# UGS MODULE
# PHYSIOLOGY(LECTURE 1)
# GLOMERULAR FILTRATION RATE (GFR)

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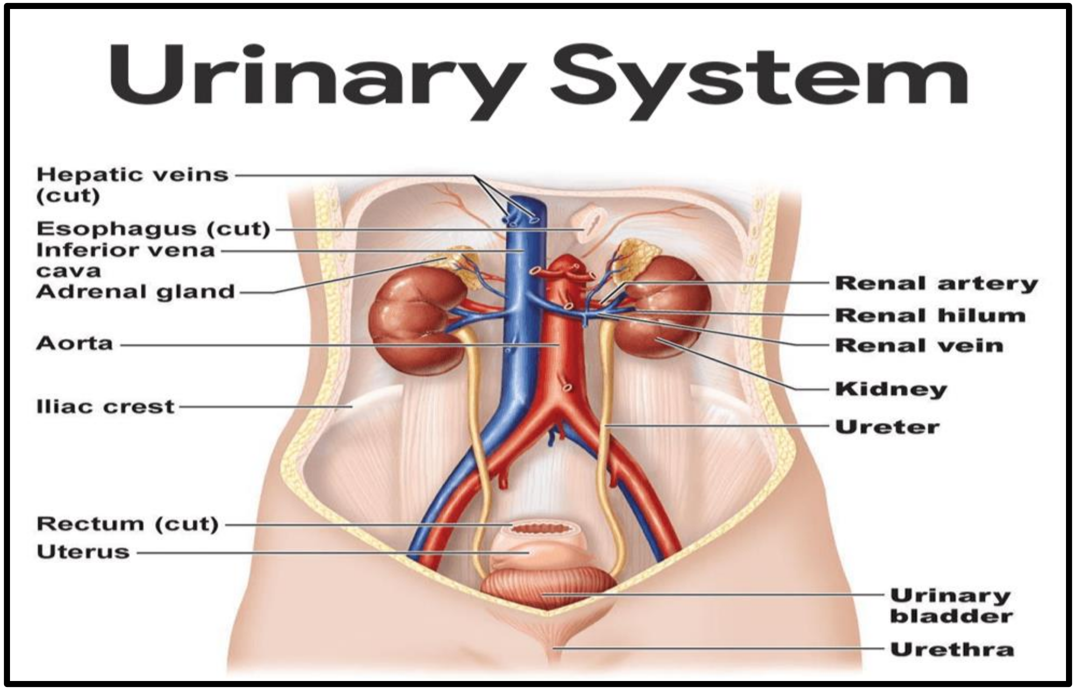
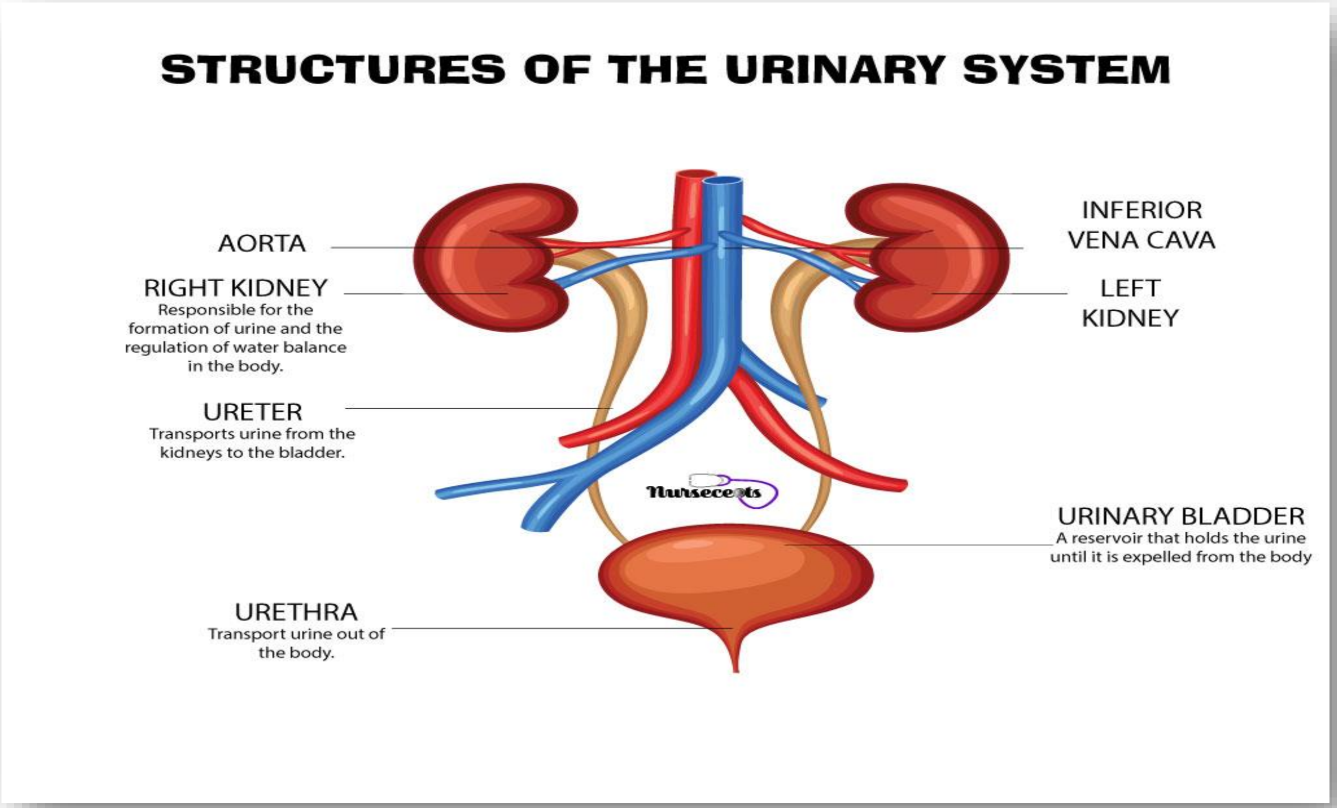


# The urinary system

The urinary system consists of two kidneys, two ureters, urinary bladder and the urethra. It is the **main excretory route in the body** since it is concerned with **formation and excretion of urine**.



# FUNCTIONS OF THE KIDNEYS

**1- Excretory function:** Through **urine excretion**, the kidneys clear the plasma from unwanted substances which include the following:

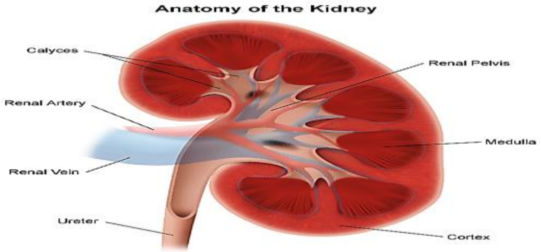
- **Non-essential substances:**
  - End products of metabolism e.g. urea, uric acid, creatinine and bilirubin.
  - Foreign substances e.g. drugs and toxins.
- **Excess amounts of essential substances** e.g. **water** and **electrolytes (regulation of water and electrolyte balance and volume of ECF)**.

**2- Homeostatic function:** By keeping the concentration of the different constituents of the body fluid constant (particularly ECF) e.g. glucose, amino acids, electrolytes, plasma osmolarity and pH……etc.

**3- Endocrine function:** Through secretion of renin, erythropoietin, prostaglandins, and active form of vitamin D3.

**4- Regulatory function:** Through regulation of **arterial blood pressure** and **acid-base balance**.

**5- Metabolism: Gluconeogenesis (during prolonged fasting) and ammoniagenesis which has an important role in acid–base homeostasis.**



## Endocrine function: The kidneys are endocrine organs

Through secretion of renin, erythropoietin, prostaglandins, and active form of vitamin D3 (1,25 dihydroxycholecalciferol; calcitriol).

1. **Renin:** A proteolytic enzyme secreted by **juxtaglomerular cells**. It acts on angiotensinogen (synthesized by liver) leading to formation of angiotensin I which is converted to angiotensin II by ACE. Angiotensin II produces generalized VC in addition to stimulation of aldosterone secretion.

**RAAS** is critical for **fluid–electrolyte homeostasis and long-term blood pressure regulation**.

- Renin secretion is stimulated by : Renal ischemia, increased sympathetic activity and catecholamines.
- Renin secretion is inhibited by: Angiotensin II, vasopressin and increased afferent arteriolar pressure .

2. **Erythropoietin:** Kidneys secrets 85% of erythropoietin which is a glycoprotein. It stimulates RBCs formation in bone marrow.
3. **Prostaglandins (PGs):** The kidneys secret 2 main types: $PGE_2$ and $PGI_2$.

Renal PGs act locally (paracrine) in the kidney and concerned mainly with autoregulation of GFR & RBF.

4. **1,25 dihydroxycholecalciferol:**

Active form of vitamin D3 formed in kidney from inactive 25-hydroxycholecalciferol in cells of **PCT by activity of 1α-hydroxylase enzyme** under control of parathormone; PTH. It regulates calcium homeostasis.

# The Nephron

**Definition:**

**It is the functional unit of the kidney.**

Nephrons work **independently** to produce urine and they constitute the functioning kidney mass.

**Each nephron consists of 2 main parts: a glomerulus and a long tubule.**

**(1) The glomerulus:** It is formed of a tuft of capillaries that are parallel, branching or anastomosing. The glomerulus is encased in the upper blind end of the renal tubule; Bowman's capsule.

**Both the glomerulus and Bowman's capsule are called renal corpuscle.**

Blood enters the glomerulus via an afferent arteriole, and leaves it via a narrower efferent arteriole. Accordingly, the glomerular capillary bed is a high pressure bed, which facilitates filtration of plasma.

**Function of glomerulus: ultrafilters (fine filters) to plasma**.

N.B. glomerulus lies between 2 arterioles and that the glomerular capillaries are the only capillaries in the body that drain into arterioles.

**(2) The renal tubule:**

- It is concerned with **urine formation**.
- It receives the glomerular filtrate (which is a filtrate from the plasma). As the filtrate flows through the tubule, substances are added to or removed from it. Ultimately, the fluid remaining at the end of each nephron combines in the collecting ducts and exits the kidneys as urine.

It consists of the following parts respectively:

**1. Proximal convoluted tubule (PCT):**

**2. Loop of Henle (LH):**

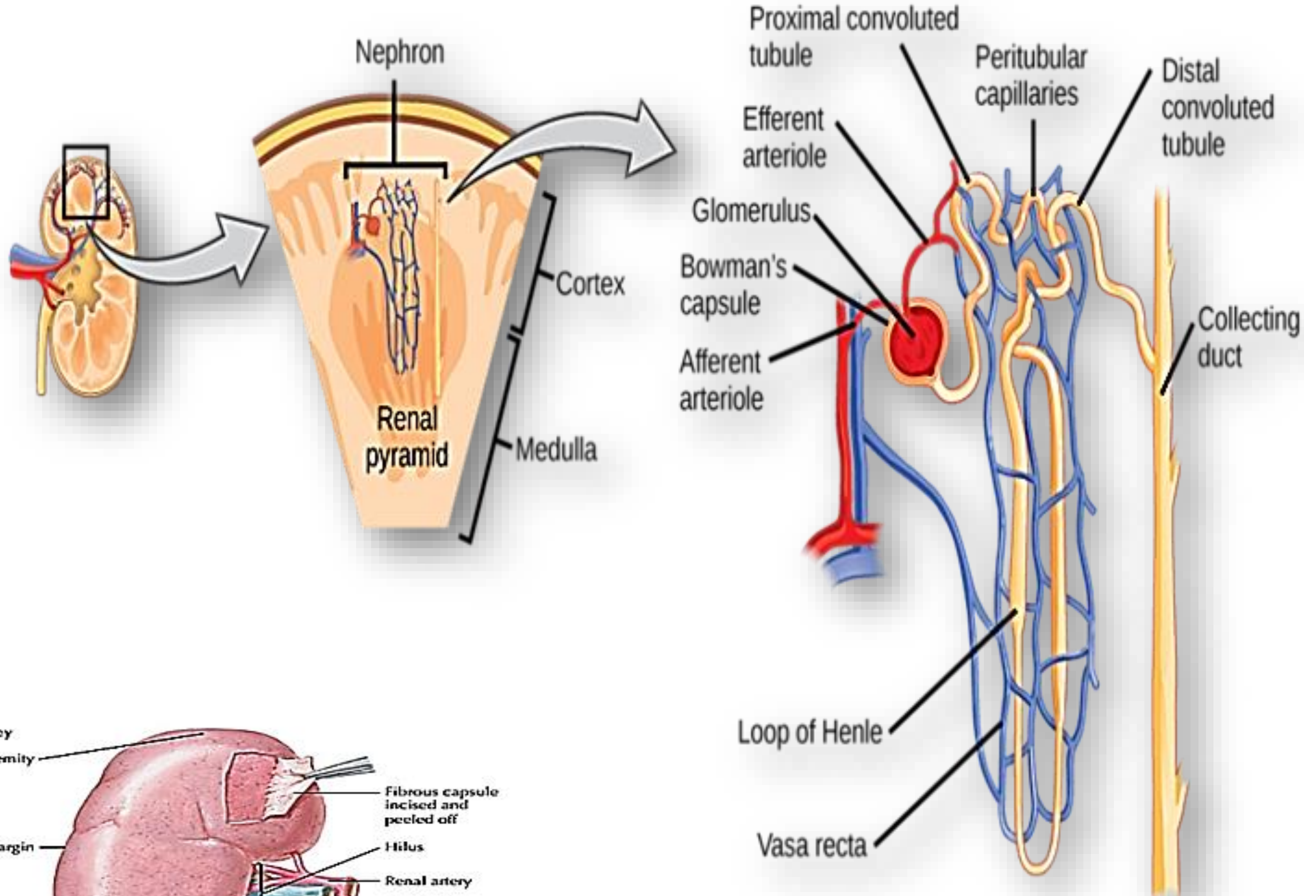
It is a **U-shaped segment of the renal tubule** that extends into the medulla for variable lengths.

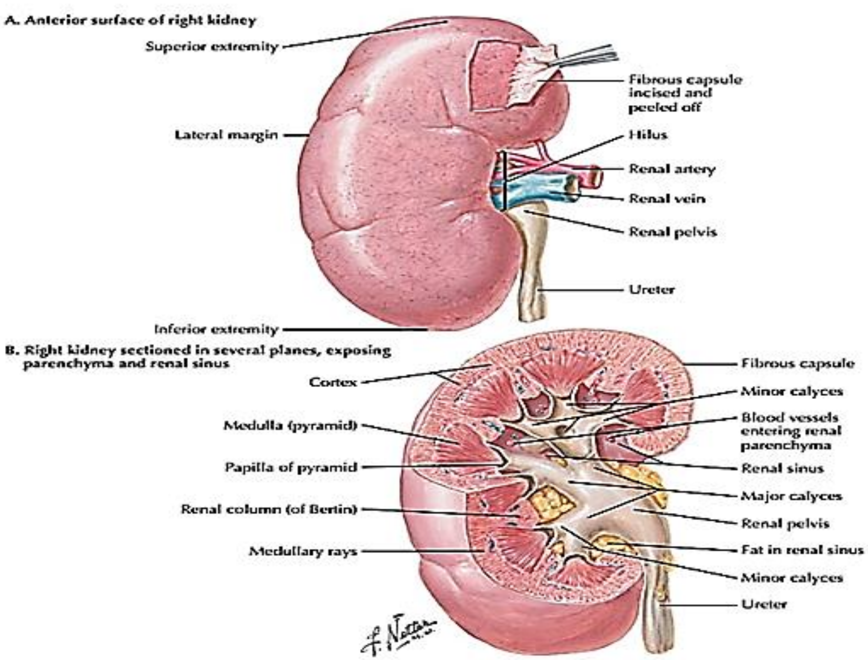
It has **descending and ascending limbs**.

**The walls of the descending limb and lower part of ascending limb are thin forming the thin segment of the LH**. On the other hand, the wall of the **upper part of the ascending limb** is thick, forming the **thick segment of the LH**.

**3. Distal convoluted tubule (DCT).**

**4. Collecting duct (CD): Cortical collecting duct (CCD)** and **medullary collecting duct (MCD)**. The later ducts merge forming larger ducts that drain into the **minor calyces** at the tips of the renal papillae. The minor calyces unite together forming **major calyces** that empty into the renal pelvis (from which the ureter arises).


Nephron
Cortex
Renal pyramid
Medulla
Proximal convoluted tubule
Peritubular capillaries
Distal convoluted tubule
Efferent arteriole
Glomerulus
Bowman's capsule
Afferent arteriole
Collecting duct
Loop of Henle
Vasa recta


A. Anterior surface of right kidney
Superior extremity
Fibrous capsule incised and peeled off
Lateral margin
Hilus
Renal artery
Renal vein
Renal pelvis
Ureter
Inferior extremity
B. Right kidney sectioned in several planes, exposing parenchyma and renal sinus
Cortex
Fibrous capsule
Minor calyces
Medulla (pyramid)
Blood vessels entering renal parenchyma
Papilla of pyramid
Renal sinus
Major calyces
Renal column (of Bertin)
Renal pelvis
Fat in renal sinus
Medullary rays
Minor calyces
Ureter

# The renal circulation

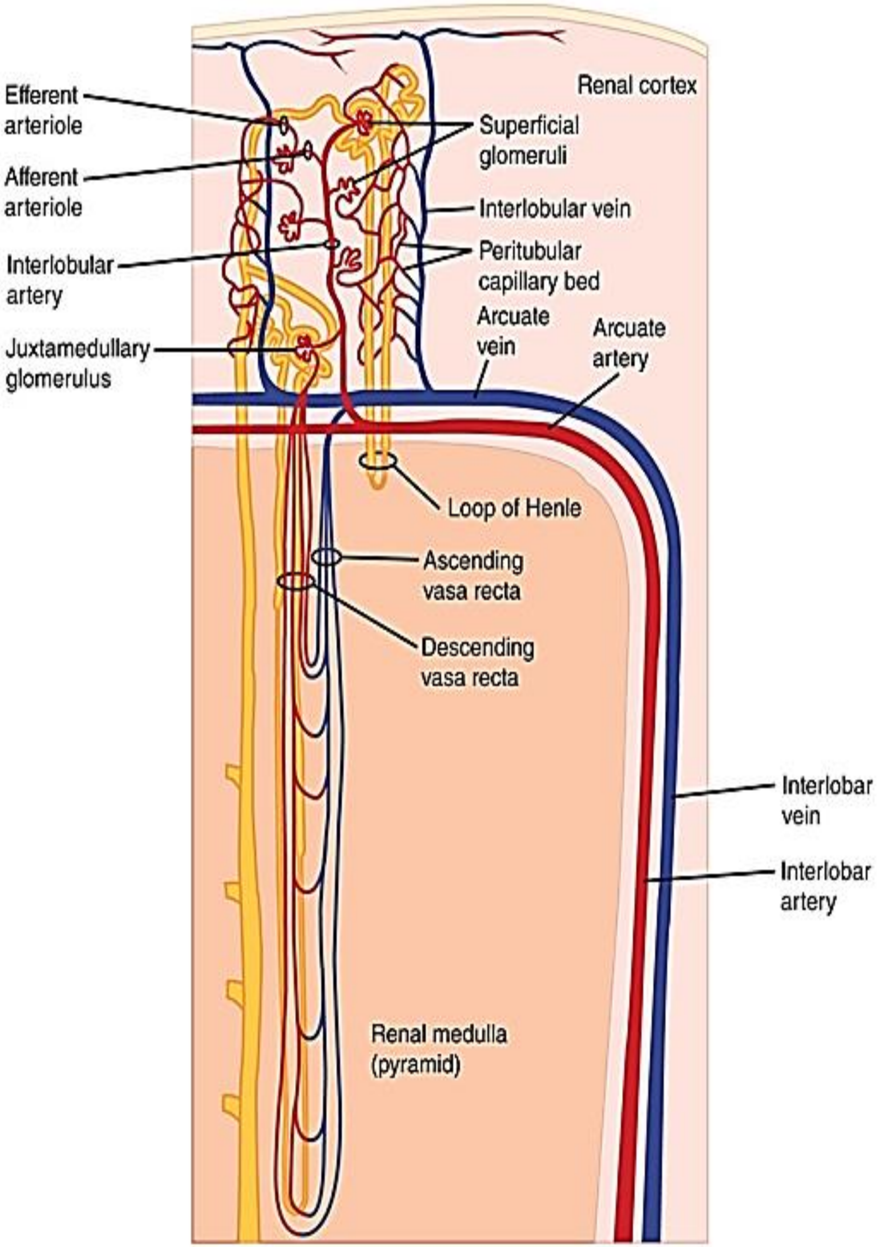
The kidney receives arterial blood via renal artery:
Aorta……renal artery……interlobar arteries in medulla……..arcuate arteries at corticomedullary junction………interlobular arteries in cortex…….wide afferent arteriole…….glomerular capillaries……narrow efferent arteriole.

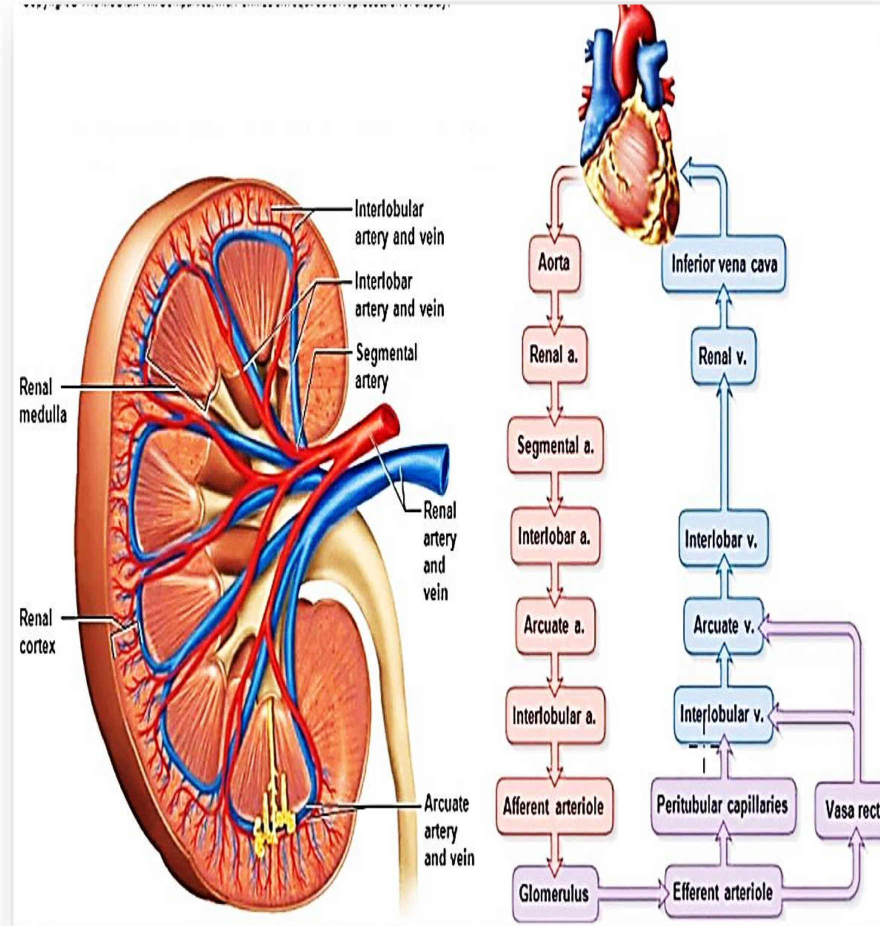
The course of circulation then differs as follows:
**Cortical nephrons:** efferent arterioles give rise to **one** network of **peritubular capillaries** that supply the tubules.

**Juxtamedullary nephrons:** Their efferent arterioles give rise **2 types of peritubular capillaries**:

- A capillary network that supplies the PCT and DCT in the renal cortex.
- Straight capillaries called **vasa recta** that accompany the long LH throughout the renal medulla then return back upwards to drain into the cortical veins.
- Average pressures in renal circulation:

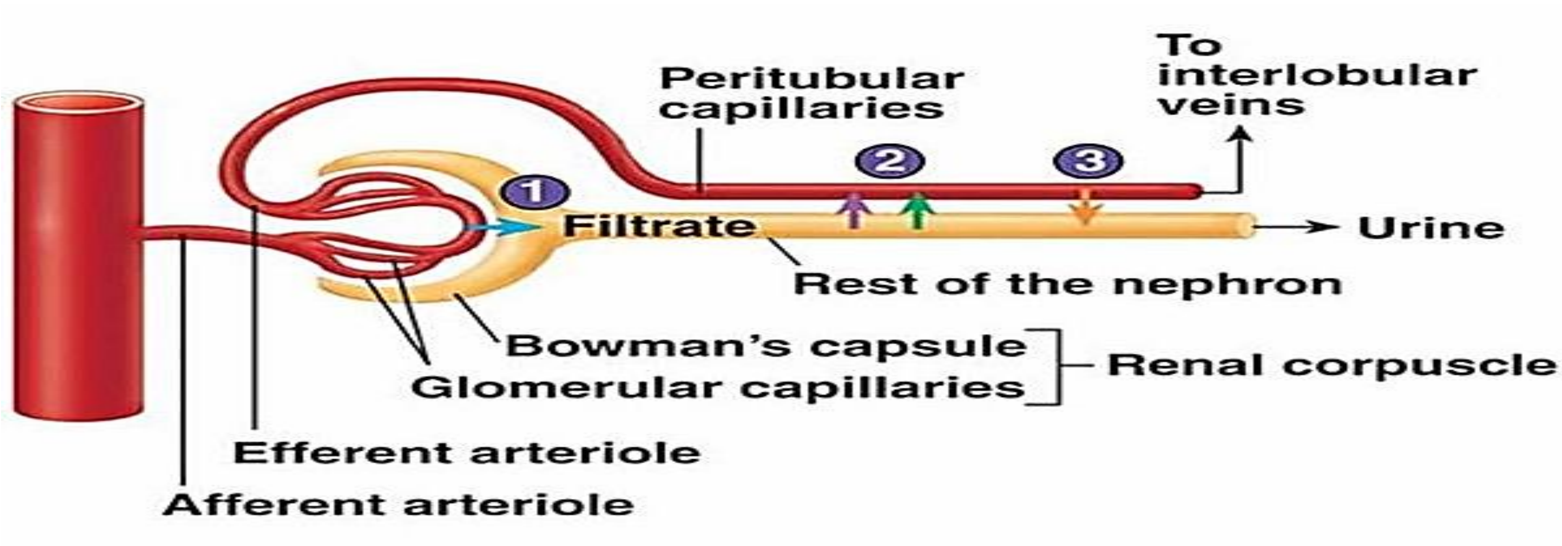
- **60 mmHg in glomerular capillaries.**
- **13 mmHg in peritubular capillaries**.


Efferent arteriole
Afferent arteriole
Interlobular artery
Juxtamedullary glomerulus
Renal cortex
Superficial glomeruli
Interlobular vein
Peritubular capillary bed
Arcuate vein
Arcuate artery
Loop of Henle
Ascending vasa recta
Descending vasa recta
Interlobar vein
Interlobar artery
Renal medulla (pyramid)


Interlobular artery and vein
Interlobar artery and vein
Segmental artery
Renal medulla
Renal artery and vein
Renal cortex
Arcuate artery and vein
Aorta
Renal a.
Segmental a.
Interlobar a.
Arcuate a.
Interlobular a.
Afferent arteriole
Glomerulus
Efferent arteriole
Peritubular capillaries
Vasa recta
Interlobular v.
Arcuate v.
Interlobar v.
Renal v.
Inferior vena cava

# Differences between glomerular and peritubular capillaries:

| | **Glomerular capillaries** | **Peritubular capillaries** |
|---|---|---|
| Origin | Afferent arteriole | Efferent arteriole |
| Drainage | Efferent arteriole | Interlobular veins |
| Pressure | High pressure bed (60 mmHg) that favors **filtration** | Low pressure bed (13 mmHg) that favors **reabsorption** |



# Types of Nephrons

**TYPES:**

There are two types of nephrons depending on the situation of the renal glomeruli:

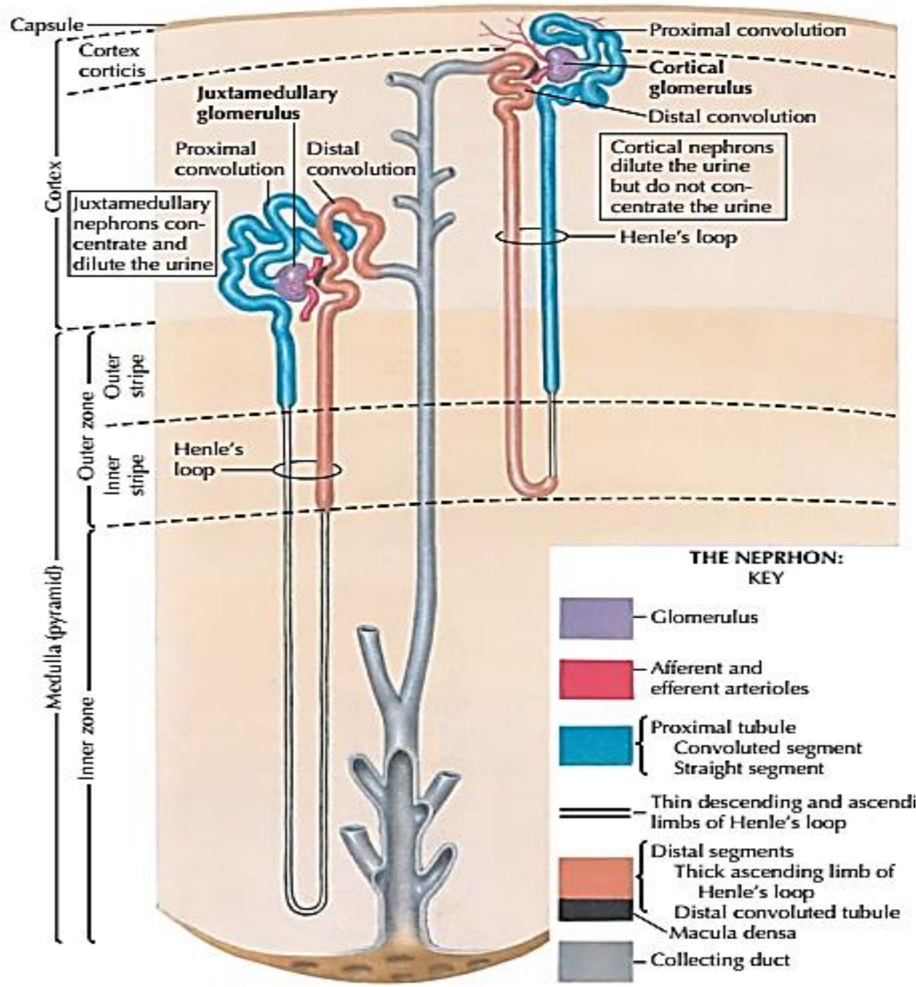
**Cortical nephrons:** (**85%** of total nephrons):

- They have their **glomeruli** in the **outer portions of the renal cortex**.
- Their **LHs** penetrated only a **short distance** **(short LH)** into the **outer part of the renal medulla**.
- Their efferent arterioles give rise to **one** network of **peritubular capillaries** that surround all parts of the tubule of nephron.

**Juxtamedullary nephrons** (**15%** of total nephrons):

- They have their **glomeruli** in the **inner portions of the renal cortex (near to the medulla)**.
- Their **LHs** penetrated **deeply (long LH)** into the **inner part of the renal medulla**.
- They are essential for the process of **urine concentration**.
- Their efferent arterioles give rise **2 types of peritubular capillaries**:
  - A network that surrounds the PCT and DCT in the renal cortex.
  - Straight capillaries called **vasa recta** that accompany the long LH throughout the renal medulla then return back upwards to drain into the cortical veins.

# Types of nephrons




| | | | |
|---|---|---|---|
| Renal blood flow | 1–1.2 L/min | Number of nerphons | 2.5 million |
| Glomerular filtration rate | 100–125 mL/min<br>140–180 L/day | Cortical | 2.1 million |
| | | Juxtamedullary | 0.4 million |
| Urine flow rate | 0.5–18 L/day | | |

# JUXTAGLOMERULAR APPARATUS (JGA)

## Definition:

**It is a secretory structure present near the glomeruli at the region where the initial portion of the distal convoluted tubule (DCT) comes in contact with the glomerulus close to its afferent and efferent arterioles, actually passing the angle between them.**

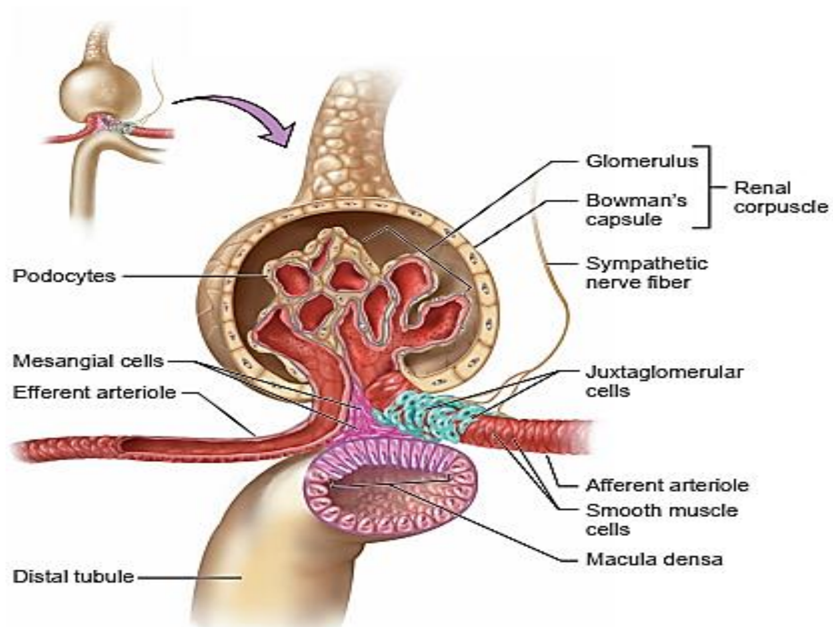



**Figure 14.5** AP|R The juxtaglomerular apparatus.

**It is formed of the following cells:**

**1. Juxtaglomerular cells:**

Juxtaglomerular (JG) cells are **secretory cells** located in the **afferent arterioles**.

**Function:**

JG cells act as **intrarenal baroreceptors** (they sense afferent arteriole pressure), which enables them to efficiently monitor ABP and maintain normal GFR through the release of **renin**, the initial enzyme in the renin-angiotensin-aldosterone system (RAAS).

**2. Macula Densa cells:**

A specialized group of epithelial cells in the **initial part of DCT** that comes in close contact with the afferent and efferent arterioles.

**Functions:**

- Are important in sensing tubular fluid flow and sodium delivery to the distal nephron.
- Because of their proximity to the afferent arteriole, macula densa cells can regulate renal blood flow (RBF) and glomerular filtration rate (GFR) **(autoregulation)**.

**Function of JGA:** Maintains the glomerular filtration rate (GFR) in response to blood pressure (BP) changes in the afferent arterioles (**autoregulation of GFR and RBF**).

## RENAL BLOOD FLOW (RBF)

Normally, **RBF is about 1200 ml/minute**. The flow is much greater in the renal cortex, only about **2 % pass in the vasa recta** resulting in a sluggish flow in the renal medulla which is important for the process of urine concentration.

**The renal fraction:**

This is the portion of the cardiac output that passes through the kidneys.

Normally, it averages about **20 %** of cardiac output (1200/5600 X100) ranging from (12 % - 30%).

## RENAL PLASMA FLOW (RPF)

Renal plasma flow is the measure of the volume of plasma delivered to the kidney in a given time.

About **650 ml/minute**.

# Mechanism of urine formation

- **Urine is formed as a result of:**

1) **Glomerular filtration:** Filtration of plasma from the glomerular capillaries into Bowman's space.

- Normally, glomerular capillary bed receives about 650 ml plasma/minute of which only about 1/5 **(125 ml)** is filtered into Bowman's capsules while the remaining 4/5 pass to the peritubular capillaries.

- Glomerular filtrate is called **primary urine** and it contains all plasma constituents except most plasma proteins (protein free fluid) which can't be filtered.

2) **Tubular reabsorption:**

Transport of substances (mainly essential substances) from the lumens of the renal tubules to blood in peritubular capillaries.

**Normal values:**

- GFR= 125 ml/minute (180 L/day).
- Tubular reabsorption: 124 ml/minute (99.2% of glomerular filtrate).
- Urine volume: 1 ml/minute (= 1.44 L/day = 0.8% of glomerular filtrate).

**3) Tubular secretion:**

Process by which substances are transported into the lumens of the renal tubules from the following sources:

- Blood of peritubular capillaries e.g. creatinine and $K^+$.
- Tubular epithelial cells e.g. $H^+$ and $NH_3$.

By these processes of reabsorption and secretion, the tubular fluid (= tubular urine) is changed into actual urine.

**Excretion = Filtration – reabsorption + secretion.**

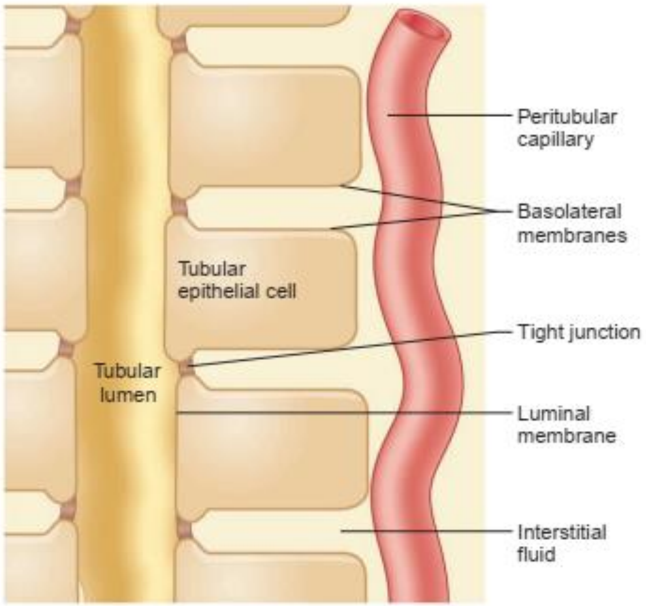
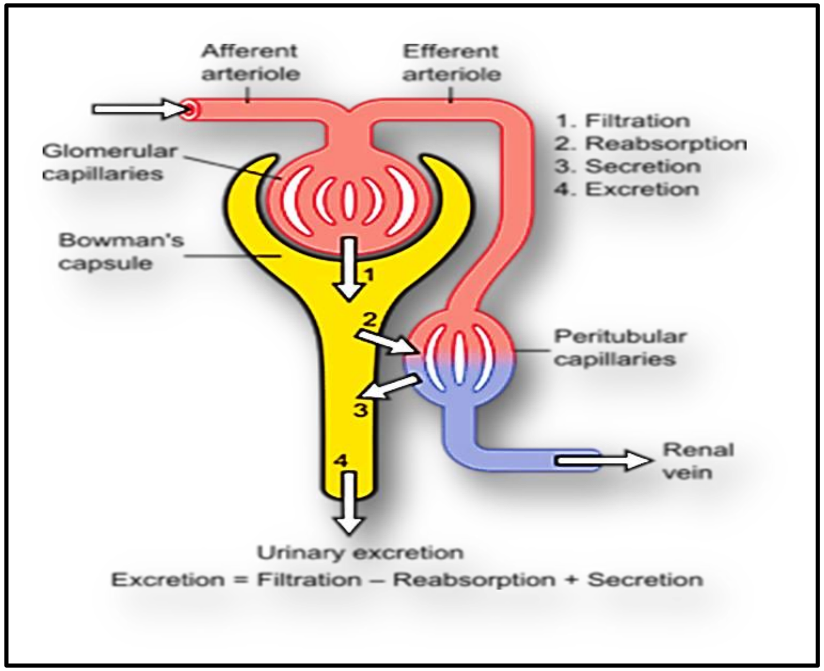
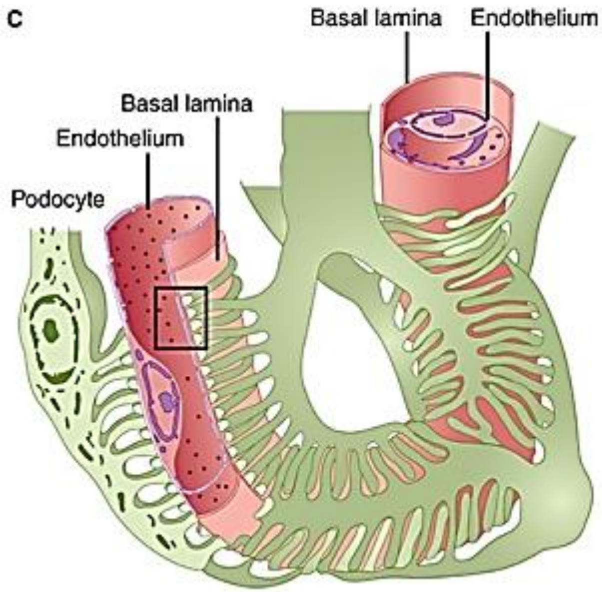


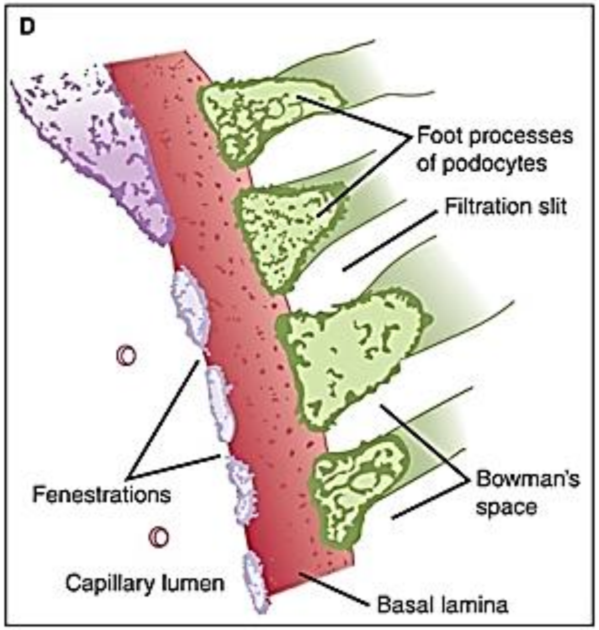

**Figure 14.10** AP|R Diagrammatic representation of tubular epithelium. The luminal membrane is also called the apical membrane.



# Glomerular Filtration

- It is the first step in urine formation.
- Filtration occurs from the glomerular capillaries to Bowman's capsule through the glomerular filtration barrier (glomerular membrane).



# Glomerular Membrane

- Glomerular membrane is a semipermeable membrane through which plasma is filtered.
- The **glomerular membrane (filtration barrier) is formed from 3 layers:**

1. **The capillary endothelial cells:** these are separated from each other by large pores called fenestrae (fenestrated).
2. **Glomerular basement membrane (GBM):**

It is composed of collagen, and proteoglycans. Proteoglycans account for the glomerular basement membrane **negative charge,** thus keeping plasma proteins, which also negatively charged, from entering the Bowman's space.

It appear poreless, but in fact it contains spaces through which fluid filtration can occur.

3. **Epithelial cells of Bowman's capsule (Podocytes)**

Line the outside of the GBM. These cells have numerous finger-like projections (pseudopodia) that interdigitate, forming slits called **slit pores**.

- The glomerular membrane is relatively impermeable to proteins; thus, the filtrate contains little protein.
- **The glomerular membrane has a high degree of selectivity:** Several factors determine whether a substance will pass through the filtration barrier:
  - **Size of its pores:** molecules with **a diameter less than 4 nm or a molecular weight less than 5500 (e.g. inulin)** are **freely (readily) filtered**, while those with a **diameter more than 8 nm or a molecular weight more than 70,000** (e.g. globulins and fibrinogen) are not filtered.
  - **Its electrical charges:** the basement membrane has strong **negative electrical charges** which repel the negatively charged substances in blood (thus decreasing their filtration). This is another cause for poor filtration of plasma proteins (which are **negatively charged**) besides their **high molecular weight** (so their concentration in glomerular filtrate is 0.03 gm%).

# Mechanism and Forces mediating filtration

**Glomerular filtration is a passive process (requiring no energy) that involves interaction between the following forces (Starling forces):**

**Filtering forces:**

**1-The glomerular hydrostatic capillary pressure (GCP):** It is about **60 mmHg**. It is the highest capillary pressure in the body. It is due to the fact that the diameter of efferent arteriole is smaller than diameter of afferent arteriole.

**2-The colloid osmotic pressure in Bowman's capsule:** Normally, it is too low to be of any significance **(zero)** due to low protein concentration in the filtrate inside Bowman's capsule.

**Opposing forces:**

**1-The glomerular colloid osmotic pressure (GOP):** This is the force due to plasma proteins. It normally averages about **32 mmHg**.

**2-Bowman's capsule pressure; capsular pressure (CP):** this is the pressure of fluid in Bowman's capsule . It is normally about **18 mmHg**.

## ✓ The net filtration pressure (NFP):

This is the driving force for glomerular filtration.

**NFP =**

**Filtering forces – Opposing forces**

**= (60+0) – (32+18) = 60-50 = 10 mmHg.**

**GFR is directly proportional to NFP**.

## ✓ The glomerular filtration rate (GFR) :

**GFR: The volume of glomerular filtrate /minute in both kidneys.**

**Volume: 125 ml/minute.**

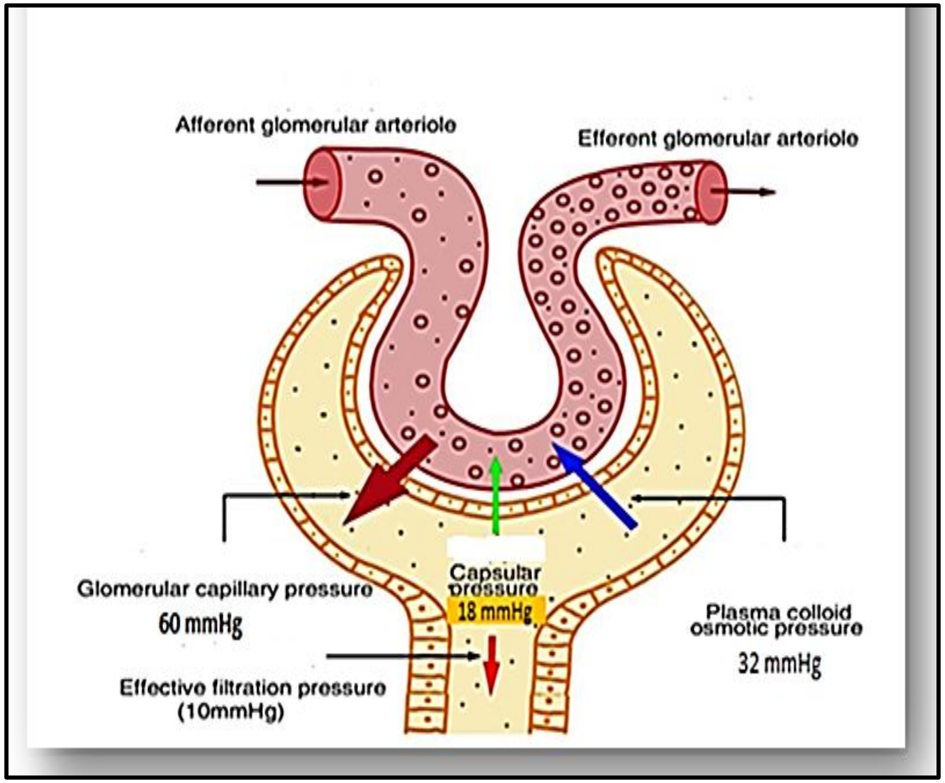
**Composition: Deproteinized plasma** (plasma free of proteins; **protein free fluid**).

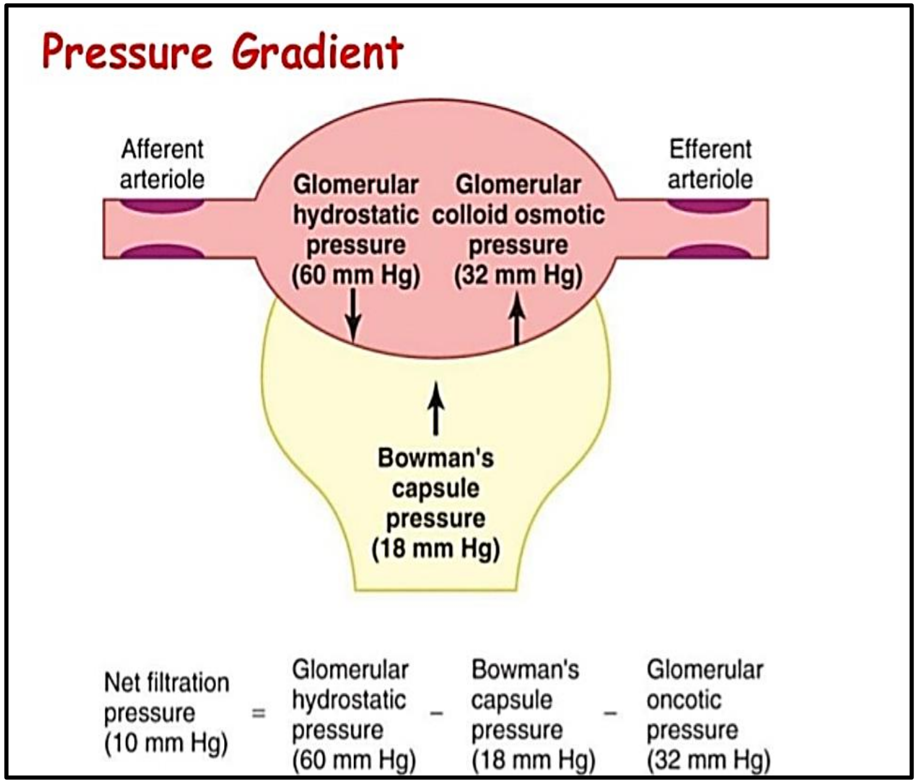
**Measurement:** This can be achieved by determination of **inulin clearance** or **creatinine clearance**.

## ✓ The filtration coefficient ($K_f$):

**This is the GFR/mmHg of net filtration pressure, and is normally about 125/10 = 12.5 ml/mmHg/minute.**

# Forces mediating filtration



# Filtration Fraction

- **Definition:**

Filtration fraction (FF) is the fraction (in %) of renal arterial plasma filtered across the glomerular membrane.

- **It is the ratio of the GFR to the RPF**.

- It can be calculated if the GFR and the RPF are known:
- $$FF = GFR/RPF \times 100$$
- = **125/650 X 100 = about 20 %. About 1/5 RPF**
- Therefore, about 20% of the RPF enters the renal tubules, while the remaining 80% leaves the glomerulus via the efferent arteriole and becomes the peritubular capillary circulation.
- When GFR is 125 ml/minute, the volume filtered 180 L/day. Since, the normal plasma volume is about 3 L, it is clear that plasma is filtered about 60 times daily.


Thank you