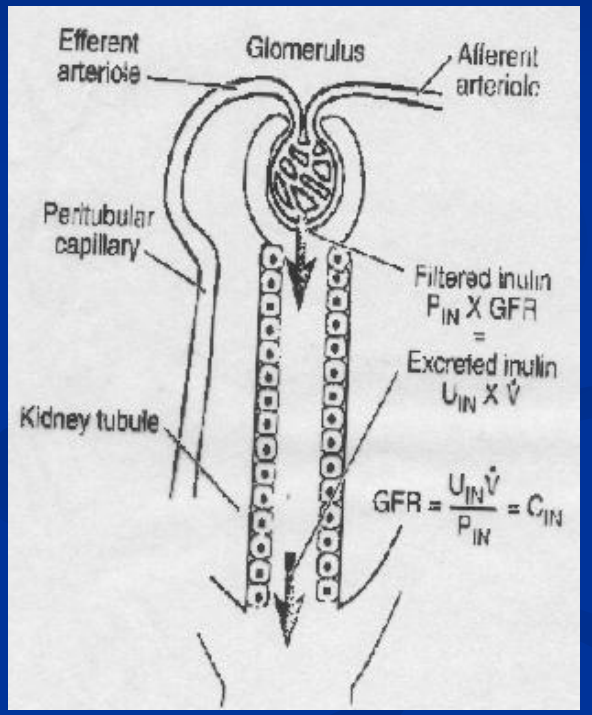
- Characteristic of substance used
  - Freely filtered (not reabsorbed or secreted)
  - Not metabolized by the kidney
  - Not toxic and stable
  - Not bound to plasma protein
  - Does not change renal plasma flow
- Inulin

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



Calculation Of GFR & FF

- GFR= K_f x net filtration pressure
- GFR = 12.5 x 10 = 125 ml/min
- $K_f \propto$ GFR ($\downarrow K_f$ in diabetes - $\downarrow$ 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 π_{GC}**
   - π_{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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