Glomerular filtration I

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GFR

1. Definition
2. Normal value
3. Variation
4. Calculation (different pressures acting on glomerular membrane)
5. Factors affecting GFR
6. Regulation of GFR
7. Measurement of GFR

QUESTIONS

LONG QUESTION

1. GFR
2. RENIN ANGIOTENSIN SYSTEM

SHORT NOTE

1. DYNAMICS OF GFR
2. FILTRATION FRACTION
3. ANGIOTENSIN II
4. FACTORS AFFECTING GLOMERULAR FILTRATION RATE
5. REGULATION OF GFR
6. RENAL CLEARANCE TEST
7. MEASUREMENT OF GFR

Collecting duct epithelium

- P Cells –

  Tall, predominant, have few organelles,

  Na reabsorption & vasopressin stimulated water reabsorption

- I cells-

  CT and DCT, less, having more cell organelles, Acid secretion and HCO_3 transport

CHARACTERISTICS OF RENAL BLOOD FLOW

- 600-1200 ml/min (high)
- AV O2 difference low (1.5 mL/dL)
- During exercise increases 1.5 times
- Low basal tone, not altered in denervated / innervated kidney
- VO2 in kidneys is directly proportional to RBF, Na reabsorption & GFR
- Not homogenous flow, cortex more & medulla less

- Vasa recta hairpin bend like structure, hyperosmolarity inner medulla
- Transplanted kidney- cortical blood flow show autoregulation & medullary blood flow don’t show autoregulation, so no TGF mechanism
- Neurogenic vasodilation not exist
- 20% of resting cardiac output, while the two kidneys make < 0.5% of total body weight.
- Excretory function rather than its metabolic requirement.
- Remarkable constancy due to autoregulation.

Processes concerned with urine formation.

1. Glomerular filtration,
2. Tubular reabsorption and
3. Tubular secretion.

- **Filtration**

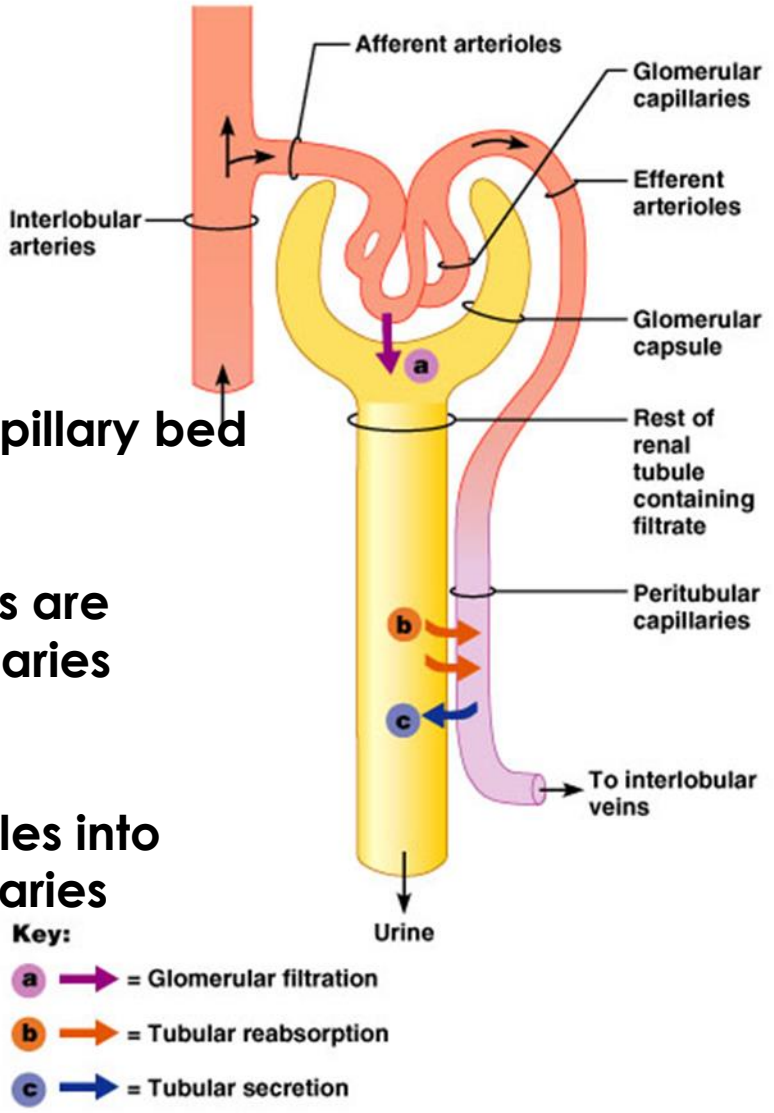
Fluid is squeezed out of glomerular capillary bed

- **Reabsorption**

Most nutrients, water and essential ions are returned to blood of peritubular capillaries

- **Secretion**

Moves additional undesirable molecules into tubule from blood of peritubular capillaries



Glomerular filtration

- Glomerular filtration refers to process of ultrafiltration of plasma from glomerular capillaries into the Bowman's capsule.

GLOMERULAR FILTRATION DEPENDS ON

1. Characteristics of filtration membrane,
2. Composition of glomerular filtrate,
3. Dynamics of glomerular filtration,
4. Glomerular filtration rate,
5. Filtration fraction,
6. Factors affecting glomerular filtration

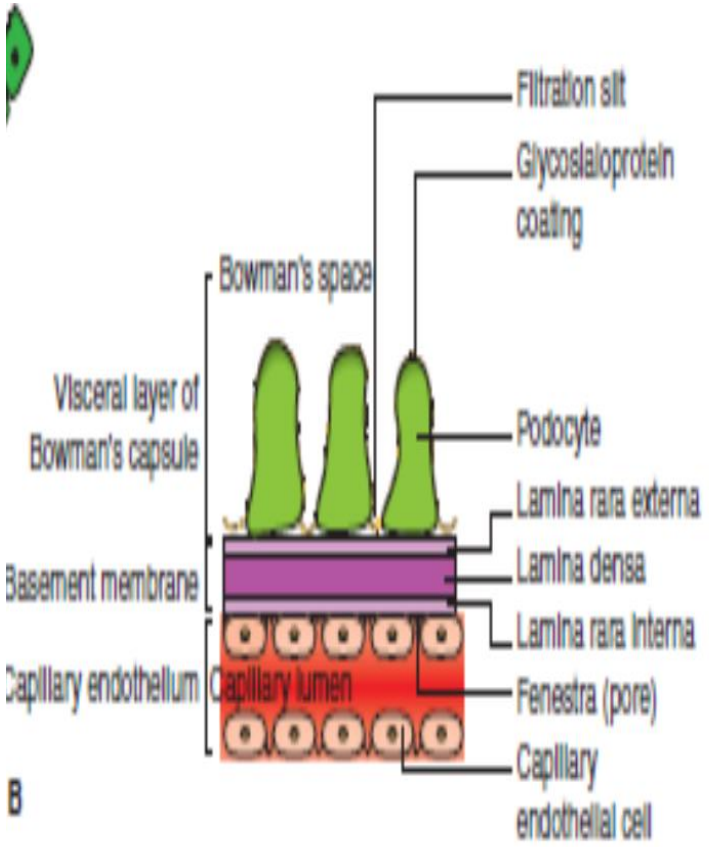
1.Characteristics of filtration membrane

- High permeability

- Permeability selectivity

1. Pore size
- Below 8mm
- Above 8 nm
- 4-8 nm

2. Electric charge
- Glycoprotein/ sialic acid
- Neutral > cationic > anionic



Filtration Membrane

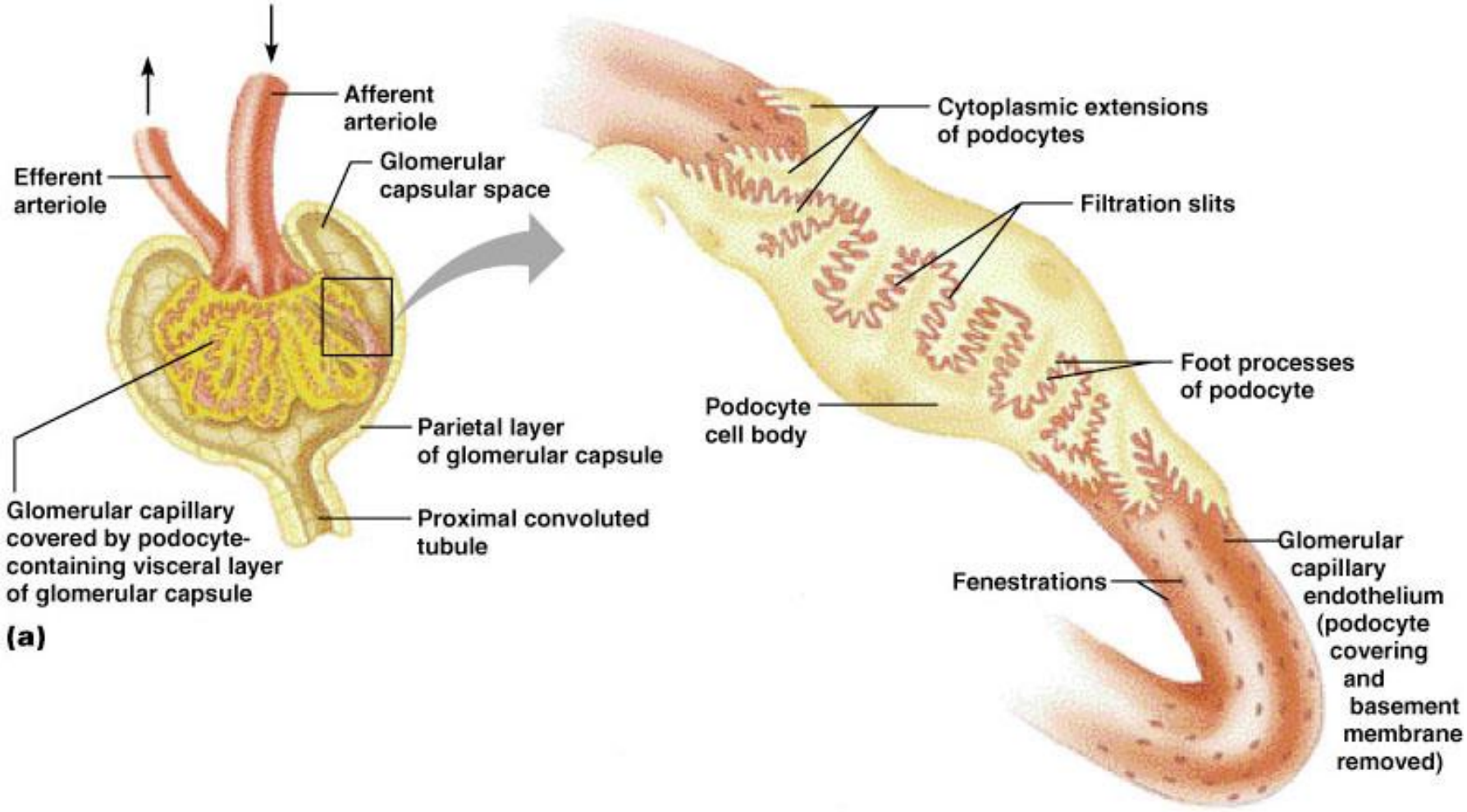


Figure 25.7a

Glomerular filtration barrier

Substance	Molecular weight (dalton)	Radius (nm)	Filterability
Water	18	0.15	1
Sodium	23	0.10	1
Glucose	180	0.33	1
Inulin	5500	1.48	1
Myoglobin	17000	1.88	0.75
Albumin	69000	3.55	0.005

2.COMPOSITION OF GLOMERULAR FILTRATE

- Normally proteins excretion in urine is less than 100 mg/dl
- Filtration membrane permeability alterted in diseases
- As a result, filtration of proteins is increased and albumin appears in urine in significant amount (albuminuria or proteinuria)

3. DYNAMICS OF GLOMERULAR FILTRATION

Forces Favouring Filtration (mm Hg)

- Glomerular capillary hydrostatic pressure = $P_{GC} = 60$
- Bowman's capsule colloid osmotic pressure = $\pi_{BS} = 0$

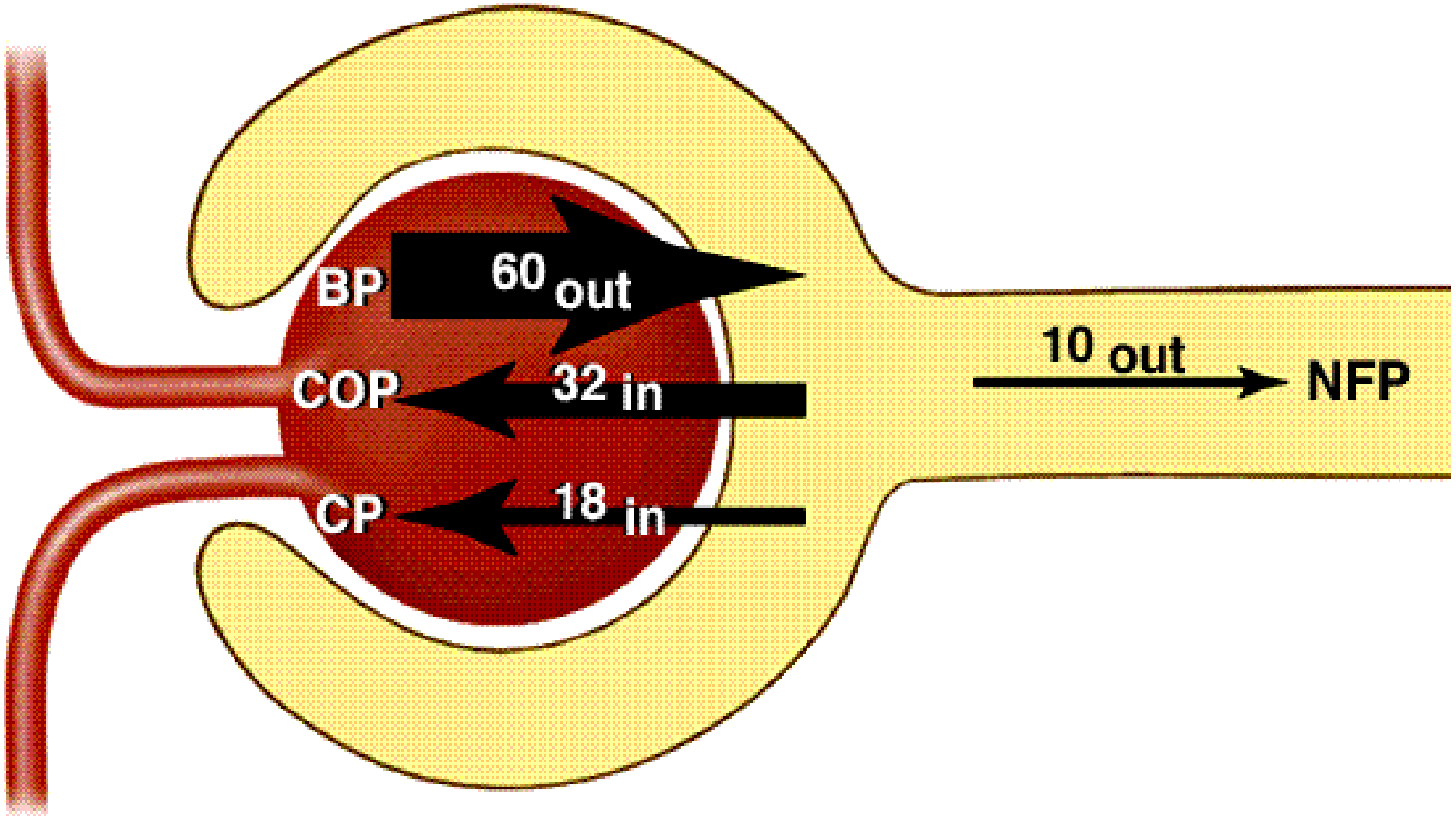
Forces Opposing Filtration (mm Hg)

- Bowman's capsule hydrostatic pressure = $P_{BS} = 18$
- Glomerular capillary colloid osmotic pressure = $\pi_{GC} = 32$

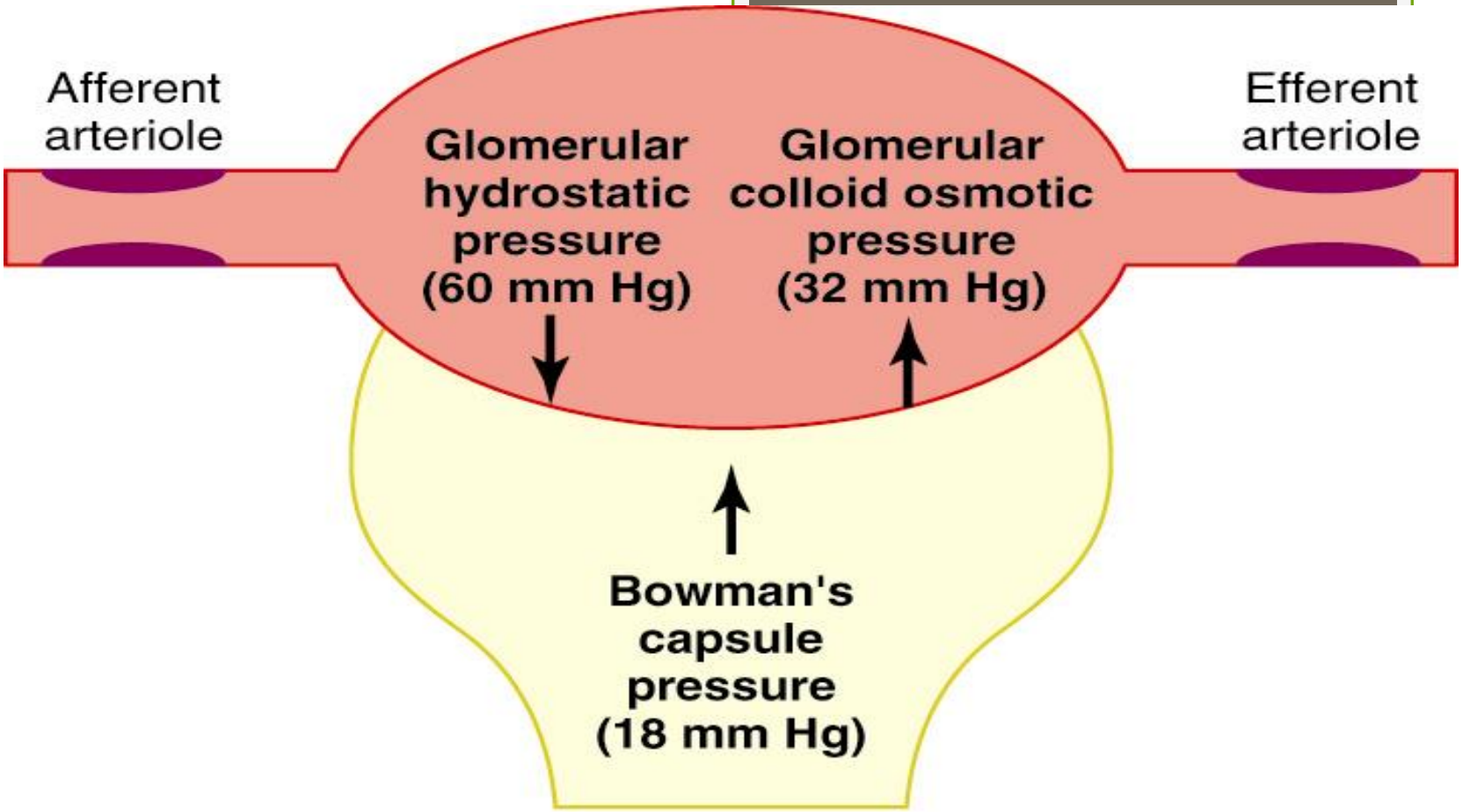
- Net filtration pressure =

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

- (60- 18) – (32-0)
- +10 mm Hg



Capillary blood pressure (BP)	60 mmHg out
Colloid osmotic pressure (COP)	– 32 mmHg in
Capsular pressure (CP)	– 18 mmHg in
Net filtration pressure (NFP)	10 mmHg out



Net filtration pressure (10 mm Hg) = Glomerular hydrostatic pressure (60 mm Hg) – Bowman's capsule pressure (18 mm Hg) – Glomerular oncotic pressure (32 mm Hg)

4.Determinants of GFR

- The total amount of filtrate formed per minute by the kidneys
- Ultrafiltration occurs because of Starling forces i.e. hydrostatic and oncotic pressures.
- Starling principle
- $$EFP = (P_{GC} - P_{BS}) - (\Pi_{GC} - \Pi_{BS})$$

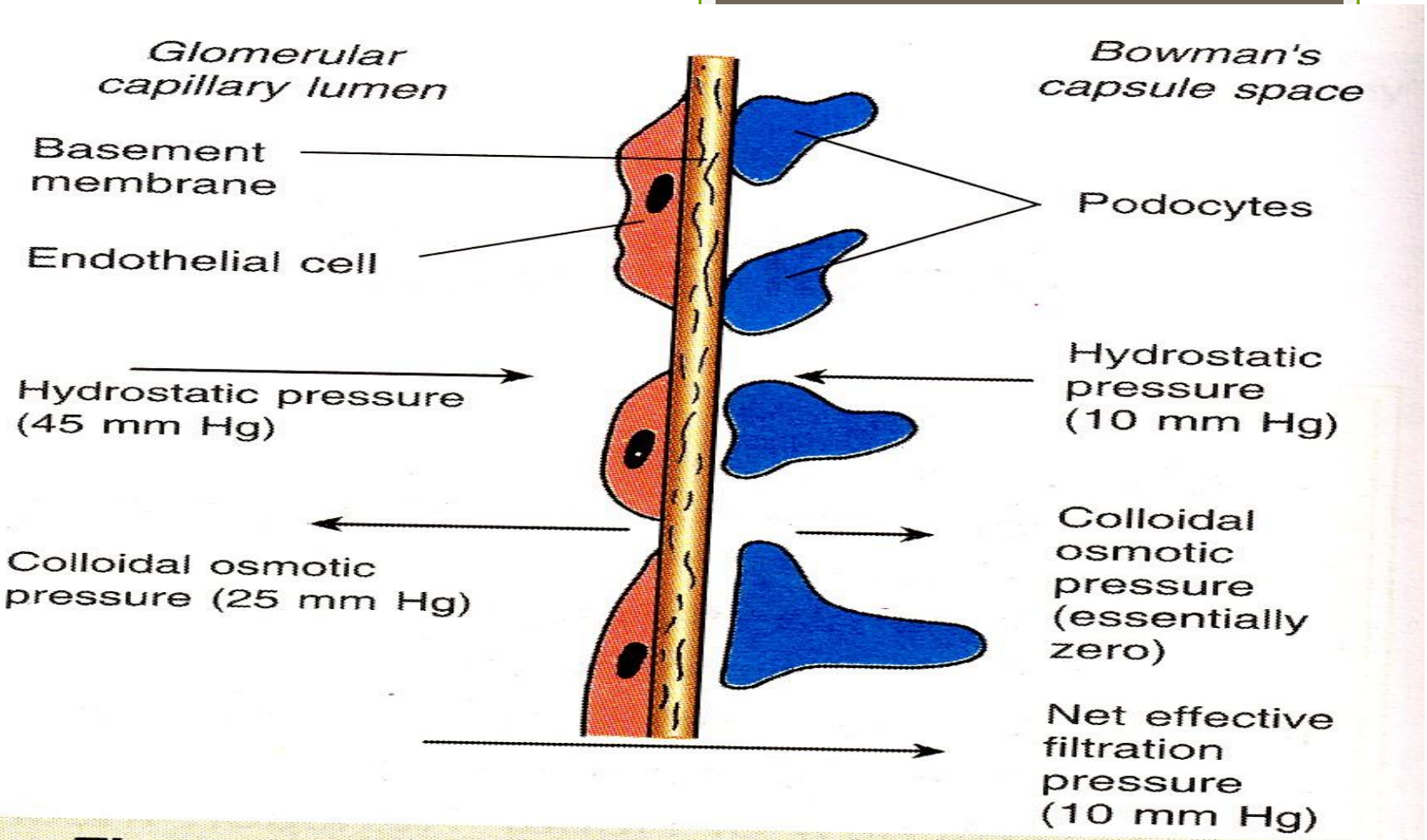


Fig. 7.2.2 A diagrammatic representation of mechanism of glomerular filtration.
(**Note**: Length of the arrows denotes magnitude and direction of the force.

- GFR = Kf X (P_{GC} - P_{BS}) – (Π_{GC} - Π_{BS})
- So, GFR = 12.5 X [(60 – 18) – (32 – 0)]

  = 12.5 X 10

  = 125 ml/min

- P_{GC} = Glomerular capillary hydrostatic pressure (60). outward= favour filtration
- P_{BS} = Bowmen space hydrostatic pressure (18). Inward = oppose filtration
- Π_{GC} = Glomerular capillary oncotic pressure (32) inward = oppose filtration
- Π_{BS} = Bowmen space oncotic pressure (0) Outward = favour filtration

- Normal GFR= 125 ml/min (range 90–140 ml/min).
- In women are 10% lower than in men.
- In 24 hr period, 180 L/day of plasma is filtered glomerulus.
- 99% or more is reabsorbed ,Only 1% or less is excreted as urine.
- After age of 30 years, GFR declines with age.
- If the GFR is too high:

Needed substances cannot be reabsorbed quickly enough & are lost in the urine

- If the GFR is too low:

Everything is reabsorbed, including wastes that are normally dispose

5.FILTRATION FRACTION

- Ratio of GFR to renal plasma flow (RPF).
- GFR 125 ml/min and RPF 650 ml/min;
- FF = 0.2 (125/650).
- Increase in FF = increase in reabsorption in PCT

6.FACTORS AFFECTING GLOMERULAR FILTRATION RATE

1. Filtration coefficient (Kf).
2. Hydrostatic pressure in Bowman's space fluid (PBS)
3. Glomerular capillary hydrostatic pressure (PGC).
4. Glomerular capillary oncotic pressure (πGC).
5. Sympathetic stimulation
6. State of glomerular membrane

1.Filtration coefficient (Kf).

- Increased Kf raises GFR & Decreased Kf reduces GFR.

Kf = permeability X filtration area (glomerular capillary membrane)

- Hypoxia and presence of toxic agents and increase in colloidal osmotic pressure of bowmen's space increase Kf by increasing permeability

- Sialoprotein have negative charge so anions have less permeability and size more than 8 nm will not filtered.
- Thickening of capillary membrane will decrease permeability.

- **Filtration area-(SIZE OF CAPILLAR BED)**

- **Contraction of mesangial cells= Vasoconstrictors Release**
  Endothelin, NE,TXA2,Histamine=
  decrease Kf = decrease GFR

- **Relaxation of mesangial cells = Vasoconstrictors Release**
  Dopamine, C-AMP, ANP, NO.PG
  increase Kf = increased GFR

Contraction of mesangial cells (decrease GFR)	Relaxation of mesangial cells (Increase GFR)
Angiotensin-I	Atrial natriuretic peptide (ANP)
Antidiuretic hormone (ADH)	Cyclic AMP
Endothelins	Dopamine
Histamine	Prostaglandins (PGE_2)
Leukotrienes–C_4 and D_4	Nitric oxide (NO)
Prostaglandins (PGF_2)	
Platelet derived growth factor (PDGF)	
Platelet activating factor	
Thromboxane-A_2	

2.Hydrostatic pressure in Bowman's space fluid (P_{BS})

- Opposes filtration
- Therefore GFR is inversely related to it.
- Odema of kidney inside tight renal tubule increase P_{BS}
- ureteric obstruction by stone increase P_{BS}

3.Glomerular capillary hydrostatic pressure (P_{GC}).

- GFR Directly related to P_{GC}.
- dependent on:

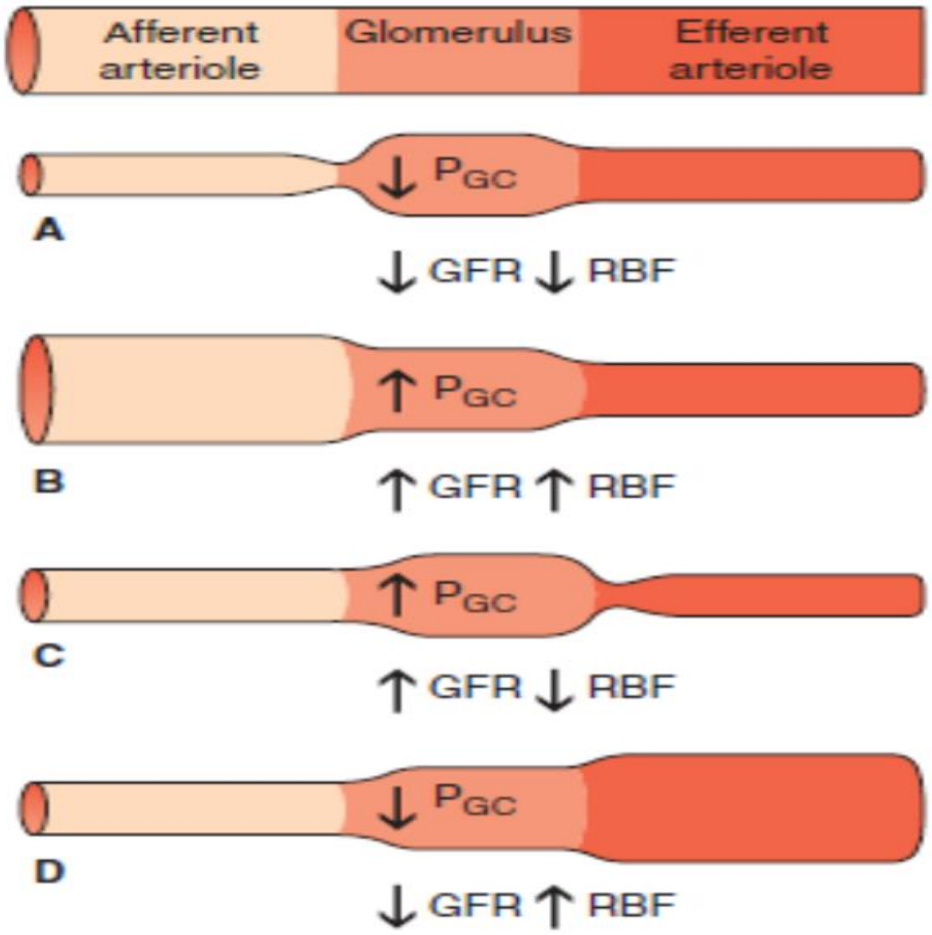
(i) Arterial pressure.

- Autoregulation (80–200 mm Hg)
- Increased above 200 mm Hg -raise GFR
- Decreased below 70 mm Hg -lower GFR.

(ii) Renal blood flow.

- GFR is directly proportional to the renal blood flow
- Autoregulatory mechanisms.

(iii) Afferent and efferent arteriolar resistance.


Afferent arteriole
Glomerulus
Efferent arteriole
↓ P_{GC}
A
↓ GFR ↓ RBF
↑ P_{GC}
B
↑ GFR ↑ RBF
↑ P_{GC}
C
↑ GFR ↓ RBF
↓ P_{GC}
D
↓ GFR ↑ RBF

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