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

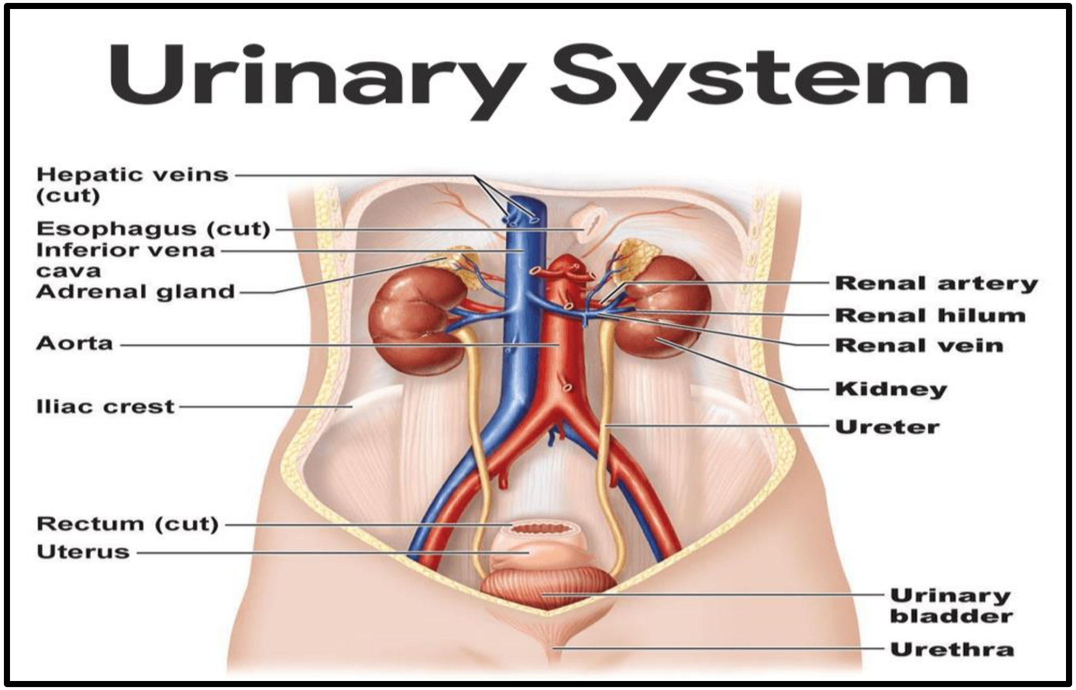
BY

Dr. Fatma Farrag Ali

Associate Professor of Medical Physiology

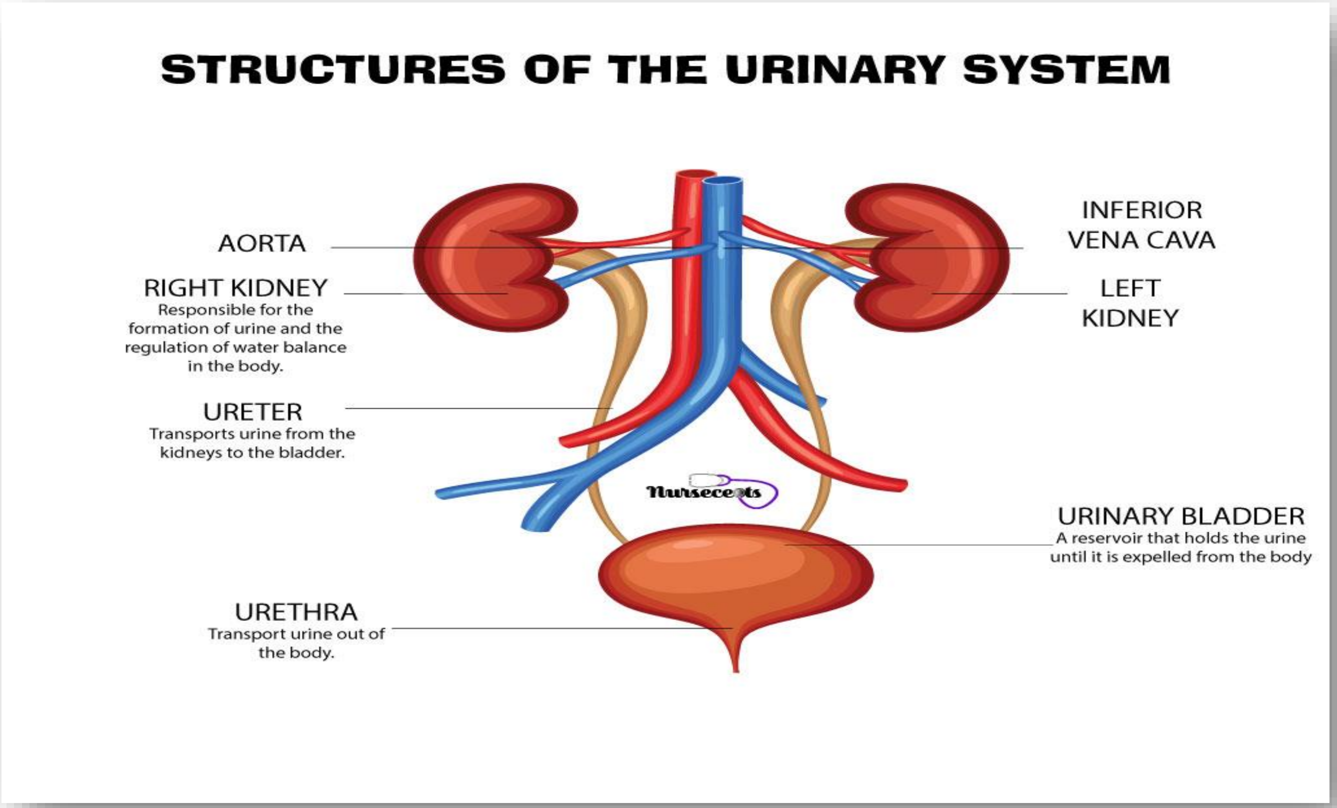
Faculty of Medicine-Mutah University

2023-2024



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 kidney:

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

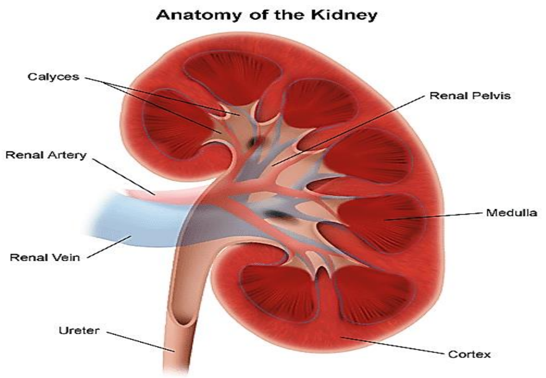
- Non-essential substances:
- End products of metabolism e.g. urea, uric acid, creatinine and bilirubin.
- Foreign substances e.g. drugs and toxins.
- Excess amounts of essential substances e.g. **water** and **electrolytes (regulation of water and electrolyte balance)**.

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 osmolality and pH……etc.

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

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

5- Gluconeogenesis (during prolonged fasting).



Endocrine function: The kidneys are endocrine organs

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

1. **Renin:** Glycoprotein 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.

Renin secretion is stimulated by : renal ischemia and increased sympathetic activity and catecholamines.

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 (parathyroid hormone).

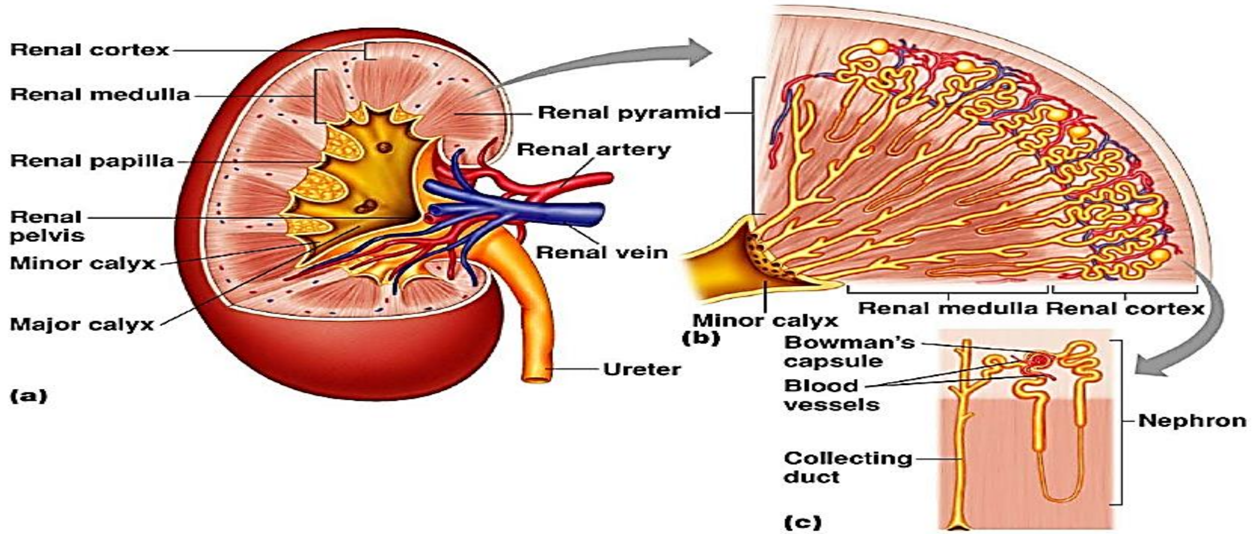
Physiologic anatomy of the kidney:

The kidney is surrounded by a thin tough fibrous capsule.

It consists of 2 distinct zones:

(1) An outer cortex: this appears red because it is richly supplied with blood, and granular because it contains the renal glomeruli.

(2) An inner medulla: this is paler than the cortex because it is poorly supplied with blood, and is striated because it contains the loops of Henle and medullary collecting ducts. It is formed of 10-15 triangular-shaped wedges of tissue called the pyramids, the apex of which drain into the calyces. The pyramids divide the kidney into lobes (each renal lobe consists of one pyramid + the facing cortical tissue) which are in turn subdivided into lobules.



The Nephron

Definition:

It is the functional unit of the kidney.

Nephrons work **<u>independently</u>** 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 about 50 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 Malpighian 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. Conversely, the efferent arterioles are the only arterioles in the body that collect blood from capillaries.

(2) The renal tubule:

It is concerned with **urine formation** and its total length including the collecting duct (about 20 mm) is 45-65 mm.

It receives the glomerular filtrate (which is a filtrate from the plasma), and its main functions are **reabsorption** of the wanted substances from the tubular fluid and **secretion** of the unwanted substances into the fluid.

It consists of the following parts respectively:

1. Proximal convoluted tubule (PCT):

This is the first part of tubule and its length averages 15 mm.

It receives the glomerular filtrate from Bowman’s capsule then delivers its fluid into the descending limb of the loop of Henle.

2. Loop of Henle (LH):

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

It is about 20 mm long, and it has descending and ascending limbs.

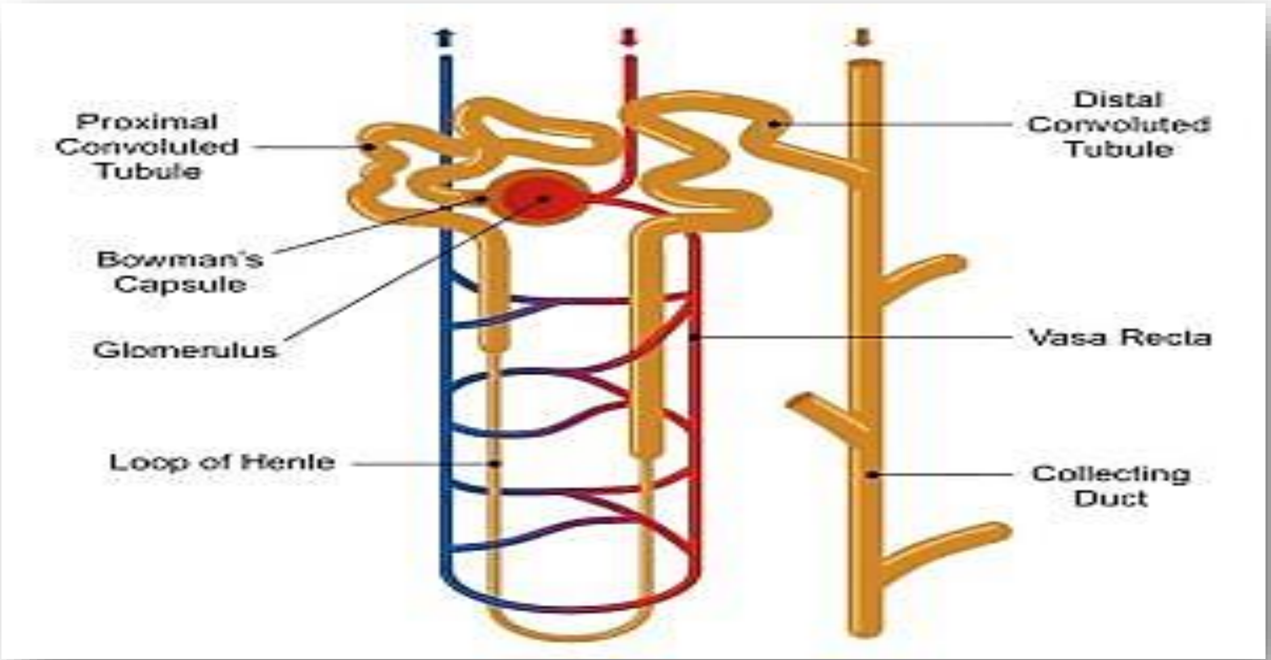
The walls of the descending limb and lower part of ascending limb are thin (because they are made up of a single layer of flat epithelial cells) **forming the thin segment of the LH** (2-14 mm). On the other hand, the wall of the **upper part of the ascending limb** is thick (because it is made of cuboid epithelial cells rich in mitochondria), forming the **thick segment of the LH** (about 12 mm).

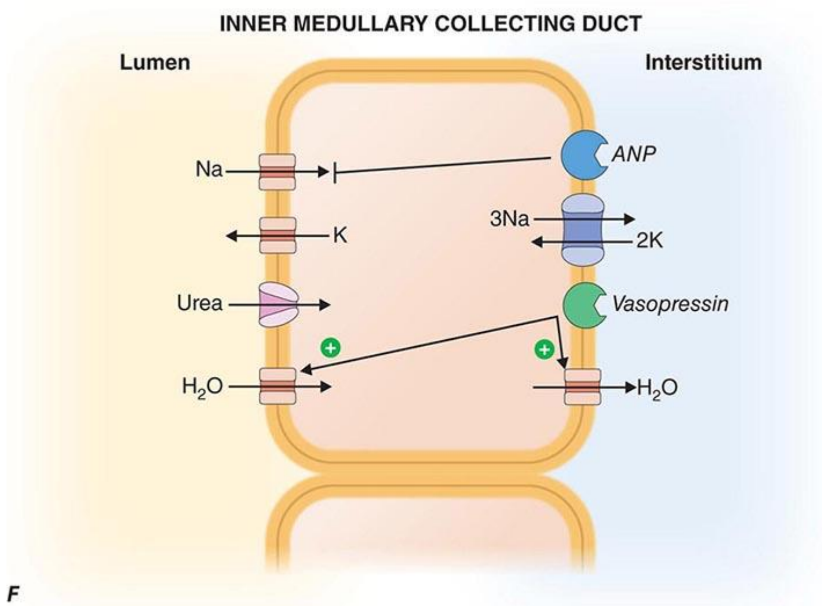
3. Distal convoluted tubule (DCT):
It receives the tubular fluid from the ascending limb of LH and is about 5 mm long.

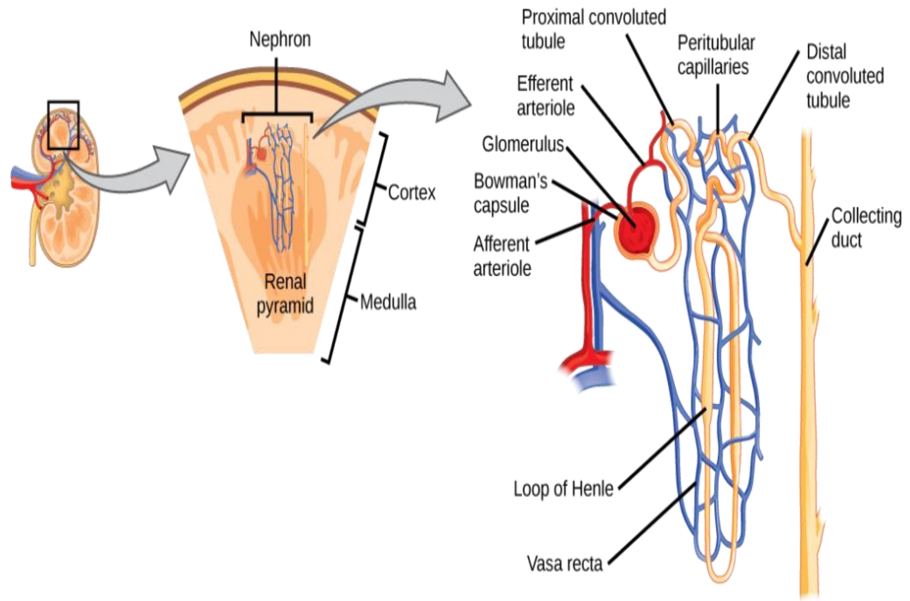
4. Cortical collecting duct (CCD) which passes downwards into the medulla where it becomes a **medullary collecting duct (MCD)**. The later ducts coalesce forming larger ducts that drain into the minor calyces at the tips of the renal papillae. The minor calyces unite together forming major calyces that empty into the renal pelvis (from which the ureter arises).

N.B.
All PCTs and DCTs as well as glomeruli and cortical collecting ducts are present in the renal cortex. The LH together with medullary collecting ducts and vasa recta are arranged parallel to each other in the medulla producing the striated appearance of the renal pyramids.

The epithelium of the collecting ducts (CD) is made up of 2 types of cells:
Principal (P) cells.
Intercalated (I) cells.
The **P cells predominate and are involved in Na^+ reabsorption and vasopressin-stimulated water reabsorption**. On the other hand, **the I cells (which are also present in the late DCTs) are concerned with H^+ secretion and bicarbonate reabsorption**.


Proximal Convoluted Tubule
Bowman's Capsule
Glomerulus
Loop of Henle
Distal Convoluted Tubule
Vasa Recta
Collecting Duct


INNER MEDULLARY COLLECTING DUCT
Lumen
Interstitium
Na
K
Urea
H_2O
ANP
3Na
2K
Vasopressin
H_2O
F


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

Types of Nephrons

TYPES:

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

Cortical Versus Juxtamedullary Nephrons:

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** 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 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** 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

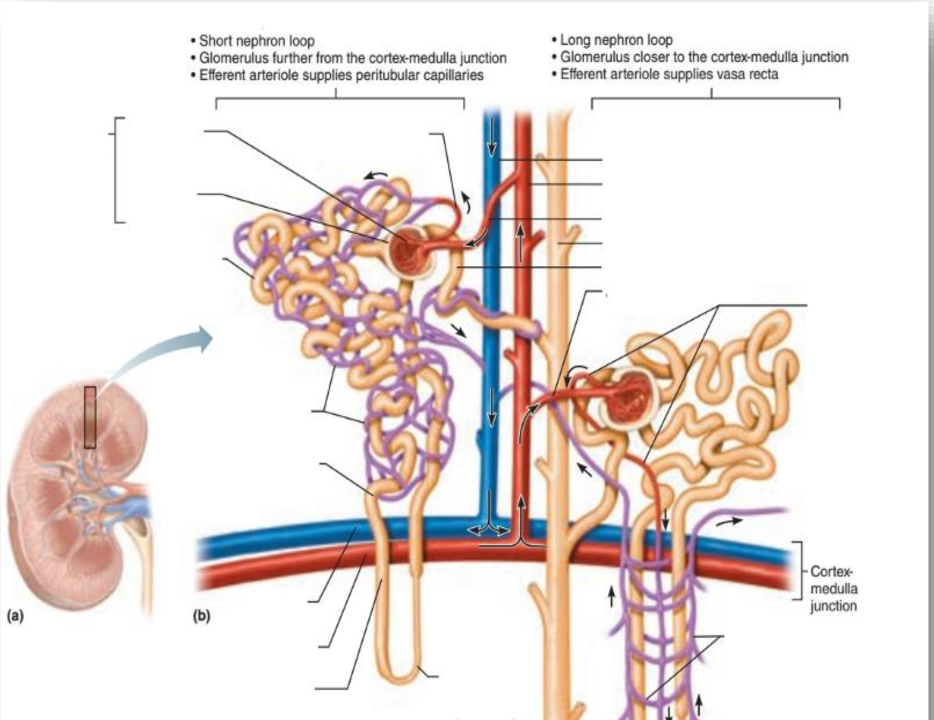
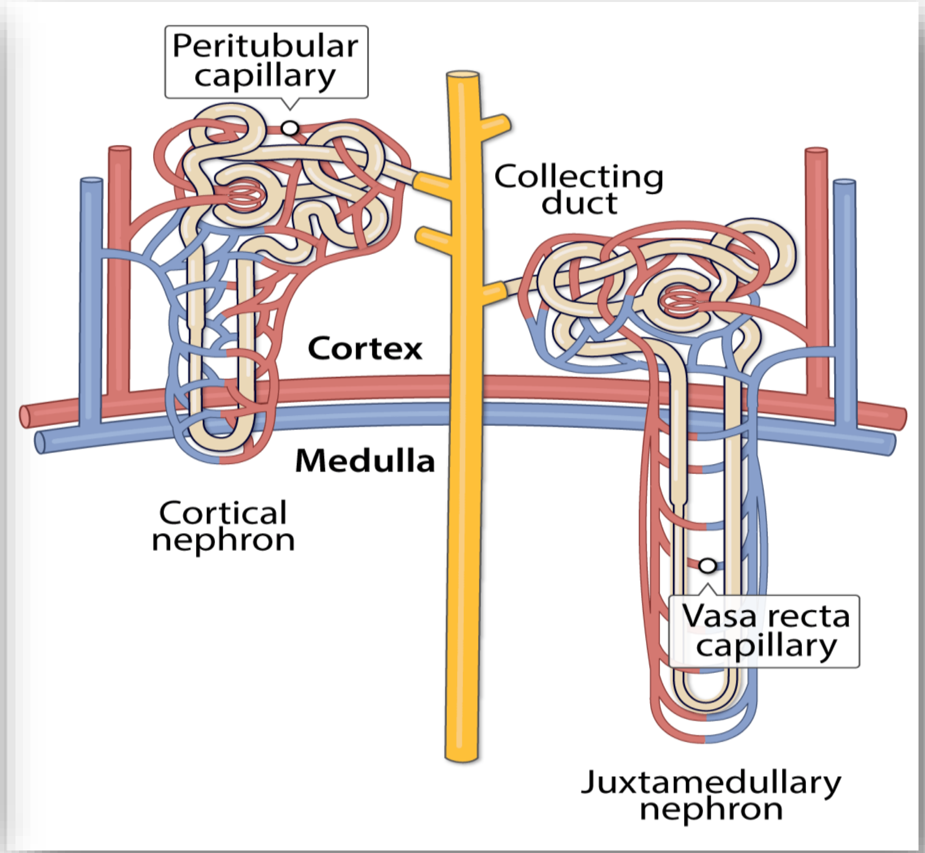


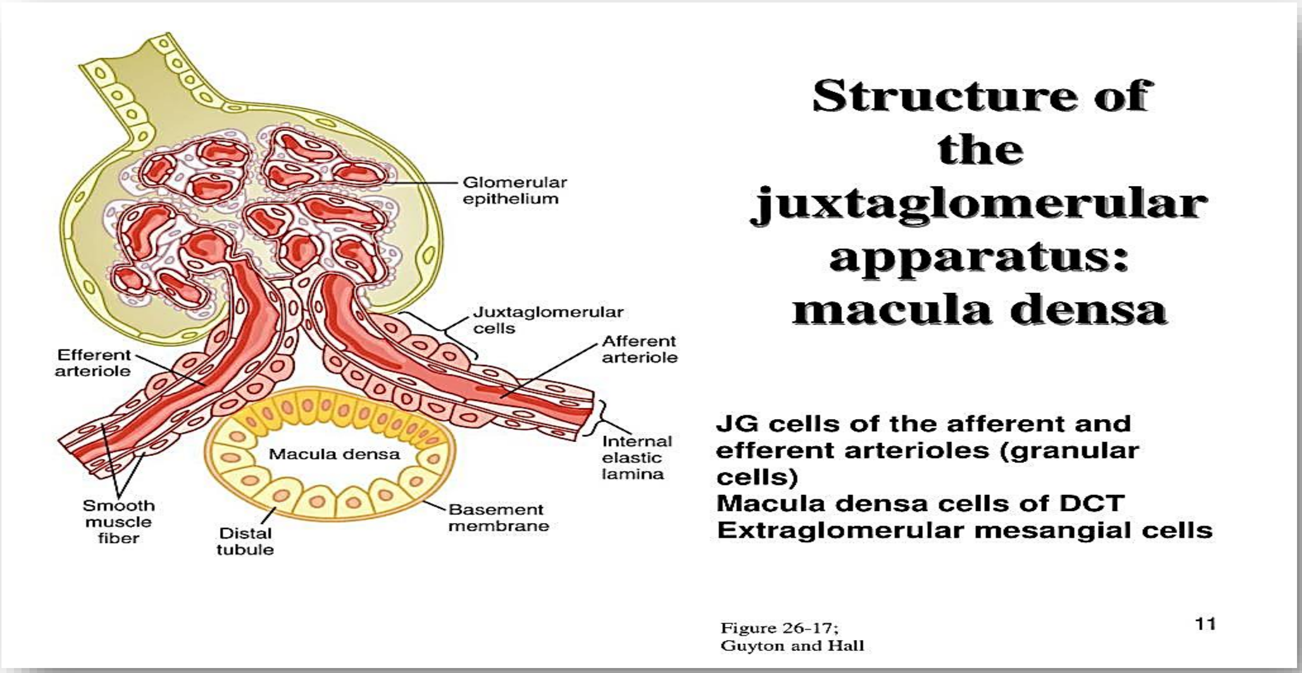
Figure 40.4 Cortical and juxtamedullary nephrons and their associated blood vessels. (a) Rectangular-shaped section of kidney tissue indicates position of nephrons in the kidney. (b) Detailed nephron anatomy and associated blood supply. Arrows indicate direction of blood flow.



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.



It is formed of the following cells:

1. Juxtaglomerular cells:

Juxtaglomerular (JG) cells are modified epithelial (smooth muscle) cells located in the **afferent arterioles**. JG cells act as baroreceptors (they sense intra-renal arteriole pressure), which enables them to efficiently monitor BP and maintain normal GFR through the release of **renin**, the initial enzyme in the renin-angiotensin-aldosterone system.

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. The cells of the macula densa are **sensitive (sensors) to NaCl concentration and rate of flow through DCT**, and **regulate GFR (autoregulation)**.

3. Lacis cells:

A granular cells present between afferent and efferent arterioles.

FUNCTION of JGA

The JGA functions to maintain 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 **21 %** (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 amount of time.

About **650 ml/minute**.

The renal circulation

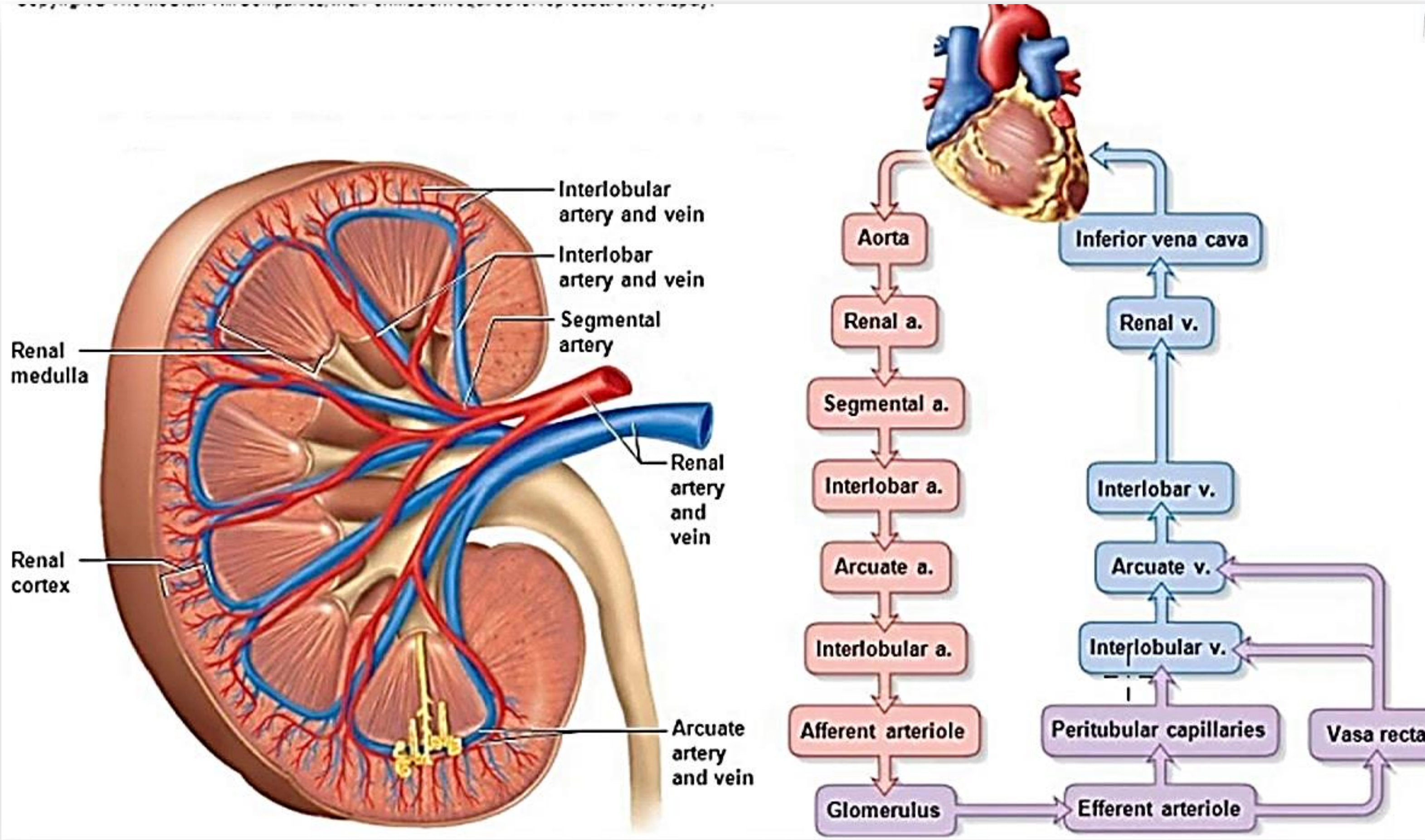
The receives arterial blood via renal artery:
Aorta……renal artery……interlobar arteries in medulla……..arcuate arteries at corticomedullary junction………interlobular arteries in cortex…….wide afferent arteriole…….glomerular capillaries……narrow efferent arteriole.

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

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**.


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

Mechanism of urine formation

- **Urine is formed as a result of:**
  - Filtration of plasma in the glomeruli (= glomerular filtration).
  - Reabsorption in the renal tubules.
  - Secretion in the renal tubules.
  - Excretion = Filtration – reabsorption + secretion.

- 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 (wanted and unwanted) except most plasma proteins which cannot be filtered because of their high molecular weight as well as other factors.

- In the renal tubules, about 124 ml are reabsorbed back into peritubular capillaries (together with the essential substances e.g. glucose and electrolytes) and more of the unwanted substances are secreted from peritubular capillaries into the tubules.
- By these processes of reabsorption and secretion, the tubular fluid (= tubular urine) is changed into actual urine (which is normally about 1 ml/minute i.e. about 0.1 % of RBF).

Tubular reabsorption:

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

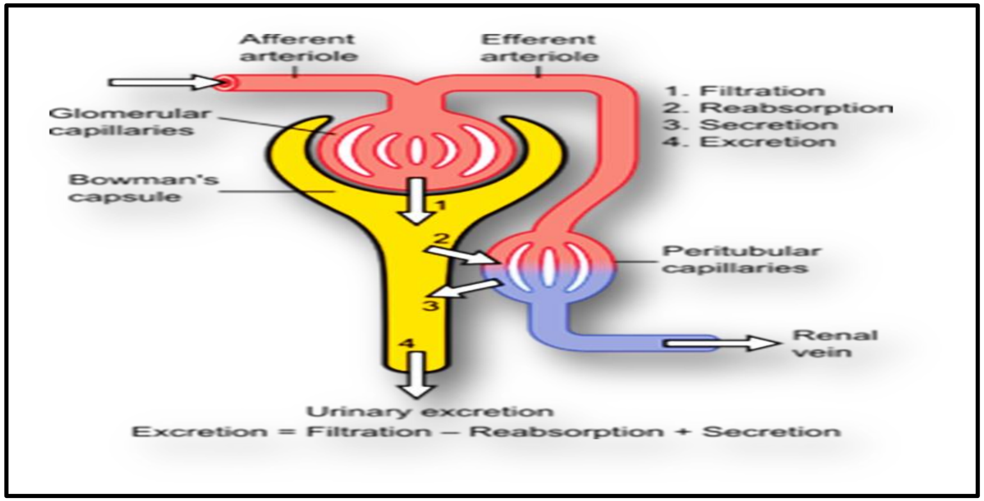
Normal values:

- 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).

Tubular secretion:

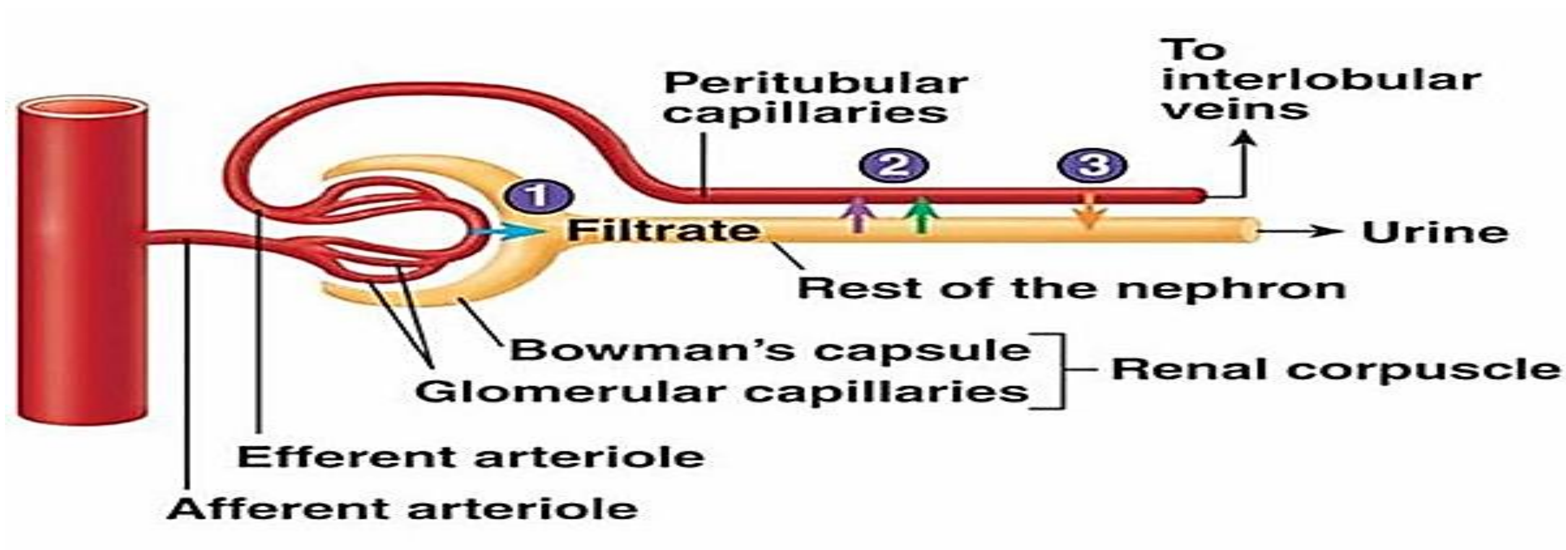
Process by which substances are transported into the lumens of the renal tubules from the following sources:

- Blood of peritubular capillaries e.g. creatinine.
- Tubular epithelial cells e.g. H^+ and NH_3.
- Both glomerular filtration and tubular secretion are processes that clear plasma from unwanted substances while tubular reabsorption is not a clearing process.



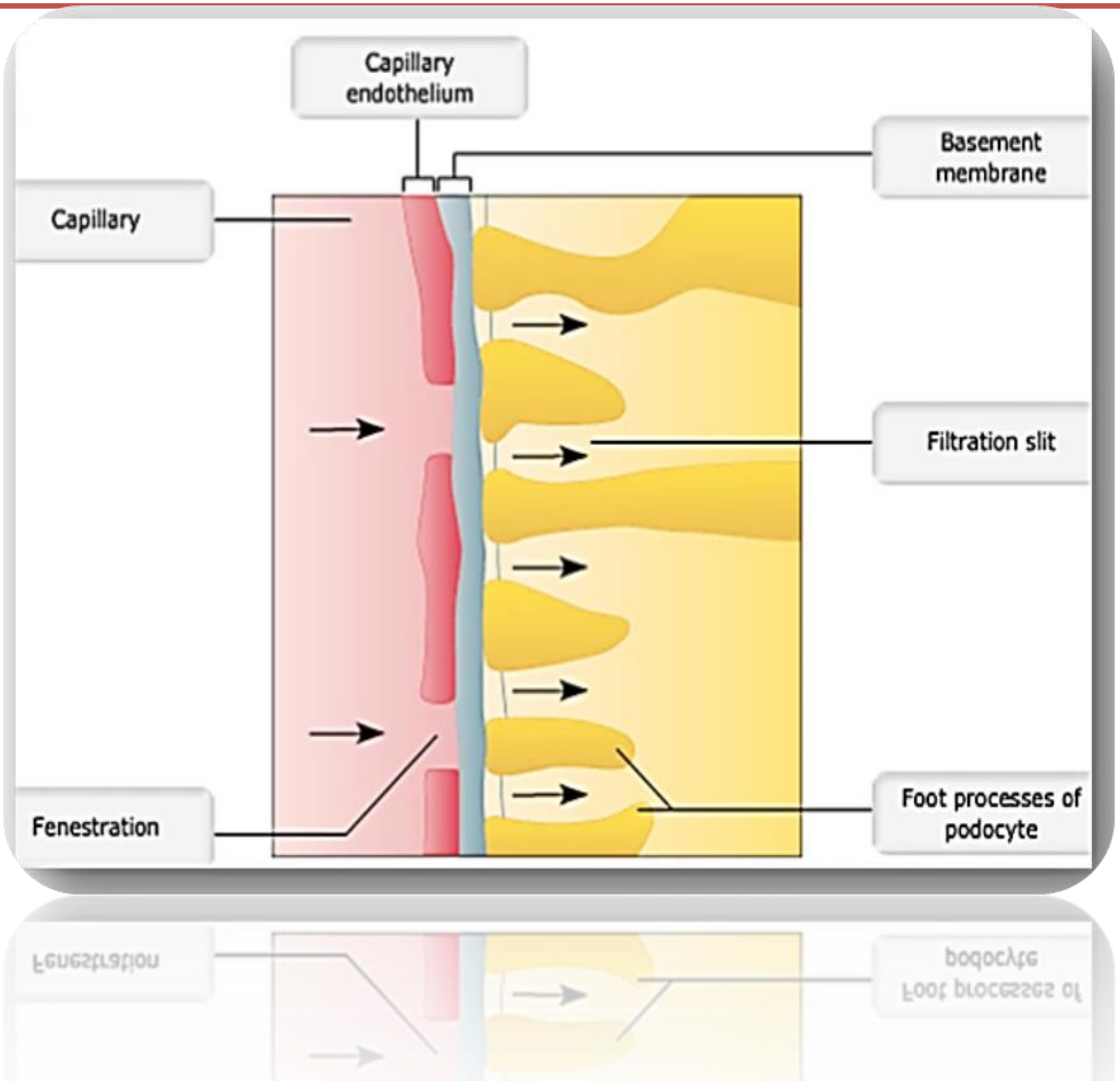
Differences between glomerular and peritubular capillaries:

	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**



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. **<u>The capillary endothelial cells:</u>** these are separated from each other by large pores called fenestrae (fenestrated); each of which is 70-90 nm in diameter.
2. **<u>Glomerular basement membrane (GBM):</u>**

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

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

3. **<u>Epithelial cells from Bowman's capsule (Podocytes)</u>**

Line the outside of the GBM. These cells have numerous finger-like projections (pseudopodia) that interdigitate, forming slits called **slit pores** each of which is about 25 nm in diameter.

In spite of these 3 layers, the permeability of glomerular capillaries is much greater than that of other capillaries elsewhere in the body (about 50 times more permeable than capillaries of skeletal muscle).

- 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 70000 (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 **large size** (so their concentration in glomerular filtrate is 0.03 gm%).

Glomerular Filtration rate (GFR)

The glomerular filtration rate (GFR): The volume of glomerular filtrate /minute in **both kidneys**.

- Volume: 125 ml/minute.
- Composition: deporteinized plasma (plasma free of proteins).
- Measurement: This can be achieved precisely by determination of **inulin clearance** but **creatinine clearance is more commonly used**.

Filtration Fraction

Definition:

Filtration fraction (FF) is the fraction (in %) of renal arterial plasma filtered across the glomerular membrane. It can be calculated if the GFR and the RPF are known:

$$FF = GFR/RPF \times 100$$

$= 125/650 \times 100 =$ about 19 % (16-20%). 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.

Mechanism and Forces mediating filtration

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

Filtering forces:

1-The hydrostatic glomerular capillary blood 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 **(0)** due to low protein concentration in the filtrate inside Bowman's capsule.

Opposing forces:

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

2-Hydrostatic pressure in Bowman's capsule (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 – Absorbing forces

= (60+0) – (32+18) = 60-50 = 10 mmHg.

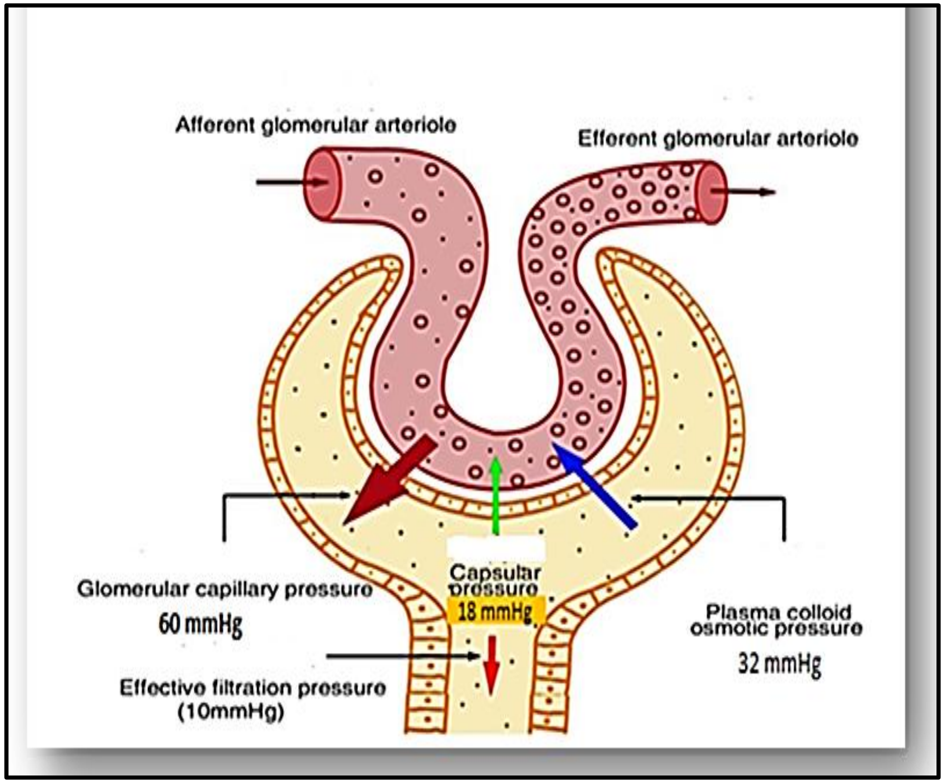
GFR is directly proportional to NFP.

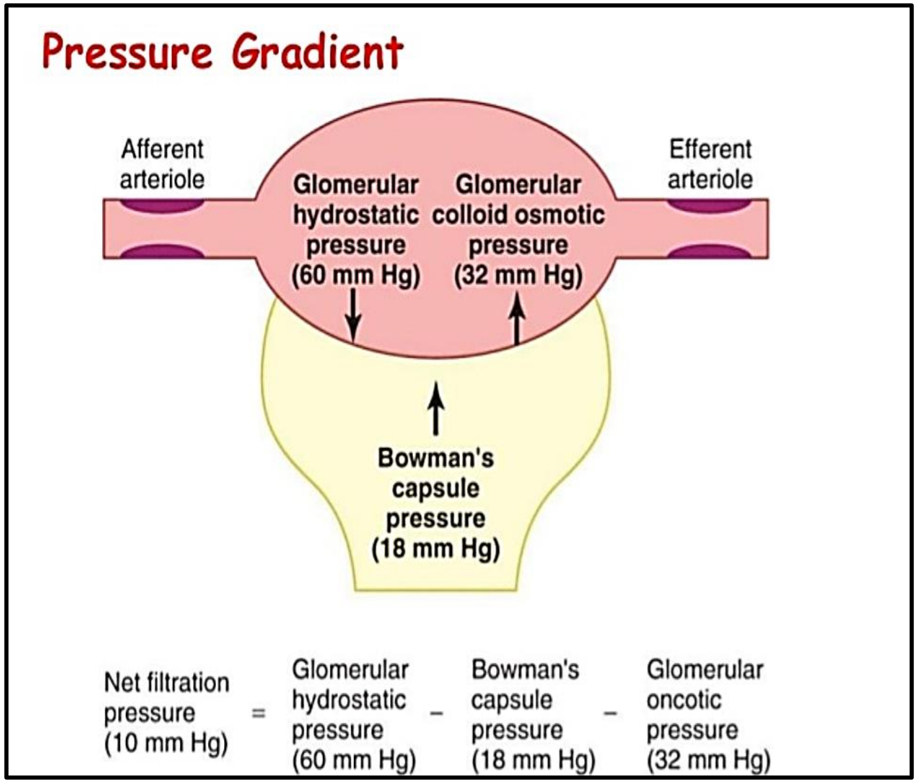
The glomerular filtration rate (GFR) = 125 ml/min.

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






THANK
YOU