Unit V – Problem 8 – Physiology: Glomerular Filtration and Renal Blood Flow

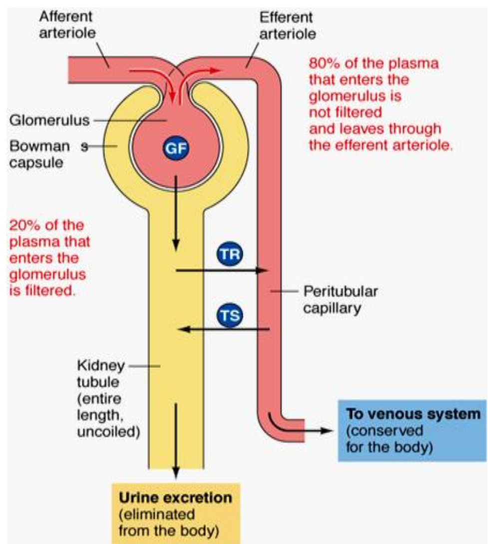
- What are the functions of kidneys?

- **Removing metabolic waste products and foreign chemicals from the blood and their excretion in urine.**
- **Regulating:**
  - ✓ Blood volume.
  - ✓ Arterial blood pressure (both blood volume and blood pressure are regulated through renin-angiotensin-aldosterone system).
  - ✓ Concentration of blood solutes: Na^+, Cl^-, K^+, Ca^{2+}, HPO_4^{2-}
  - ✓ Acid-base balance.
  - ✓ Blood cell synthesis (through the secretion of erythropoietin).
- **Conversion of vitamin D (25-OH vitamin D) to its active form (1,25-$(OH)_2$ vitamin D) through the enzyme 1α-hydroxylase that is present in kidneys.**
- **Gluconeogenesis (especially in with prolonged starvation).**

- Renal Blood Flow (RBF):

- **Definition**: it is the volume of blood delivered to kidneys per unit time. This represents 25% of cardiac output which is equal to 1200 ml/min.
- Notice that 80% of (RBF) perfuses the renal cortex and only 20% perfuses the medulla.
- **(RBF)** = $\frac{(Arterial\ pressure - Venous\ pressure)}{Total\ renal\ vascular\ resistance}$ **or** $\frac{Renal\ Plasma\ Flow\ (RPF)}{1 - hematocrit}$
- **(RBF) and O_2 consumption:**
  - ✓ 20% of O_2 consumption is for metabolic needs.
  - ✓ 80% of O_2 consumption is for active reabsorption of ions and active secretion of others.

- Urine formation/excretion:

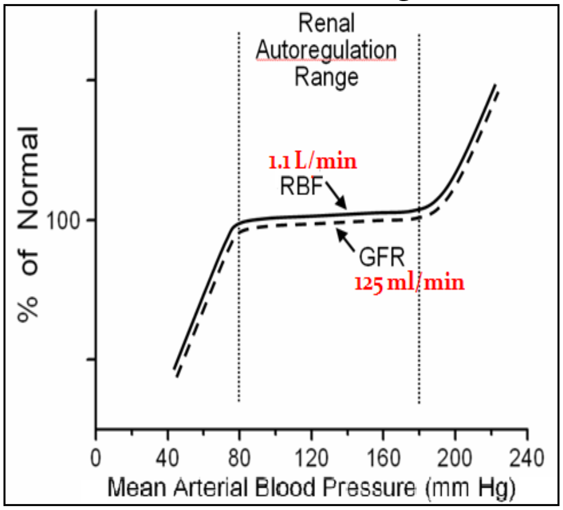


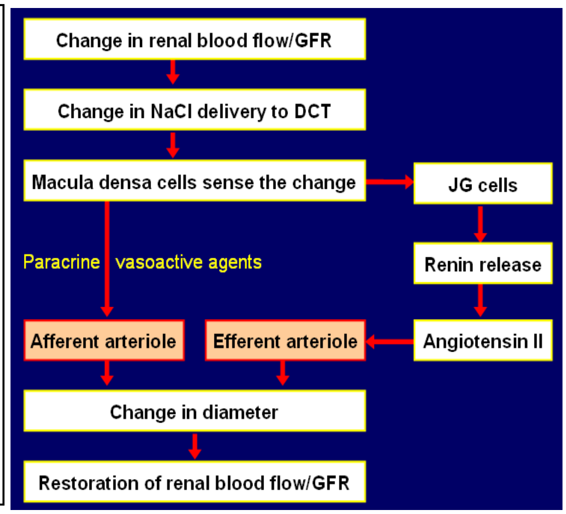
- Blood is delivered through renal arteries to glomerular capillaries where it will be filtrated to enter renal tubules.
- Reabsorption of water and different ions occur through the course of renal tubules into peritubular capillaries.
- Some ions are actively secreted in renal tubules to be excreted in the urine.
- Filtered blood will return to systemic circulation through interlobular veins.

- Glomerular Filtration Rate (GFR):

- Inulin clearance can be used to calculate (GFR) because it is freely filtered and is neither reabsorbed nor secreted.
- Notice that creatinine clearance is an approximate measure of (GFR). Slightly overestimates (GFR) because creatinine is moderately secreted by the renal tubules.
- **(GFR) = C_{inulin} = $\frac{U_{inulin}\ x\ V}{P_{inulin}}$ ml/min**
  - ✓ U_{inulin}: urine concentration of inulin (mg/ml).
  - ✓ V: urine flow rate (ml/min).
  - ✓ P_{inulin}: Plasma concentration of inulin (mg/ml).
- **Normal (GFR) = 125 ml/min (180 L/day).**
- **Glomerular capillary filtration coefficient (K_f) is depending on:**
  - ✓ Premeability coefficient of membrane.
  - ✓ Surface area (A) of filtration membrane.

- **Physiologic control of (GFR): it is controlled by the following mechanisms:**
  - ✓ <u>Intrinsic feedback mechanisms (they normally keep RBF and GFR constant despite marked changed in arterial blood pressure):</u>
    - ❖ *Autoregulation:*
      - ➢ Myogenic (relatively minor in kidneys).
      - ➢ Tubuloglomerular feedback.

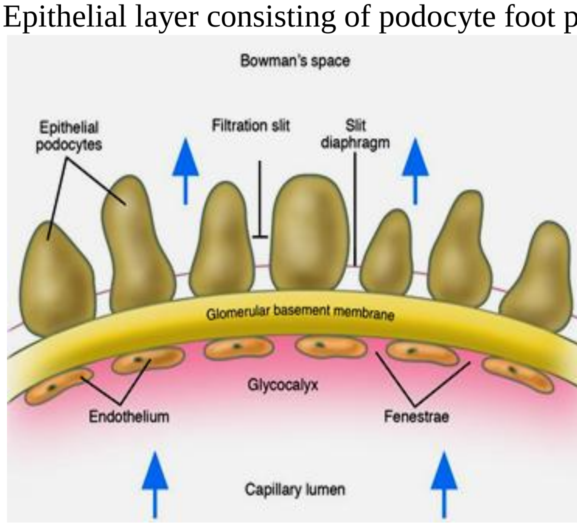


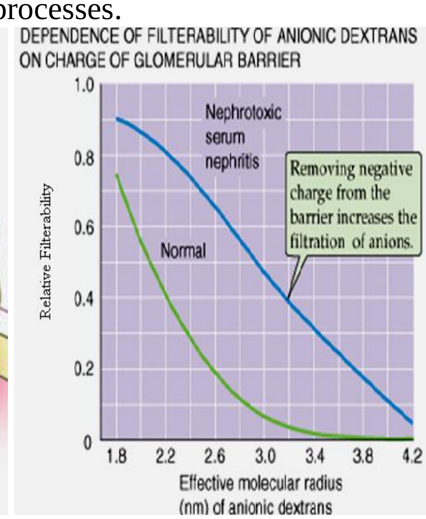


    - ❖ *Autocoids.*
  - ✓ <u>Extrinsic feedback mechanisms:</u>
    - ❖ *Sympathetic nervous system activation.*
    - ❖ *Hormones.*

  These mechanisms are directed to adjust (RPF) and (P_{GC}) by mainly regulating arteriolar resistance or mesangial cells.

- **<u>Glomerular filtration barrier:</u>**
- Responsible for filtration of plasma according to size and net charge.
- **Composed of:**
  - ✓ Fenestrated capillary endothelium (size barrier).
  - ✓ Fused basement membrane with heparin sulfate (negative charge barrier).
    - ❖ Effect of charge on filterability: anions (negatively charged molecules) do not pass easily through glomerular filtration barrier.
  - ✓ Epithelial layer consisting of podocyte foot processes.





- **Disruption of glomerular filtration barrier in type-II diabetes:**
  - ✓ Reduced endothelial glycocalyx.
  - ✓ Reduced endothelial fenestrations.
  - ✓ Thickened glomerular basement membrane.
  - ✓ Increased foot process width with decreased filtration slit frequency.

- **Net filtration pressure:**

Force	Effect	Magnitude (mmHg)
Glomerular capillary blood pressure	Favors filtration	55
Plasma-colloid osmotic pressure	Opposes filtration	30
Bowman's capsule hydrostatic pressure	Opposes filtration	15
Net filtration pressure (difference between force favoring filtration and forces opposing filtration)	Favors filtration	10 (how?) → 55 – (30 + 15) = 10

- **Bowman's capsule hydrostatic pressure (P_{BC}) and (GFR):**
  - ✓ Increased (P_{BC}) → decreases (GFR).
  - ✓ Can increase markedly in certain pathological states:
    - ❖ Urinary tract obstruction.
- **Glomerular capillary colloid osmotic pressure (л_{GC}) and (GFR):**
  - ✓ Increased (л_{GC}) → decreases (GFR).
  - ✓ There are two factors which influence (л_{GC}):
    - ❖ Arterial plasma colloid osmotic pressure.
    - ❖ Filtration Fraction ($= \frac{GFR}{RPF}$)
      - ➢ ↑FF → ↑(л_{GC}) → ↓(GFR) and vice versa.
- **Glomerular capillary hydrostatic pressure (P_{GC}) anf (GFR):**
  - ✓ Magnitude of (P_{GC}) depends on (RPF) which is determined by:
    - ❖ Mean Arterial Pressure (MAP).
    - ❖ Arteriolar resistance.

- **Changes in glomerular dynamics:**

Effect	RPF	GFR	FF (GFR/RPF)
Afferent arteriole constriction	↓	↓	-
Efferent arteriole constriction	↓	↑	↑
↑Plasma protein concentration	-	↓	↓
↓Plasma protein concentration	-	↑	↑
Constriction of ureter	-	↓	↓