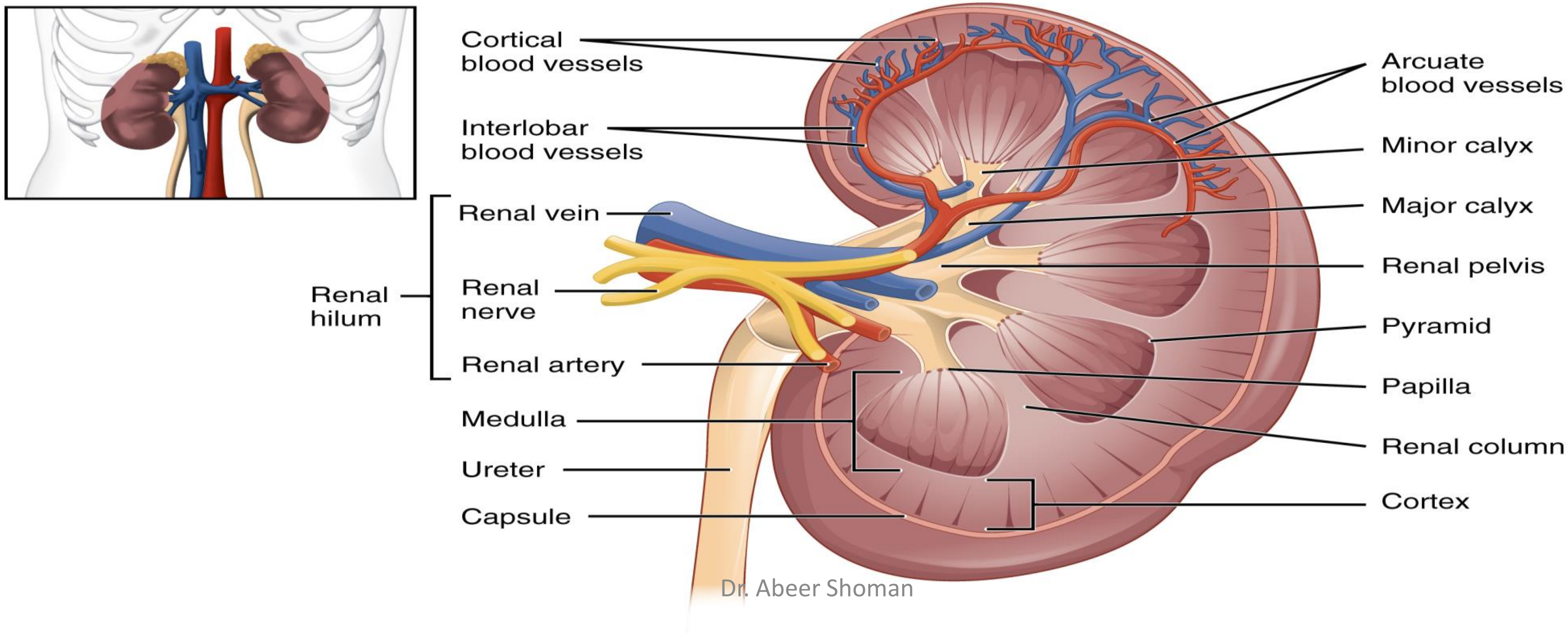
THE KIDNEY

FUNCTIONAL ORGANIZATION OF THE KIDNEY



objectives

1-Kidney functions

2-Physiological anatomy of the kidney

3- Blood flow of the kidney

4- juxta glomerular apparatus

Kidney Functions

1- **Excretion of waste products**: Urea, uric acid.

2- **Control of** volume, osmotic pressure and electrolyte of the ECF.

3- **Endocrine functions :**

a) Renin – Angiotensin b) Erythropoietin hormone c) Formation of 1-25 DHCC(Vit. D)

4- **Regulation of arterial blood pressure:** A) Short term , b) Long term

5- **Regulation of acid base balance:** A) Elimination of acids b) Regulation of buffer stores.

6- **Gluconeogenesis:** during prolonged fasting.

7- **Secretion of** prostaglandins and bradykinin: they are paracrine hormones

Physiological Anatomy of the Kidney

The kidney is: Paired organ lies on either side of the vertebral column. Below the diaphragm, just behind the peritoneum of the abdominal cavity.

- **Structure of the kidney:**

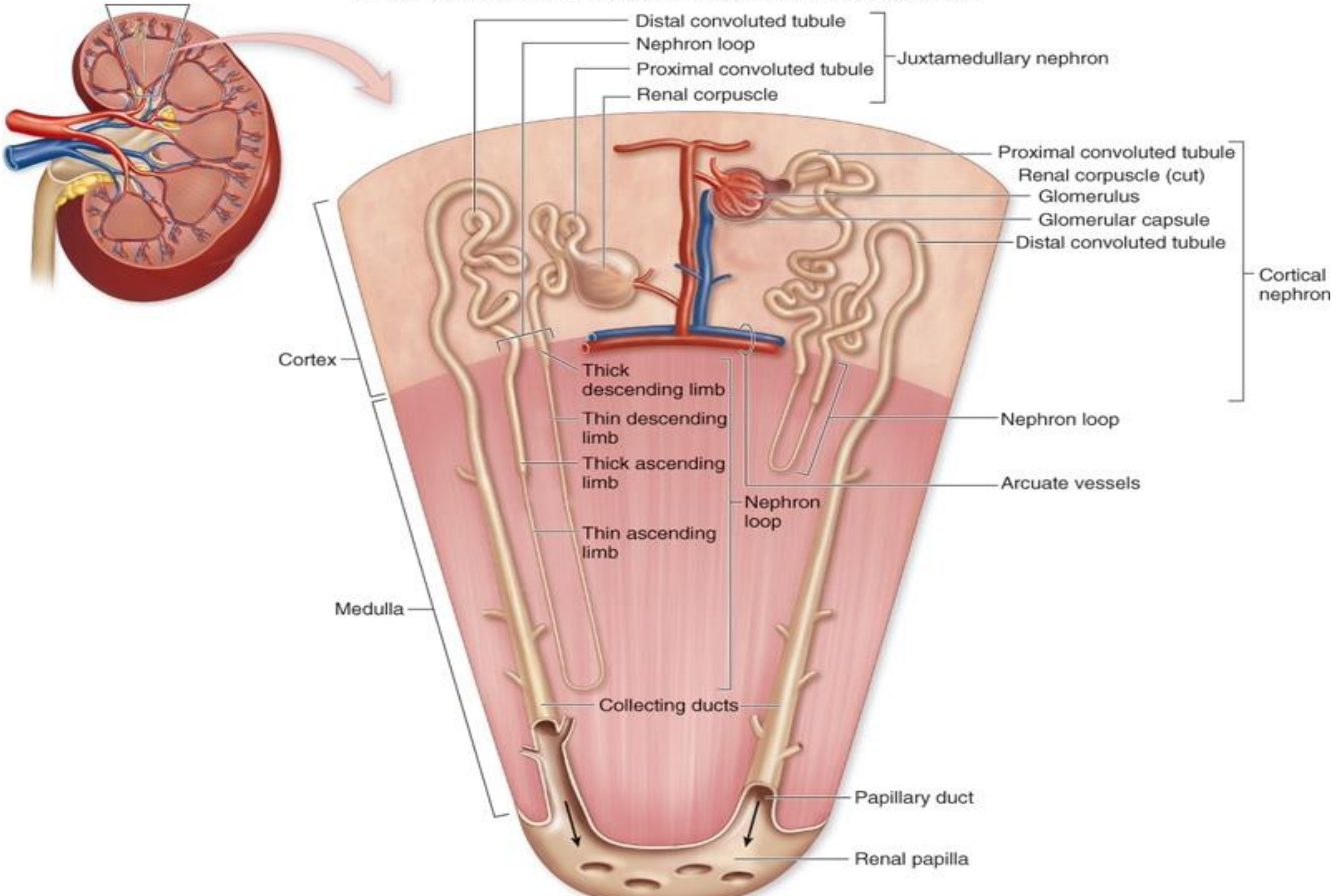
The kidney is formed of:

A-Cortex.

Is the outer granular part because of its many capillary beds (glomeruli)

B-The Medulla.

- It is the deep part lighter in color formed of tubules and long blood vessels.
- The medulla consists of 8-15 renal pyramids. The apex of these pyramids drain urine into minor calyx, several minor calyces unit to form major calyx. Major calyx unit to form the renal pelvis.



Distal convoluted tubule
Nephron loop
Proximal convoluted tubule
Renal corpuscle
Juxtamedullary nephron
Proximal convoluted tubule
Renal corpuscle (cut)
Glomerulus
Glomerular capsule
Distal convoluted tubule
Cortical nephron
Cortex
Thick descending limb
Thin descending limb
Thick ascending limb
Thin ascending limb
Nephron loop
Nephron loop
Arcuate vessels
Medulla
Collecting ducts
Papillary duct
Renal papilla

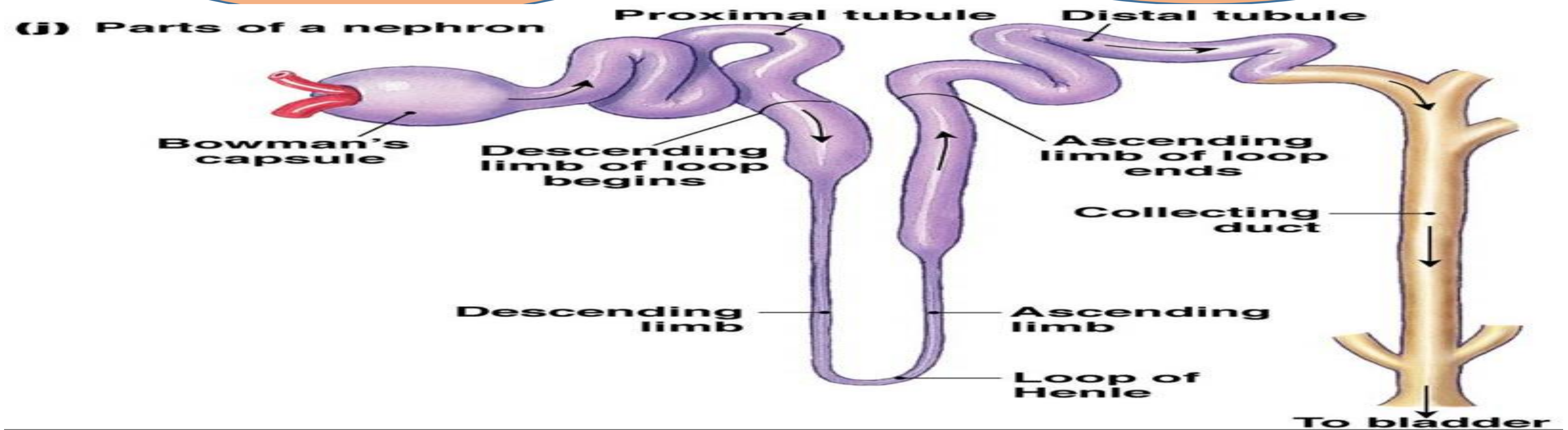
Nephron

is the functional unit of kidney.

- There are 1.3 million nephrons in each human kidney
- The **Nephron** consists of:

(1)Renal corpuscle
It is formed of:
Glomerulus and Bowman's capsule

(2) Renal tubule:
It is divided into:
PCT, loop of Henle , DCT

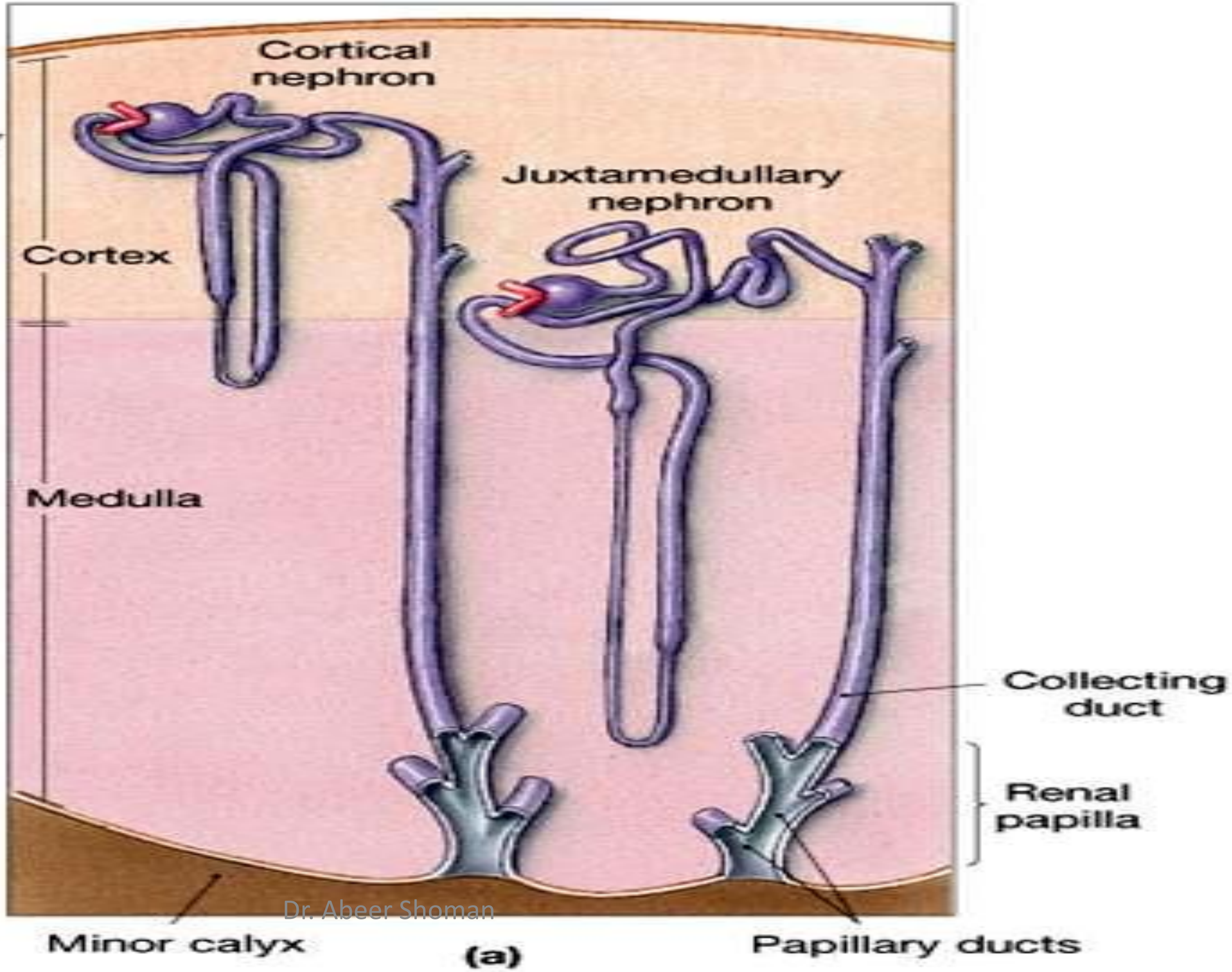


- **Glomerular capillary :** the only capillary lying between **2 arterioles.**

There are two types of nephrons:

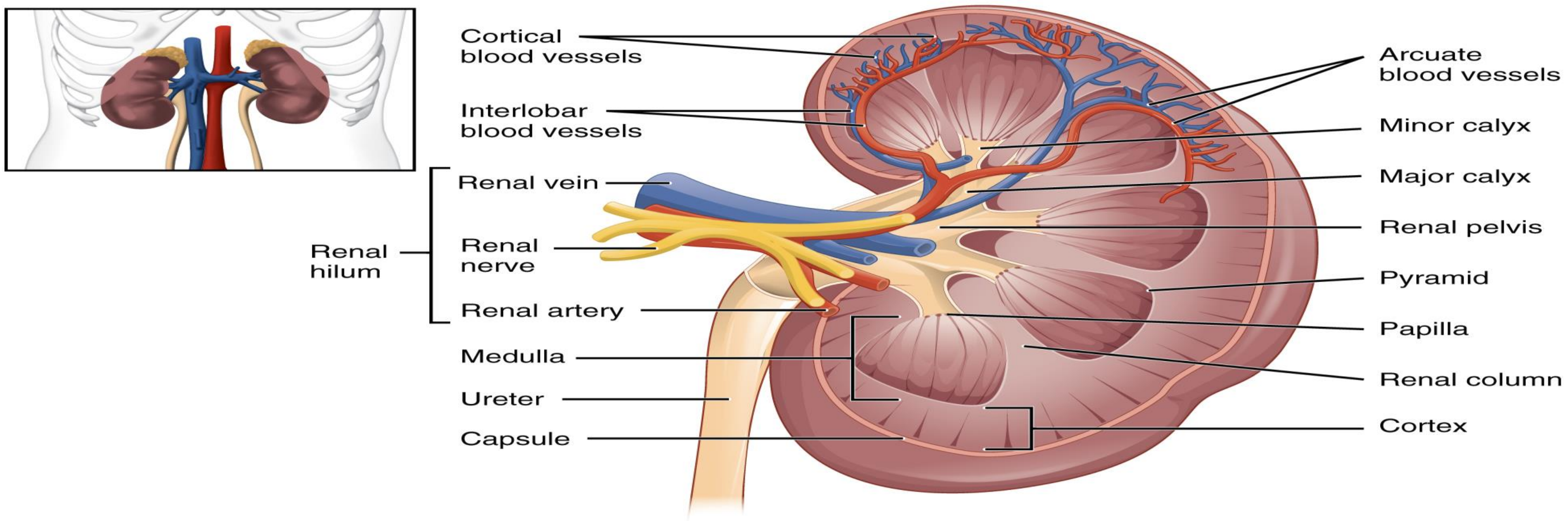
Cortical nephrons(85%)	Juxta medullary nephrons(15%)
Their glomeruli lie close to surface	Their glomeruli lie deep near the medulla
They have very short loop of Henle	They have very long loop of Henle
Network of peritubular capillaries	U shaped peritubular capillary that lie side by side with loop of Henle
Its function is formation of urine	play a role in urine concentration

Types of Nephron

Renal Blood Flow

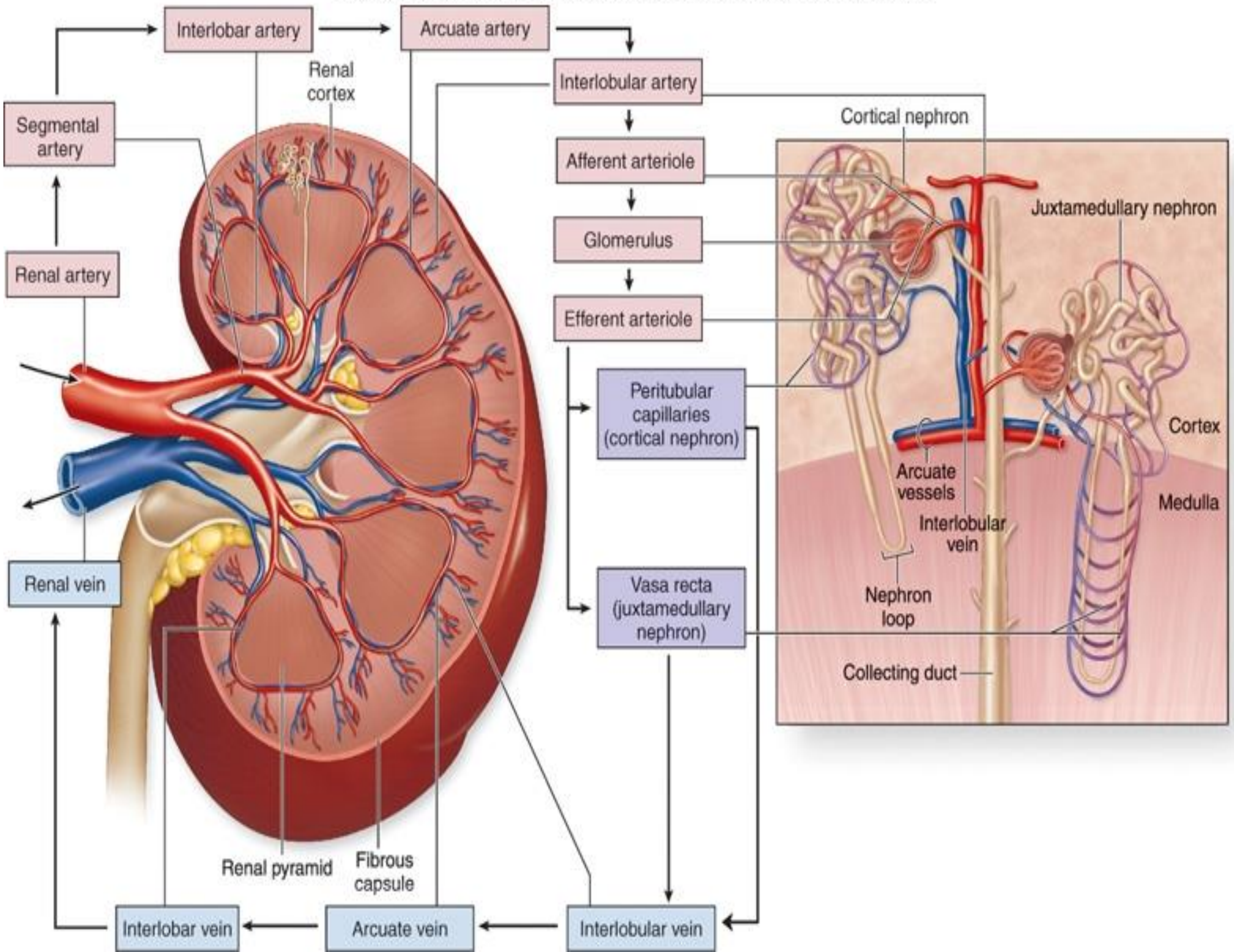
- **Blood flow to kidney is 1200 ml/min (20% of Cardiac output)**
- **plasma flow** = 650 ml/min



……Renal Blood Flow

- **Renal artery arises directly from the abdominal aorta**
- enters the kidney at hilum dividing into:

1. interlobar
2. arcuate,
3. interlobular,
4. afferent arterioles,
5. glomerular capillaries,
6. efferent arterioles,
7. peritubular capillaries which give vasa recta

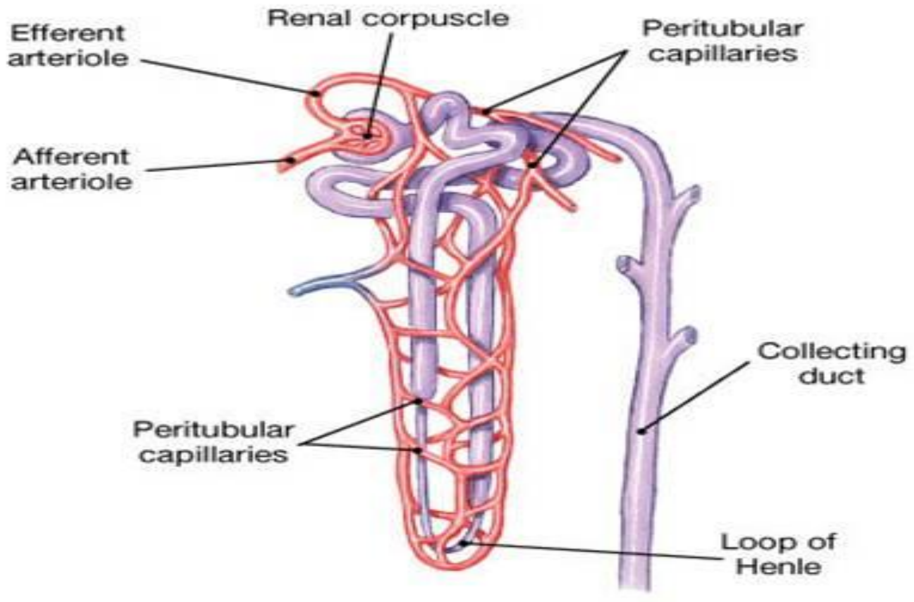

Interlobar artery
Arcuate artery
Interlobular artery
Renal cortex
Segmental artery
Renal artery
Afferent arteriole
Glomerulus
Efferent arteriole
Peritubular capillaries (cortical nephron)
Vasa recta (juxtamedullary nephron)
Cortical nephron
Juxtamedullary nephron
Cortex
Medulla
Arcuate vessels
Interlobular vein
Nephron loop
Collecting duct
Renal vein
Renal pyramid
Fibrous capsule
Interlobar vein
Arcuate vein
Interlobular vein

Vasa Recta:

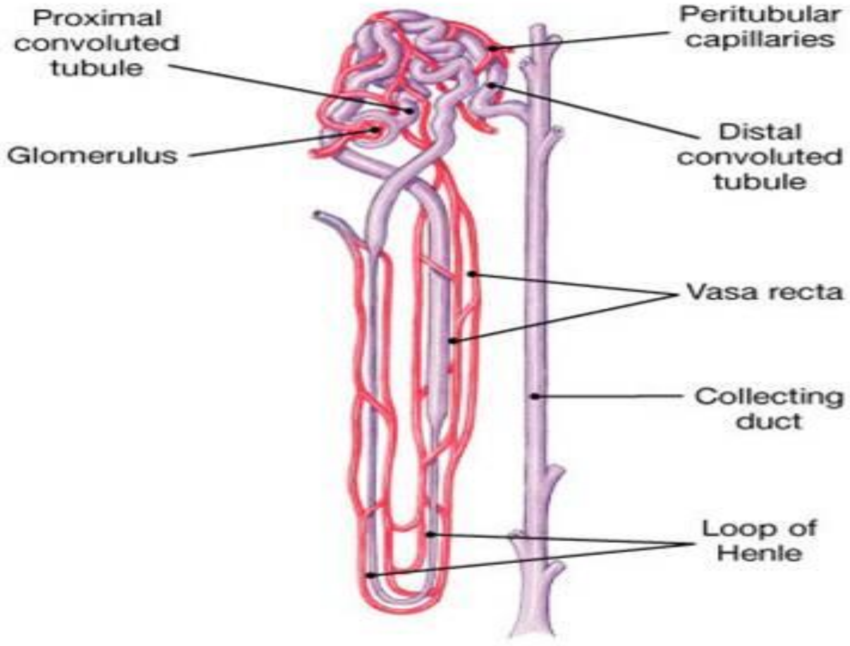
These are capillaries that descend in medulla along juxtamedullary nephrons & reascend into cortex supplying lower part of loop of Henle

•They are concerned with concentration of urine (with collecting duct) .

•The great length of vasa recta results in a high resistance to blood flow → low blood flow in the medulla (1-2% of blood flow).



(b) Cortical nephron



(c) Juxtamedullary nephron

Glomerular capillary

-Arises from afferent arteriole

-High pressure bed

- Capillary pressure = 60 mmHg

-Plasma is filtered

Peritubular Capillary

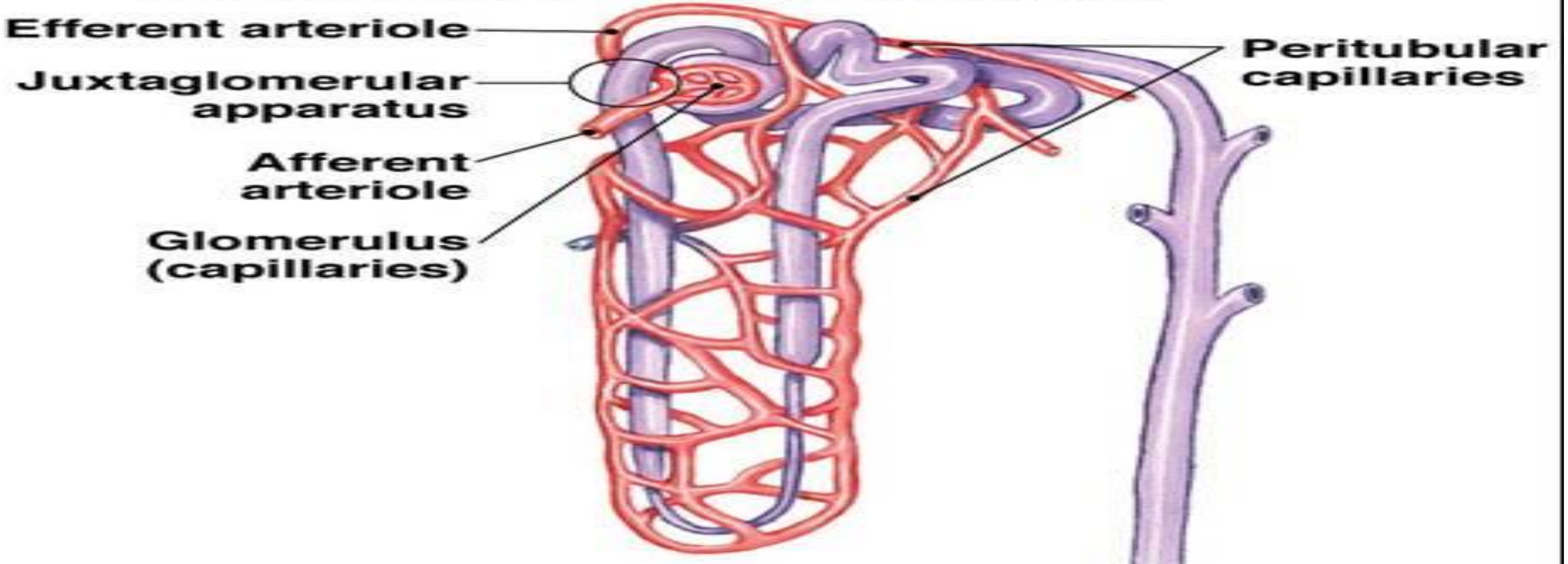
-Arises from efferent arteriole

-Low pressure bed

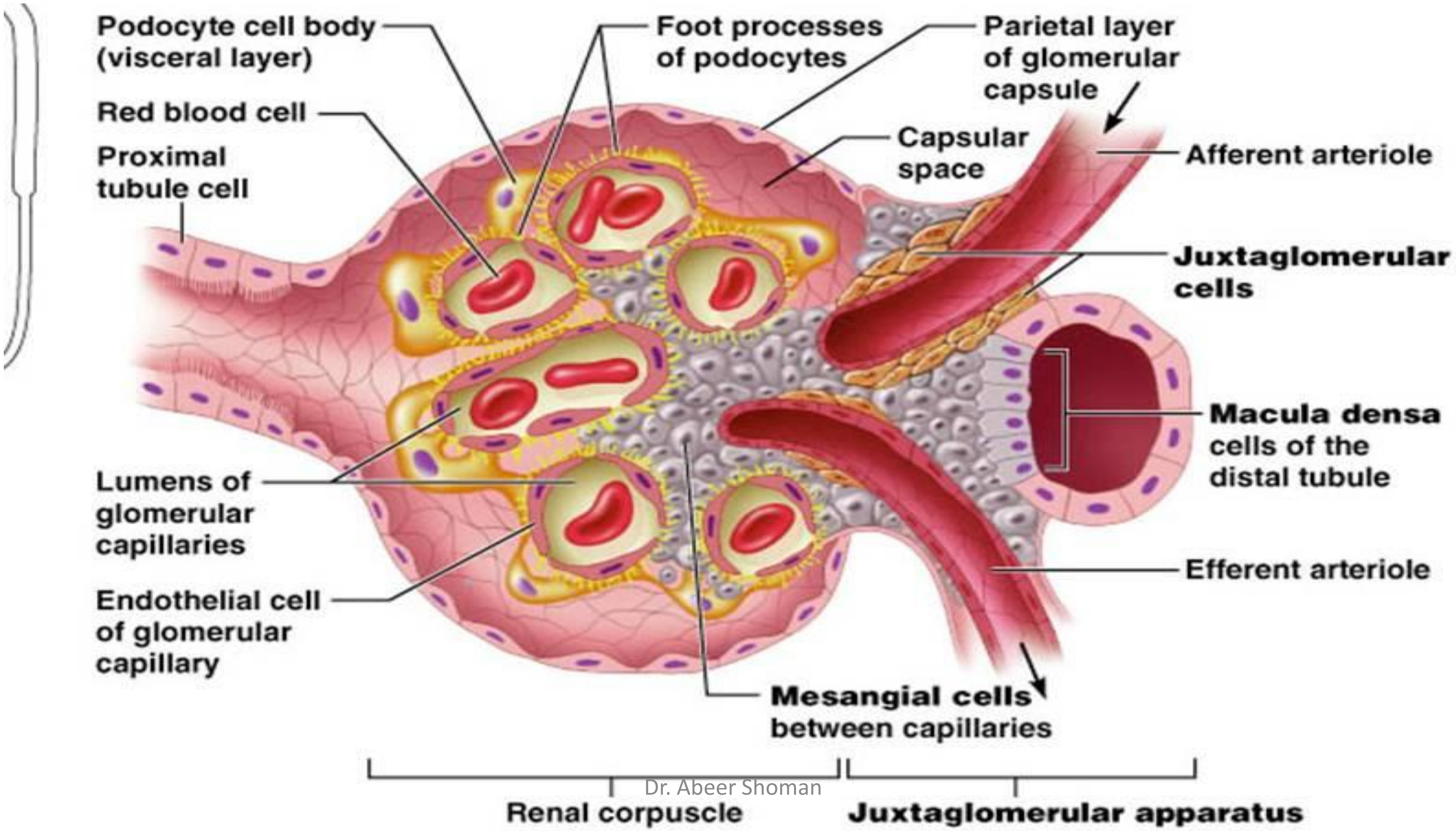
-Capillary pressure =13 mmHg

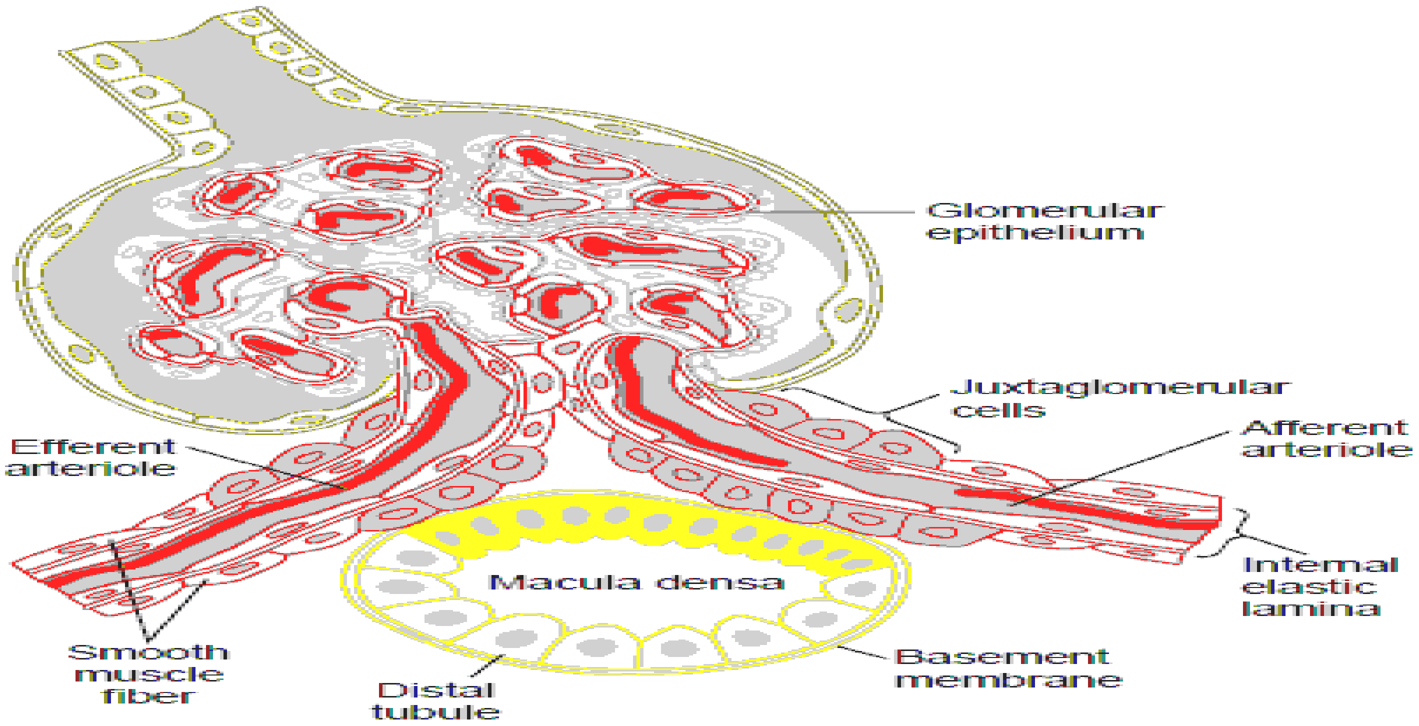
-Filtrate is reabsorbed.

(g) Each nephron has two arterioles and two sets of capillaries associated with it.



Juxta glomerulus apparatus



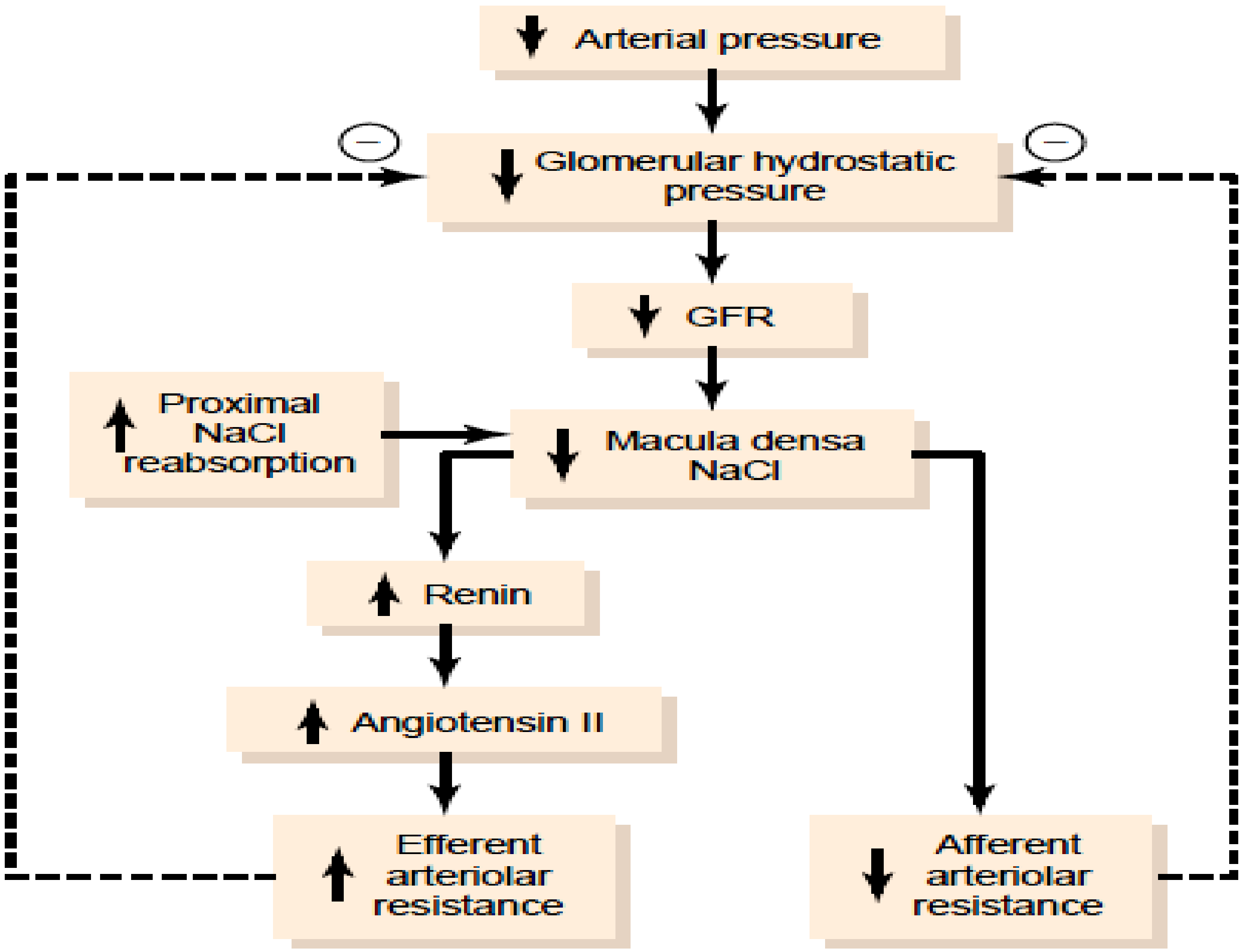


It lies at the area of contact between distal convoluted tubule, and the afferent arteriole and efferent arteriole, formed of:

1-Macula densa: The tubular epithelium show dense crowding of cells & nuclei

2-Juxta glomerular cells: The smooth muscles of arterioles (afferent & to a lesser extent efferent) have an appearance like epithelial cells. They secrete renin.

3-Lacis cells: agranular cells between afferent & efferent arterioles. They contain renin.



Macula densa feedback mechanism for autoregulation of glomerular hydrostatic pressure and glomerular filtration rate (GFR) during decreased renal arterial pressure.

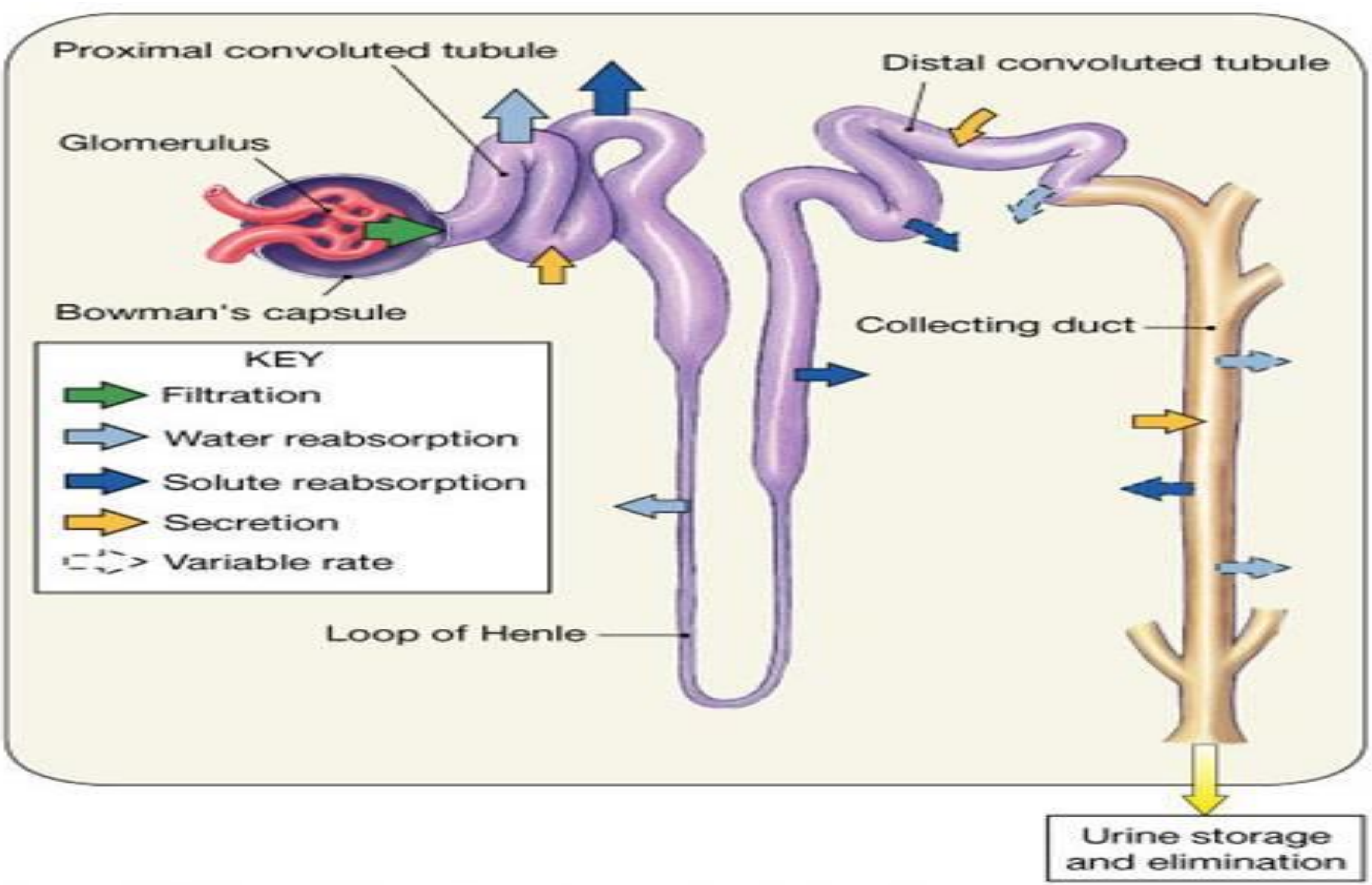
Urine formation

Glomerular filtration rate (GFR)

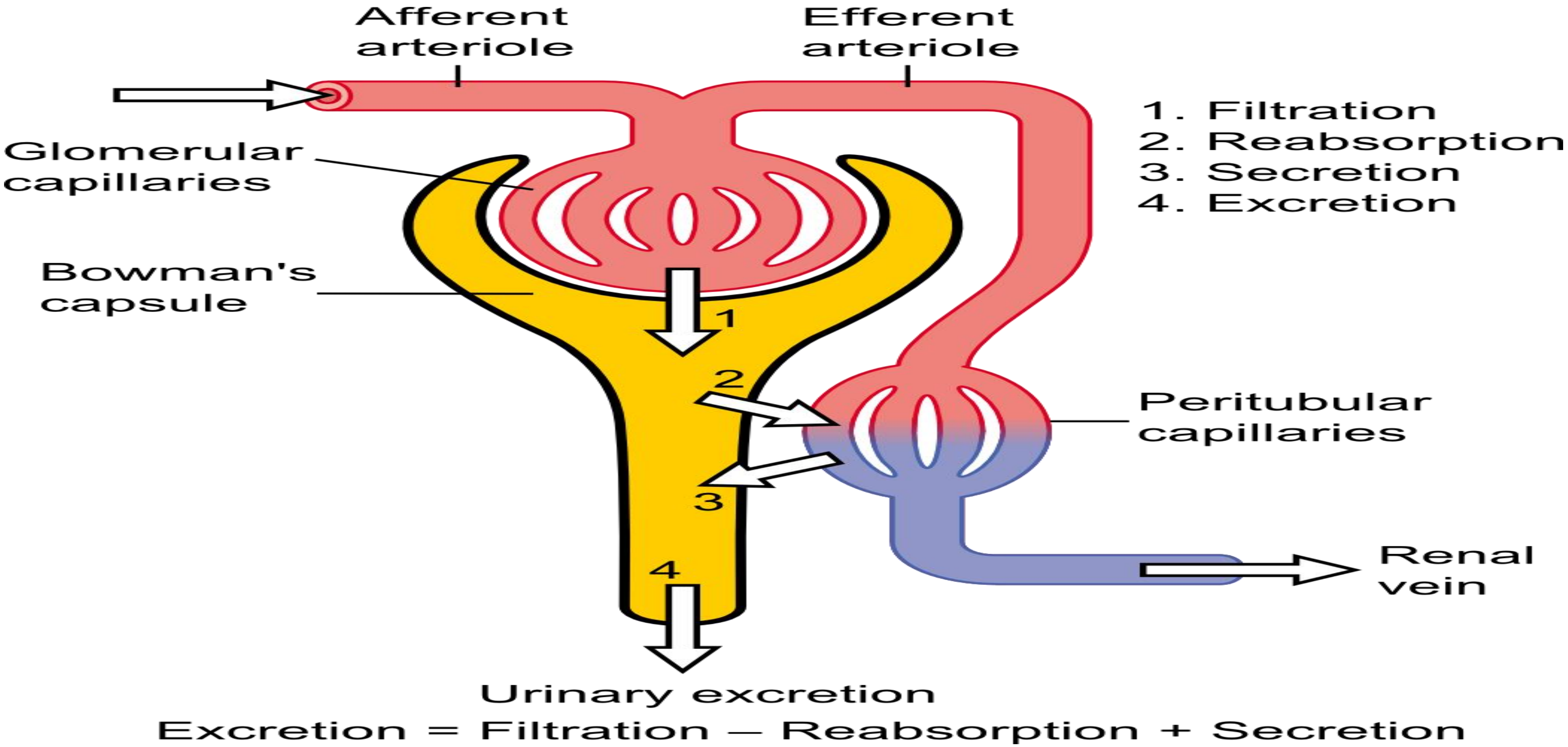
ILOs

1. Describe the three layers of the glomerular filtration barrier and explain how size and charge selectivity prevent plasma protein filtration.
2. State the composition of glomerular filtrate and compare it to plasma.
3. Define the Starling forces (hydrostatic and osmotic pressures) that determine the Net Filtration Pressure (NFP).
4. Calculate the Net Filtration Pressure given the values of the individual forces.
5. Predict how changes in afferent or efferent arteriolar resistance will affect glomerular hydrostatic pressure and GFR.

Urine formation



Urine formation



Glomerular Filtration Rate: GFR

*Glomerular Filtrate: is the fluid that filters through glomeruli into Bowman's capsule.

*Glomerular Filtration Rate: is the amount of glomerular filtrate formed each minute in all nephrons of both kidneys.

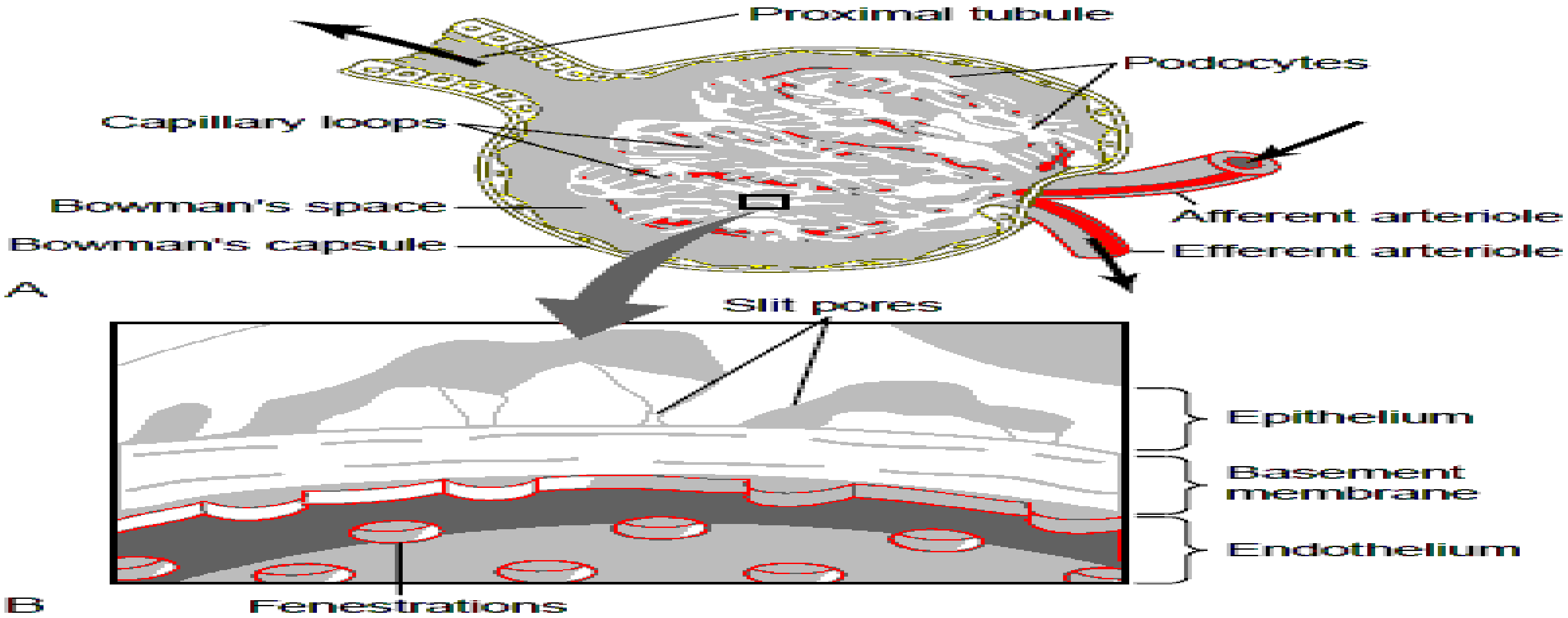
It equals : 125 ml/min - 180 litre/day

Glomerular filtrate is an ultrafiltrate of plasma through the glomerular capillary membrane not contain plasma proteins.

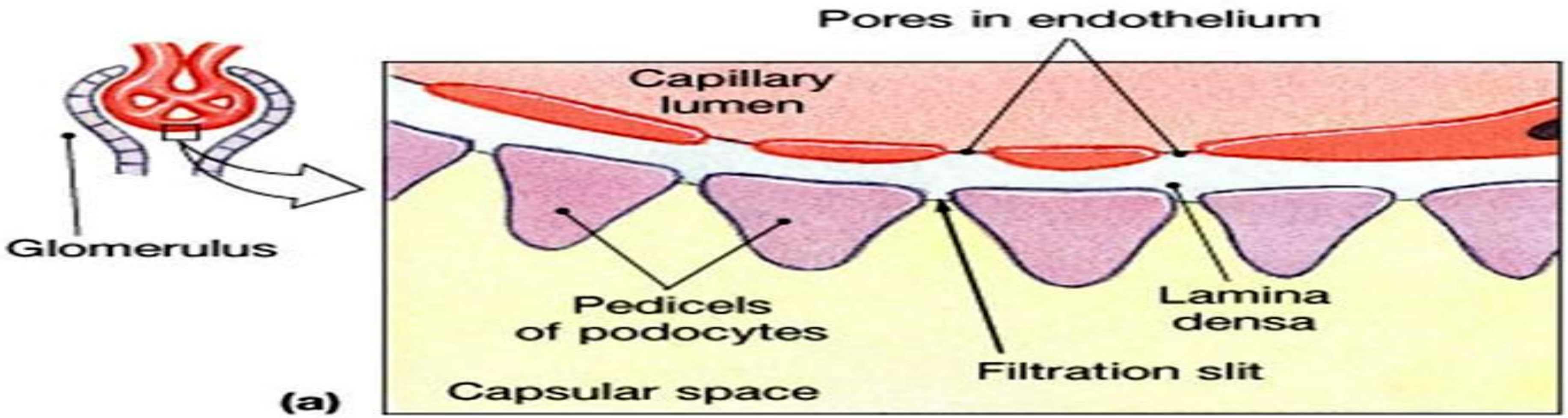
*Glomerular Capillary Membrane:

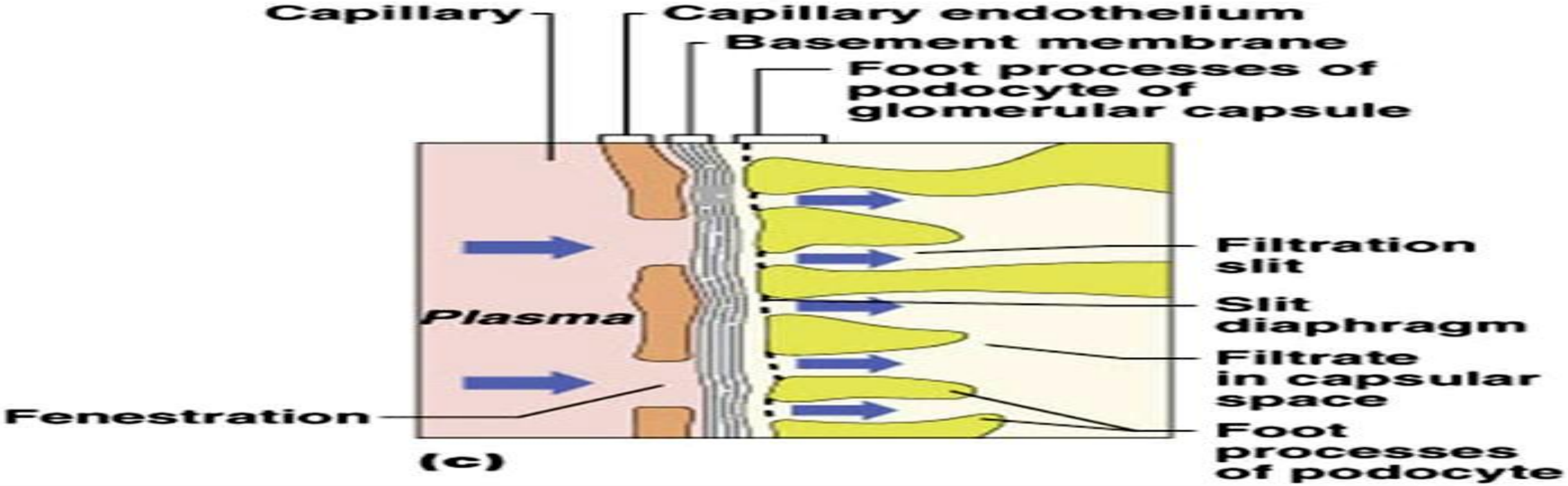
is formed of 3 layers:

1) **Capillary endothelium** : contain wide pores 70-90 nm
2) **Basement membrane:** which has no pores, it is negatively charged repel anions of plasma
3) **Bowman's capsule epithelium:** podocytes with slit pores(25



Glomerular membrane





Forces causing glomerular filtration:

(1)Hydrostatic pressure of glomerular capillary (HP_{GC}) =(**60** mmHg)

- It helps filtration. It is the highest capillary pressure all over the body………why?

(2)Colloidal Osmotic Pressure of Bowman's capsule (CO_{BC})= (**zero**)

- It helps filtration

(3)Colloidal Osmotic Pressure of Glomerular capillary (CO_{GC}) =**32** mmHg

- It opposes filtration.

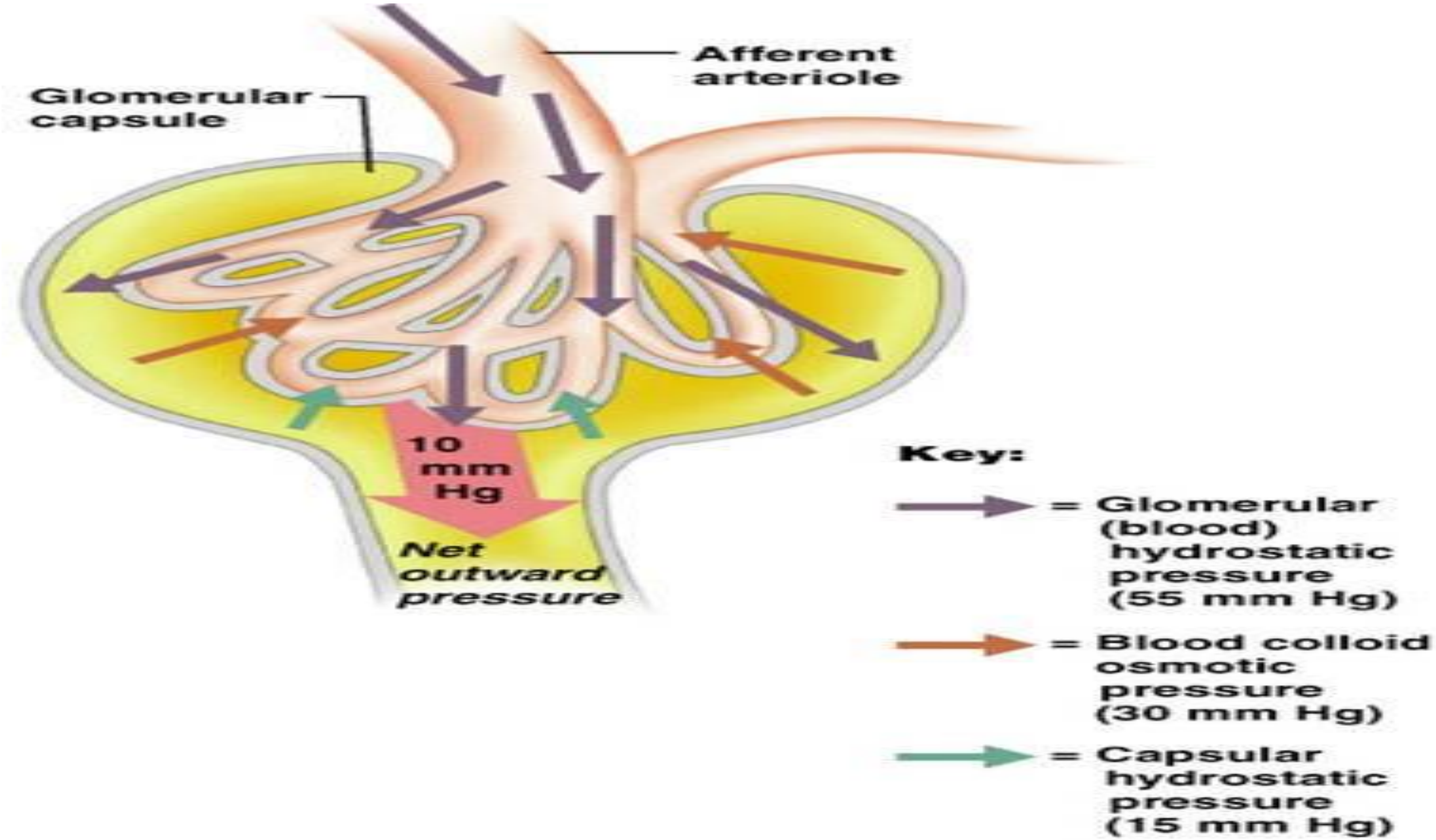
(4)Hydrostatic pressure of Bowman's capsule (HP_{BC})=**18** mmHg.

- It opposes filtration.

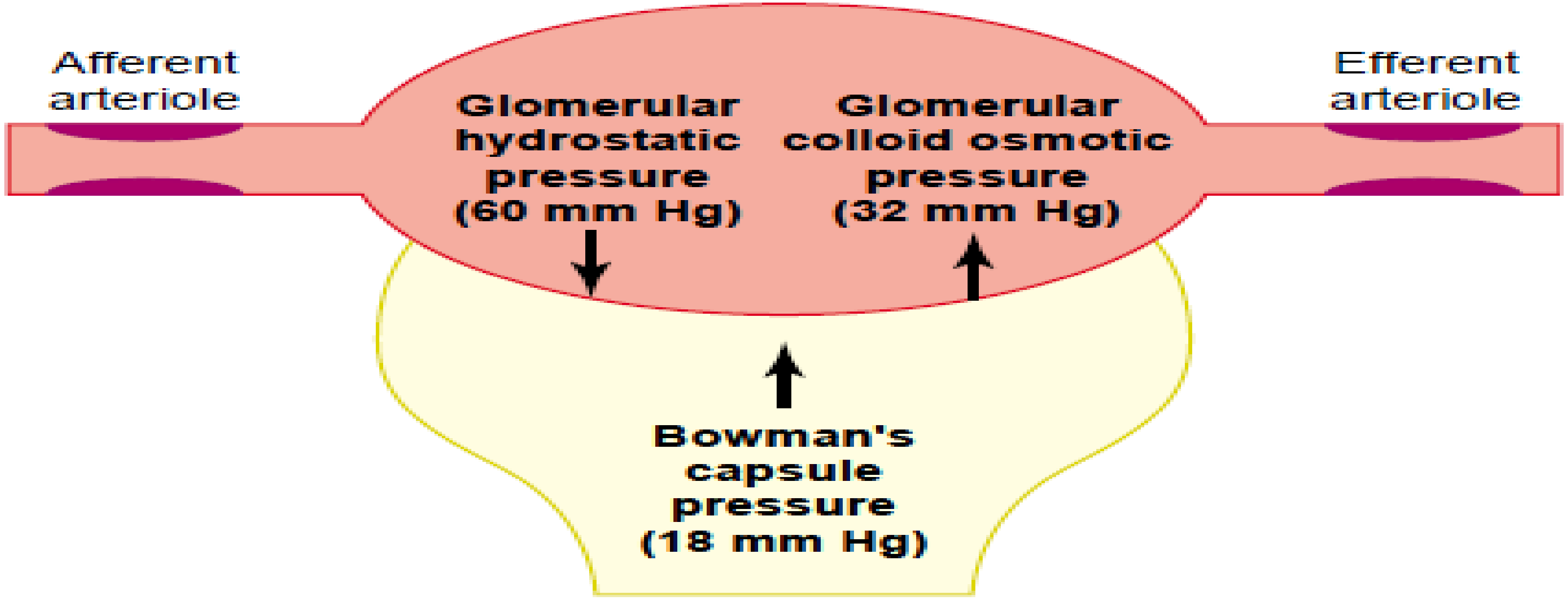
The Net filtering forces or the filtration pressure (NFF)

NFF= CHP + COPB – (COPG + HPB) = 60 + 0 - (32 + 18)= 10 mmHg

Filtration forces



Starling forces



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)

Factors affecting GFR

[1] Changes in glomerular hydrostatic pressure (GHP)

[2] Changes in glomerular colloidal osmotic pressure (OP_{GC})

[3] Increase hydrostatic pressure in Bowman's capsule (HP_{BC})

[4] Increase colloidal osmotic pressure in Bowman's capsule (OP_{BC})

[5] Conditions affecting Kf

[6] Changes in Arterial blood pressure ABP & or renal blood flow

Changes in glomerular hydrostatic pressure (GHP):

Glomerular Hydrostatic Pressure is affected by:

A) Afferent arteriolar dilatation (by prostaglandin & bradykinin) leads to increase $HP_{GC} \rightarrow$ increase GFR

B) Afferent arteriolar constriction (by sympathetic & adenosine) leads to decrease $HP_{GC} \rightarrow$ decrease GFR.

C) Moderate Efferent arteriolar constriction leads to increase $HP_{GC} \rightarrow$ slight increase of GFR

D) Severe efferent arteriolar constriction→plasma remains for a longer time in Glomerulus with more filtration with more increase in colloidal osmotic pressure (O.P)→ decrease GFR.

It is called paradoxical decrease in GFR despite elevated HP_{GC}.

2]Changes in glomerular colloidal osmotic pressure (OP_{GC})

Increase in OP_{GC} (as in dehydration) leads to decrease GFR.

Decrease in OP_{GC} (as in hypoproteinemia) leads to increase GFR

3]Increase hydrostatic pressure in Bowman's capsule (HP_{BC}):

As in urinary tract obstruction →decrease GFR.

[4] Increase colloidal osmotic pressure in Bowman's capsule (OP_{BC}):

As in increased glomerular membrane permeability → increase GFR

[5] Conditions affecting Kf:

• **Membrane permeability:**

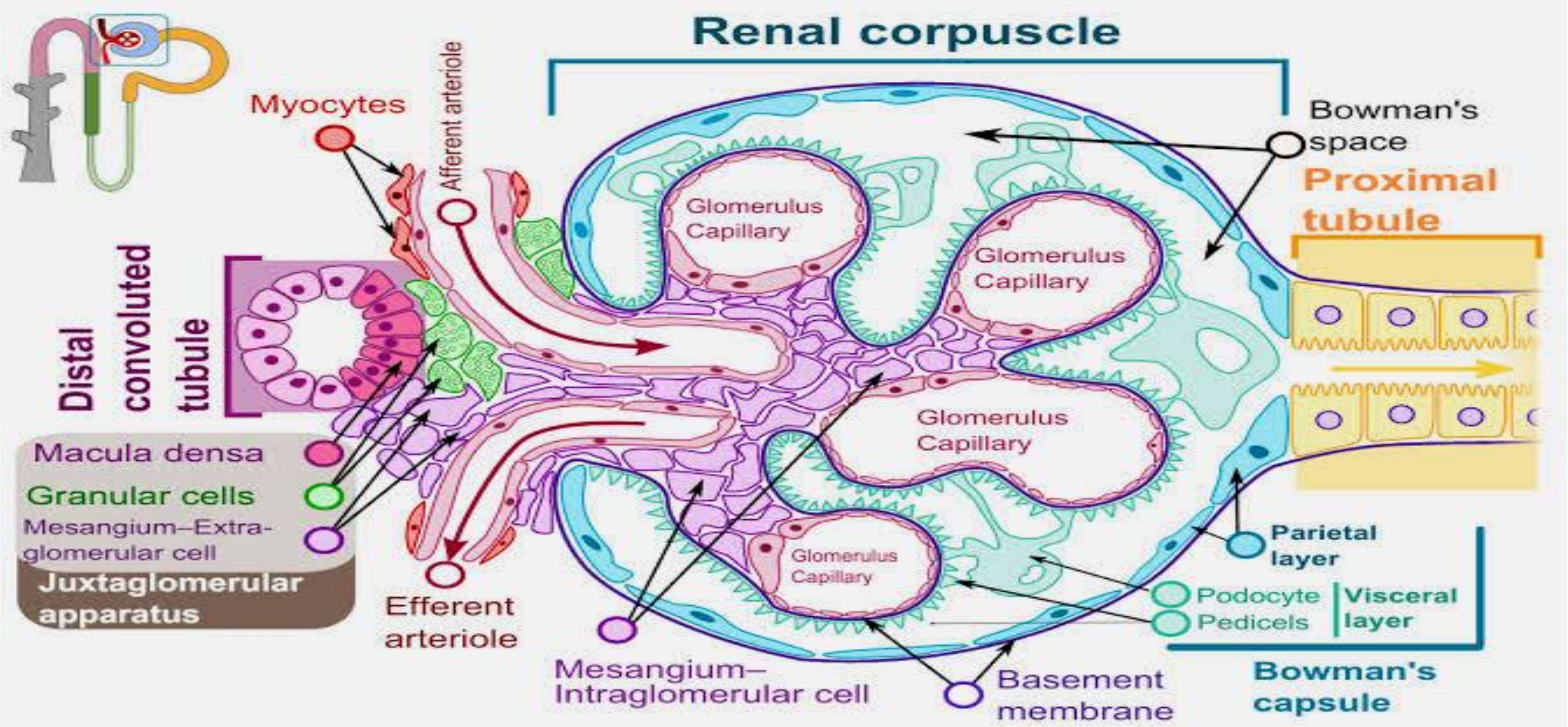
• Increase thickness of glomerular membrane → decrease membrane permeability → decrease Kf → decrease GFR.

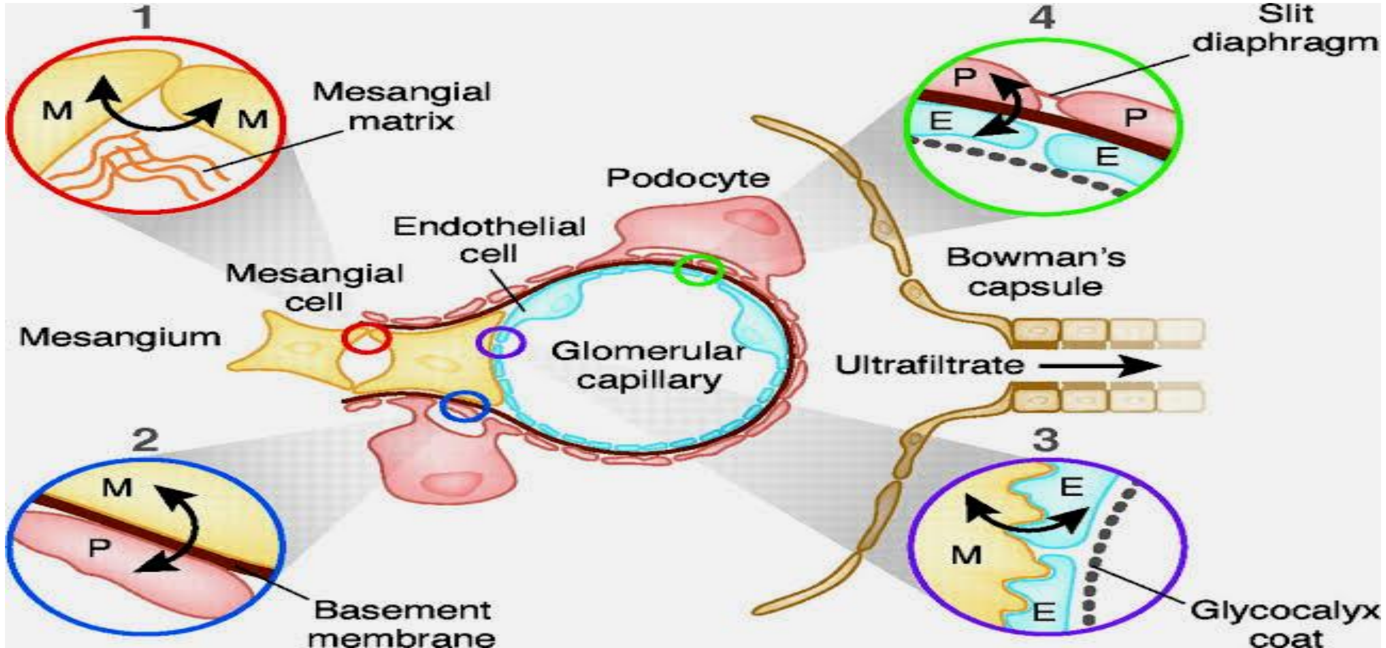
• **Surface area of glomerular capillaries:**

_it is affected by:

***Contraction of mesangial cells which** reduce surface area and decrease GFR. caused by: Angiotensin II, Nor epinephrine, Vasopressin & Endothelins.

***Relaxation of mesangial cells which** increase surface area and increase GFR. caused by: ANP, CAMP, PGE2 & Dopamine.


Renal corpuscle
Myocytes
Afferent arteriole
Bowman's space
Proximal tubule
Distal convoluted tubule
Glomerulus Capillary
Glomerulus Capillary
Glomerulus Capillary
Glomerulus Capillary
Macula densa
Granular cells
Mesangium–Extra-glomerular cell
Juxtaglomerular apparatus
Efferent arteriole
Parietal layer
Podocyte
Pedicels
Visceral layer
Mesangium–Intraglomerular cell
Basement membrane
Bowman's capsule


1
M
M
Mesangial matrix
4
Slit diaphragm
P
E
P
E
Podocyte
Endothelial cell
Mesangial cell
Mesangium
Glomerular capillary
Bowman's capsule
Ultrafiltrate
2
M
P
Basement membrane
3
E
M
E
Glycocalyx coat

[6] Changes in ABP & renal blood flow:

- GFR is kept constant despite of changing ABP between 90 - 200 mmHg.
- This is called **autoregulation** of GFR.

The mechanisms involved in autoregulation of GFR are :

1- Tubuloglomerular balance

2- Myogenic autoregulation

1- Tubuloglomerular balance

Decrease ABP → decrease GFR → decrease Na^+, cl^- concentration at macula densa leading to:

Efferent arteriolar V.C. feedback	**afferent arteriolar VD feedback**
Macula densa send signals to release Renin →increase **angiotensin II**→ VC of efferent arteriole → increase Glomerular pressure→ increase GFR	Macula densa send signals to cause VD of afferent arteriole → increase GFR

2- <u>Myogenic autoregulation :</u>

- It is a rapid mechanism and the first line of defense against rapid change in blood pressure.
- Increase ABP → stretch wall of arteriole→ increase tension → contraction of plain muscle of arteriole → decrease diameter → decrease blood flow.
- Conversely a decrease in ABP results in relaxation of smooth muscles.

Determination of GFR By:

1) Inulin clearance test
2) Creatinine clearance test &
3) Radio Isotope as Cr^{51}

P

Plasma Clearance

***Definition:** The volume of plasma (in ml) that is cleared from a certain substance which is excreted in urine/min.

* **Calculation:**

Amount of substance cleared/min= amount of substance excreted in urine/min

$$C \times P = U \times V$$

Where: C is volume of cleared plasma/min

P is the concentration of the substance in plasma

U is the concentration of substance in urine

V is the volume of urine/min.

$$C = \frac{U \times V}{P}$$

Plasma Clearance

$$Cl = \frac{[U] \times V}{[P]}$$

- **A Substance that is filtered freely and neither reabsorbed nor secreted**. Its clearance equal GFR. For example : **inulin**

- **A substance that is reabsorbed by the renal tubules** will have clearance below GFR. Since tubular reabsorption returns the filtered substance back to the blood, i e.g. **urea and K^+.**

- **A substance that is secreted by the renal tubules** will have clearance above GFR. Since tubular secretion increases its removal (clearance) from the plasma e.g. **creatinine**.

** Importance of plasma clearance:

- It is an early index of renal disease.
- It is used for measurement of GFR using inulin or Mannitol
- It is used for study of behavior of different substances.
- Determination of effective renal plasma flow ERPF : A substance as"PAHA" is completely secreted through a single circulation in kidneys.

Its clearance = 650 ml/min

N.B: Clearance of endogenous substance as that of urea & creatinine: is preferred in investigating renal functions to avoid administration of exogenous substances.

Substance	Clearance	Behavior
Inulin	125 ml/min	Neither reabsorbed nor secreted
Urea, K+	< 125	Partially reabsorbed
Creatinine(140)	125 – 650	Partially secreted
PAHA	650	Completely secreted
Ammonia	>650	Completely secreted + manufactured by kidney
Glucose	Zero	Completely reabsorbed

** Disadvantage of clearance

It gives the net effect and not the detailed study of renal tubule e.g. K+ clearance = 75 ml/min which suggests that K+ is partially reabsorbed but K+ is:

65% reabsorbed in Proximal Convoluted Tubules “PCT” & then secreted in Distal Convoluted Tubules “DCT”.

1] Inulin clearance test:

Inulin is:

a) A polymer of fructose MW = 5200

b) Neither reabsorbed, nor secreted by renal tubule, i.e. amount filtered = amount excreted.

c) Non toxic.

d) Not metabolized.

e) Not stored by kidney and not affect GFR.

f) Can be easily measured in urine & plasma.

Inulin clearance

Since it is neither **reabsorbed nor secreted**

….. Amount filtered = Amount Excreted

$$C \times P = U \times V$$

C is the volume of glomerular filtrate/min (unknown)

P is the concentration in plasma which is equal to that in filtrate

U is the concentration in urine.

V is the volume of urine/min.

$$\therefore \mathbf{GFR = \frac{U \times V}{P} = \quad = 120\ ml/min}$$

2]Creatinine Clearance

Creatinine is an **endogenous substance** that is formed from creatine in muscle.

It is easily measured.

a) Freely filtered

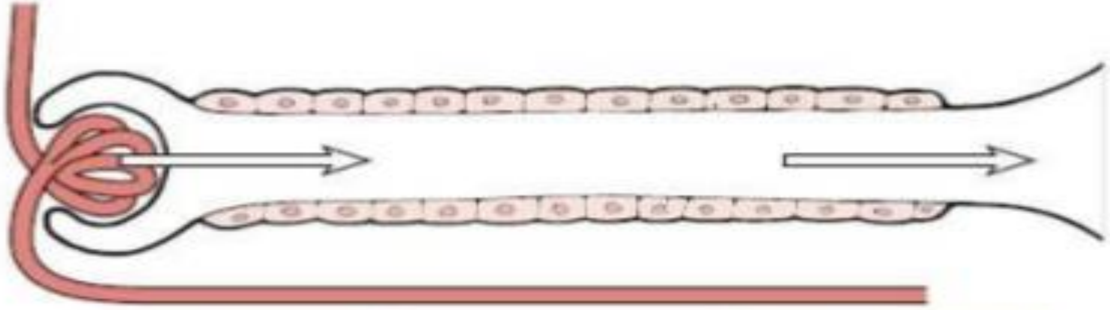
b) Not reabsorbed.

c) Partially secreted by the renal tubule.

………….Plasma clearance

Inulin Clearance Equals the Glomerular Filtration Rate

Reasons:
- freely filterable
- not reabsorbed or secreted
- not synthesized, destroyed, or stored in the kidneys.
- nontoxic.
- concentration in plasma and urine can be determined by simple analysis.



Filtered inulin $P_{IN} \times GFR$ = Excreted inulin $U_{IN} \times \dot{V}$

$$GFR = \frac{U_{IN}\dot{V}}{P_{IN}} = C_{IN}$$

Inulin clearance : highest standard
highly accurate

Others : iothalamate, an iodinated organic compound, EDTA, Vit B_{12}

Not commonly used in the clinical practice.

1. infused intravenously,
2. the bladder is usually catheterized;
3. inconvenient

$$\frac{\text{Effective Renal Plasma Flow}}{\text{Extraction Ratio}} = \text{Actual RPF}$$

$$\frac{\text{RPF}}{1 - \text{Hematocrit}} = \text{Renal Blood Flow}$$


Thank
You