MED439
KING SAUD UNIVERSITY

Physiology Team 439

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PHYSIOLOGY

RENAL FUNCTION AND GLOMERULAR FILTRATION

Black: in male AND female slides
Red : important
Pink: in female slides only
Blue: in male slides only
Green: Notes
Gray: extra information

Editing file

Functions of the Kidney

Synthetic Function

Glucose (Gluconeogenesis)
(In case of starvation will form Glucose from amino acid , so it's not occurring daily life)
Erythropoietin
(That stimulates the bone marrow for RBS formation)
1,25-dihydroxy Vitamin D (calcitriol)
(By addition of hydroxide group to increase Ca absorption)
Renin
(In order to regulate the ABP)

Excretion

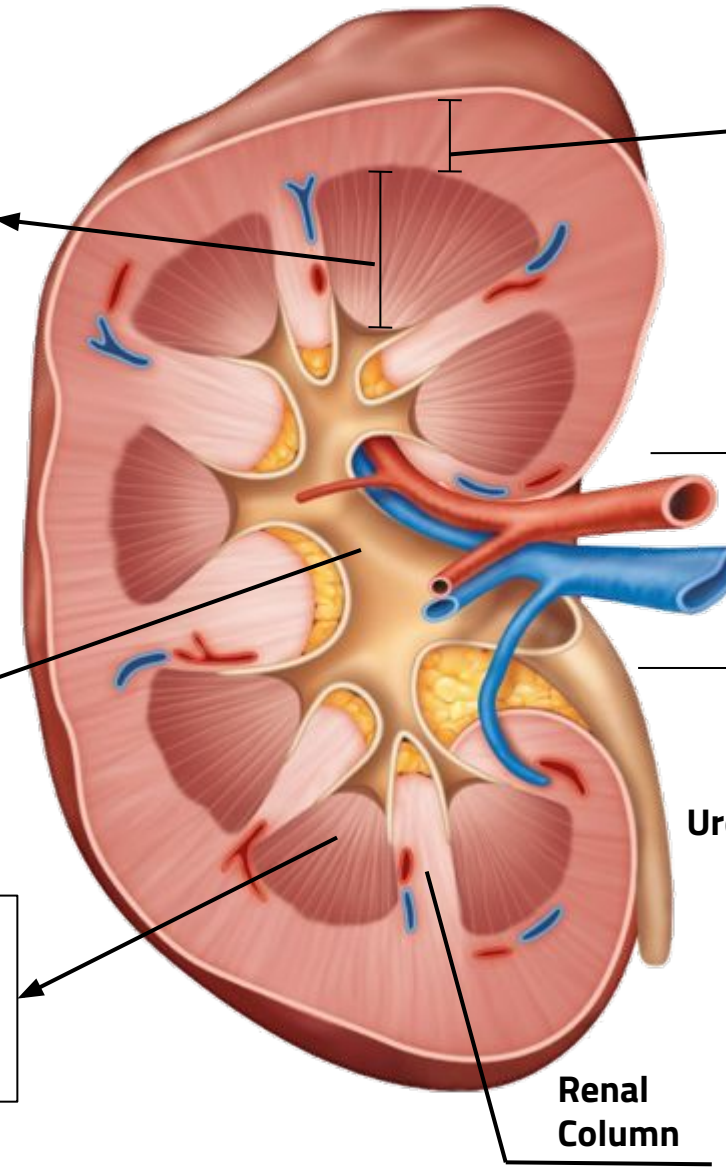
Blood with **metabolic waste products** e.g.
Urea, Creatinine, Uric Acid & Bilirubin

Ingested Toxins e.g. Drugs & Pesticides

Regulation

Water & electrolytes
Acid-base (through that and a long with renin = regulate ABP)
Arterial BP

Three Distinct Regions



Cortex
Granular Superficial Region

Medulla
Exhibits cone-shaped pyramid

Renal Hilum

Renal pelvis
flat, funnel-shaped tube

Ureter

Pyramids
bundles of collecting tubules

Renal Column

Functional unit of Kidney (Nephron)

The nephron is the functional and structural unit of the kidney, each kidney has 1 Million nephrons, each nephron is capable of urine formation.

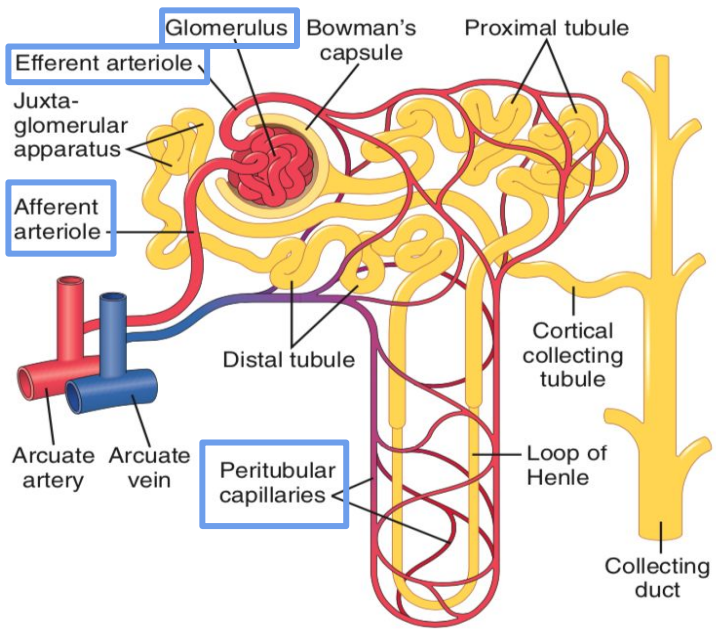
Renal Blood Vessels

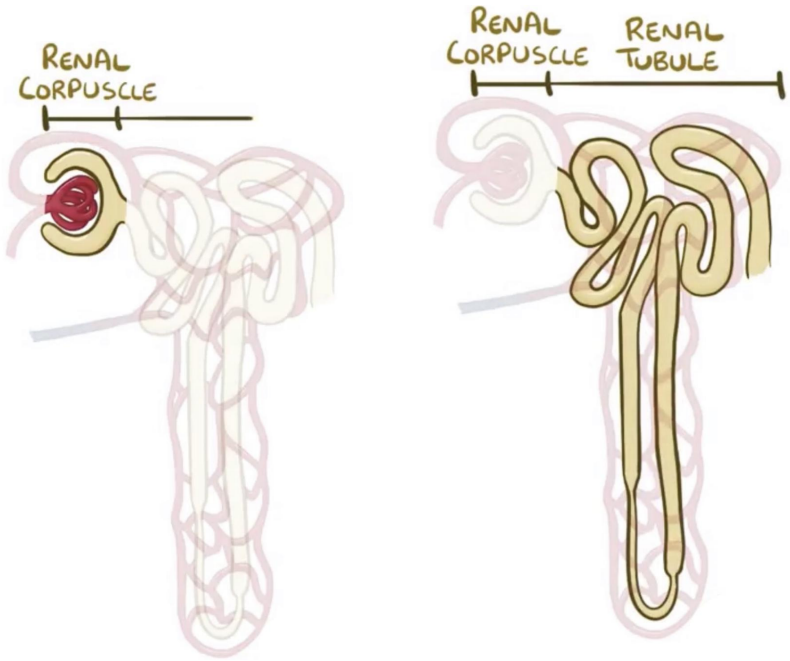
Afferent arteriole: (Arrive)
Delivers blood into the glomeruli. It has a bigger diameter compared to Efferent, it has high pressure.

Glomeruli:
Capillary network that produces filtrate that enters the urinary tubules. Higher pressure than all the other capillaries of the body because it's located between two arterioles with high pressure and this high pressure = favor filtration

Efferent arteriole: (Exit)
Delivers blood from glomeruli to peritubular capillaries , (high pressure)

Peritubular capillaries:
Vasa recta. (vasa= blood vessels , recta=مستقيم)





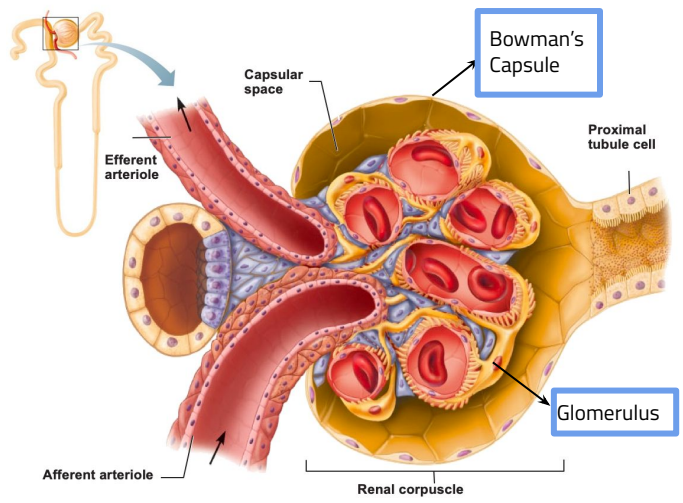
Structure of a Nephron

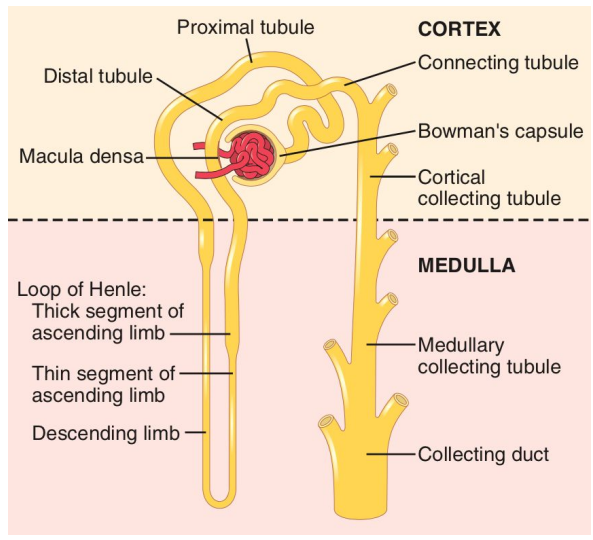
The glomerulus:
A capillary tuft associated with a renal tubule, In which large amount of fluid is filtered from blood.

Bowman's Capsule:
Blind end of the tubules, completely surrounds the glomerulus and receives the filtrate.

Tubules:
In which filtered fluid eventually is converted into urine, they're divided into different sections with different structural and functional characteristics:

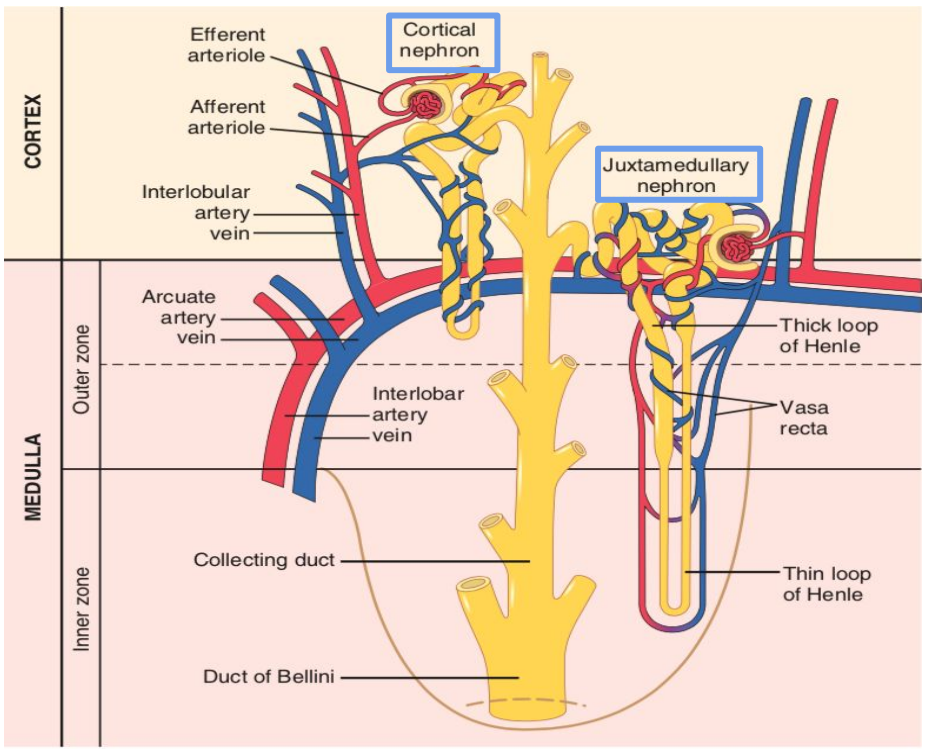
- Proximal tubules (in the cortex)
- Loop of henle
- Distal tubule (in the cortex)
- Connecting tubule, cortical collecting, and the cortical collecting ducts, which run downward in the medulla and become: medullary collecting ducts





Types of Nephron

	Cortical (85%)	Juxtamedullary (15%)
Site and features	Originate in outer ⅔ of cortex. Glomeruli in the outer portion of cortex and have **short** loops of Henle	Originate in Inner ⅓ of cortex. **Long** loops of henle extended into the medulla
Function	used daily except in case of dehydration	maints salt gradient, helps conserve water (due to vasa recta) , only in dehydration. 1-2% of blood flows through it (موجودة بكثرة عند الجمل لأنه يعيش بالصحراء فتساعده) (will be explained more in next lectures)
Capillary Type	Peritubular capillaries	Vasa Recta



Renal Blood Flow

- Renal blood flow to the kidney represents **20% of cardiac output.** The blood flows to each kidney through a **renal artery.**

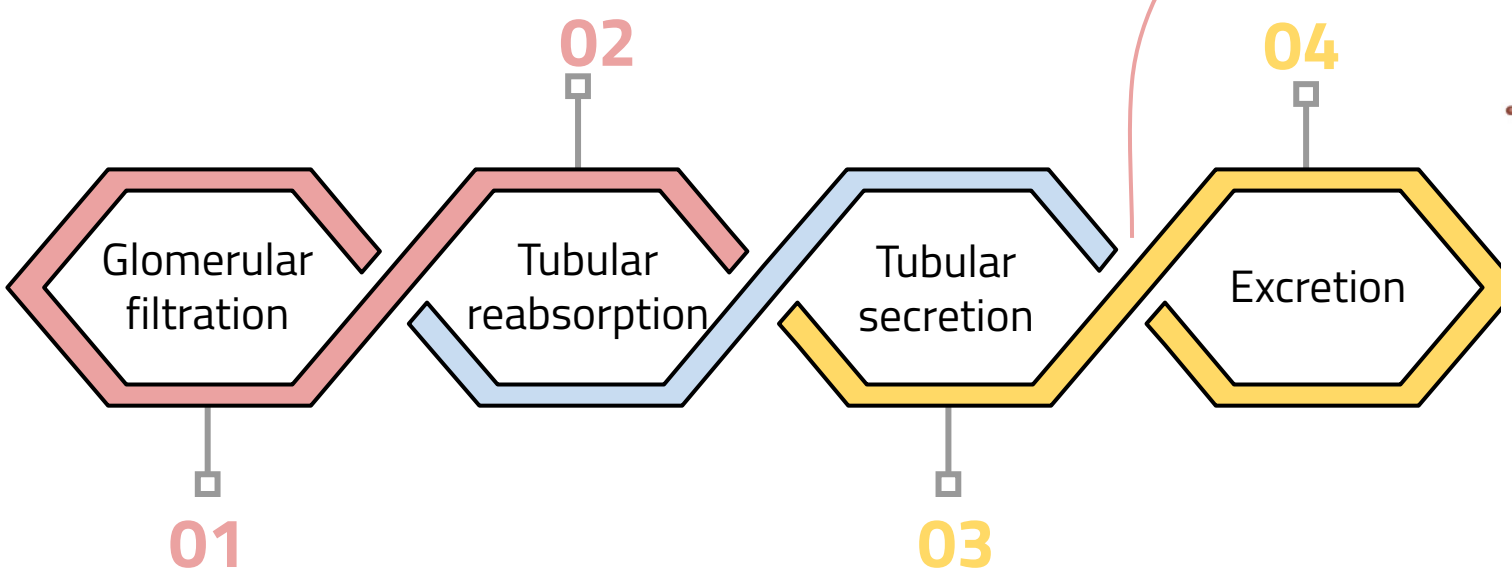
- Features of renal circulation:
  1- High blood flow rate (1200 ml/min). 20% × 5 L = 1 L/min ≈ 1200 ml/min
  2- Presence of two capillary beds: **glomerular** and **peritubular**.
- Efferent and afferent arterioles are major sites of renal resistance. they have high blood pressure.

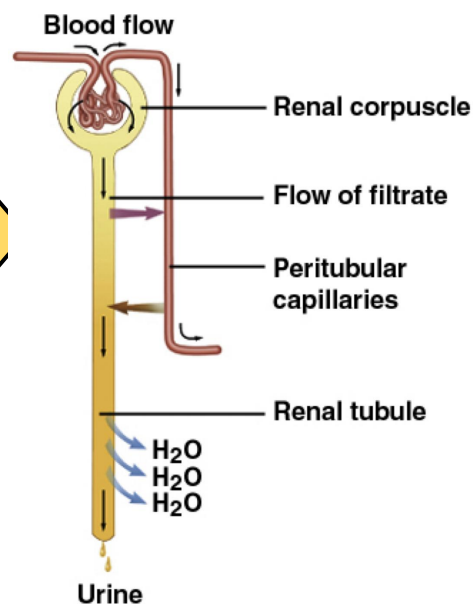
Urine Formation

- The primary function of kidney is to **clear** unneeded substances from the blood to be excreted in urine.
- **Steps of urine formation:**

Removes useful solutes from the filtrate, and returns them to the blood. (From tubules to the peritubular).

Water conservation: (happens before excretion and it's only for juxtamedullary)
Removes water from the urine and returns it to blood, concentrates wastes.





Filtration of fluid from Glomerular capillaries into the renal tubules. It's the first step of urine formation. It contains all substances present in plasma, **except proteins.**

Removes additional wastes from the blood, adds them to the filtrate. (From peritubular to the tubules).

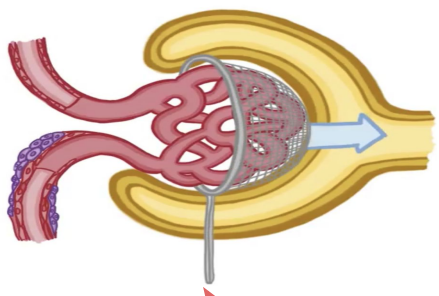
Common components of Glomerular filtrate:

- **Organic molecules:** Glucose, Amino acids. (but not proteins)
- **Nitrogenous waste:** Urea, Uric acid, Creatinine.
- **Ions:** Sodium, Potassium, Chloride.
- **Water.**

Urinary excretion = Filtration - Reabsorption + Secretion

Glomerular Filtration Rate:

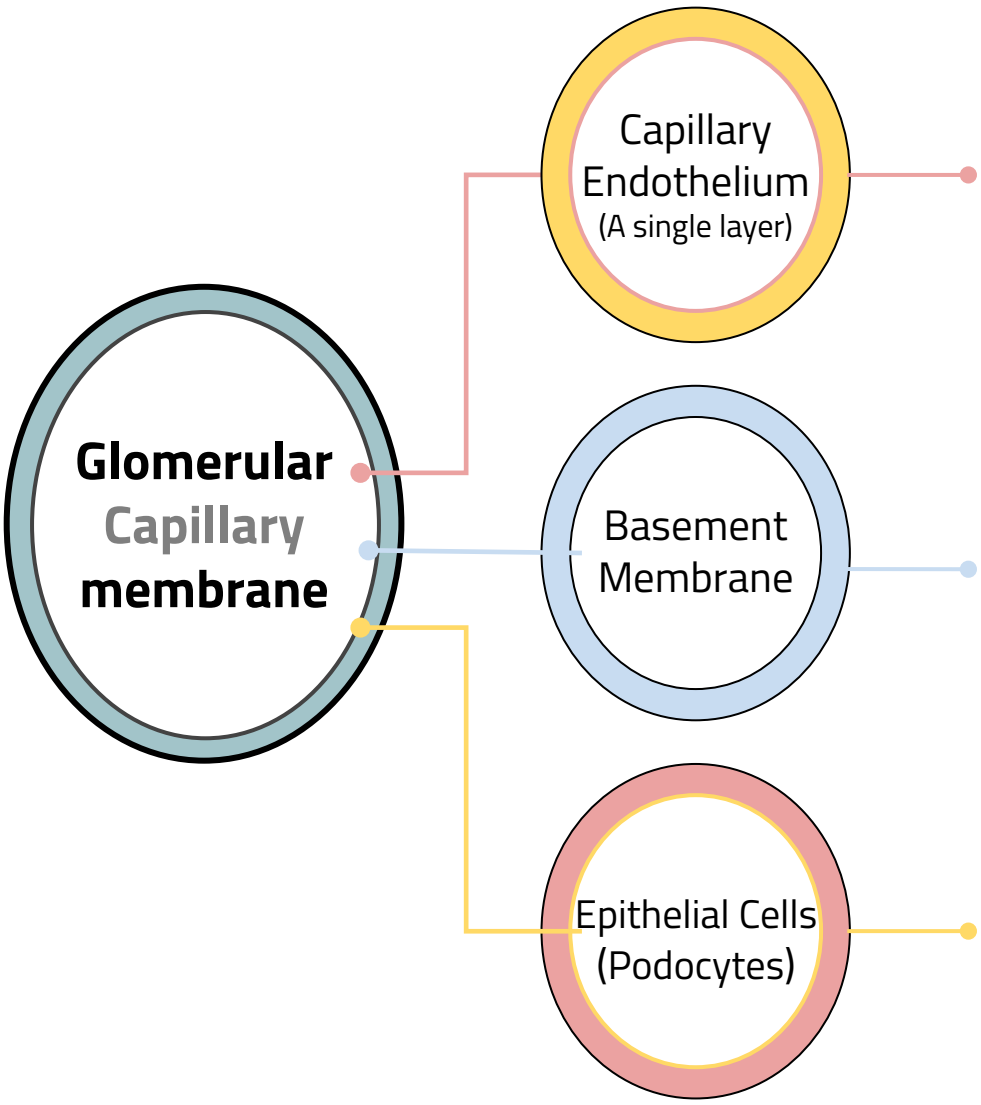
- **Defined as:** The volume of Filtrate produced by both kidneys per minute. It's mentioned in the 2ed Lecture.
- GFR is normally 125 ml/min= 20% renal plasma flow.the other 80% will go to the peritubular capillaries which means back to the blood.
- It's a good index of kidney function (GFR<90 is an indicator of kidney disease).
- (The plasma filtration is occured 60 times in a day for homeostasis)



This device basically **Filters** the blood that passes into the tubules, so it prevents substance like proteins to pass. This device represent the 3 layers of Glomerular capillary membrane. Which will be discussed in the next slide.

Glomerular Membrane

- Blood in the Glomerulus is separated from the fluid in the Bowman's space by a filtration barrier **(Glomerular membrane)** .
- It allow the passage of molecules up to 70,000 D. (Due to the higher pressure)
- **Albumin** does not normally pass as they are repelled by the negative charge of Glycoproteins material of Basement membrane. (So there's a disease called small change disease due to the low of negativity of basement membrane)
- Blood cells **don't** normally pass through the membrane. because of their large size.
- consisting of **Three Layers (all layers are negative in charge) :**



- It has pores that are 70-100 nanometers in diameter, which is relatively big, so it allows fluid, dissolved solutes, and plasma proteins, to filtrate (pass) into the basement membrane..
- Pores aren't large enough for RBCs to pass, but plasma will pass.
- Blood - RBCs = Plasma.

- It lays between the the Endothelium and Epithelium.
- It consist of a small pores that are 8 nanometer in diameter, which prevents the protein passage.
- The molecular diameter of the plasma protein albumin is only about 6 nanometers, **BUt** it still does not pass! As explained above.

- During filtration the fluid moves between their foot processes (psudopodia).
- The epithelial cell layer consists of specialized cells called **podocytes,** which are attached to the basement membrane by **foot processes.** Between the foot processes are **filtration slits,** 25 to 60 nm in diameter.

Filtration Membrane

- It is a Filter that lies between the blood and the interior of the glomerular capsule
- The filtration or the passages through the Glomerular membrane depend on the Charge, if it's -ve it won't pass,+ve will pass and the size if it's Small it passes easily.
- **Composed of Three layers:**

1. **Fenestration** (pore) of glomerular endothelial cells but allows all component of **blood plasma** to pass through.
2. Basal lamina of glomerulus: prevents filtration of larger proteins.
3. **Slit membrane between pedicels**: prevents filtration of medium-sized proteins.

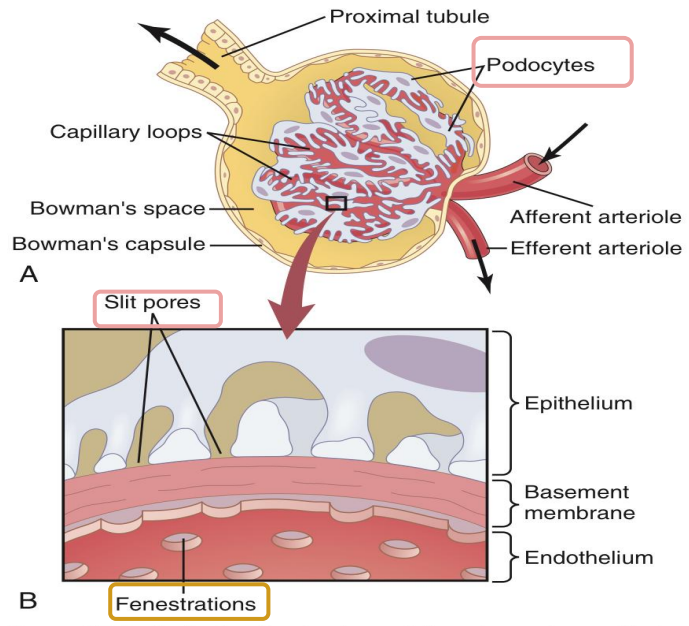


Figure 27-2. A, Basic ultrastructure of the glomerular capillaries. **B,** Cross section of the glomerular capillary membrane and its major components: capillary endothelium, basement membrane, and epithelium (podocytes).

Glomerular Filtration Rate:

GFR is determined by

- The sum of the forces acting across the membrane (starling forces) → **Net filtration pressure (NFP)**
- Factors related to the membrane itself
  - Permeability
  - Filtering surface area

  → **Capillary filtration coefficient (Kf)**

GFR= Kf **x** NFP → 12.5 **x** 10= **125 ml/min.**

Net Filtration Pressure (NFP)

❖ The net filtration pressure represents the sum of the hydrostatic and colloid osmotic forces that either **favor or oppose filtration across the glomerular capillaries.**

	Forces Opposing Filtration (mm Hg)	Forces Favoring Filtration (mm Hg)
Hydrostatic	Bowman's capsule hydrostatic pressure **18** (PB). If it increases ⟹ GFR will Decreases. It can increases in urinary obstruction e.g. stones, tumor. (يحبس السوائل من انها تطلع من الكبسول فيزيد الضغط)	Glomerular hydrostatic pressure **60** (PG). If it increases ⟹ GFR also Increases. (تذكرون الضغط هنا عالي بس الارتريولز وبالإضافة إلى زيادة السوائل بتزيده عشان تزيد الفلتريشن ، لان زي ما نعرف هالقوة تدفع السوائل برا)
Osmotic	Glomerular capillary colloid osmotic pressure **32** (πG). If it increases ⟹ GFR will Decreases. (High due to the proteins since it's not filtered)	Bowman's capsule colloid osmotic pressure **0** (πB). (No protein pass to Bowman's capsule due to their negative charge so it will rise only in pathological conditions)
Net filtration pressure = 60 – 18 – 32 = +10 mm Hg		

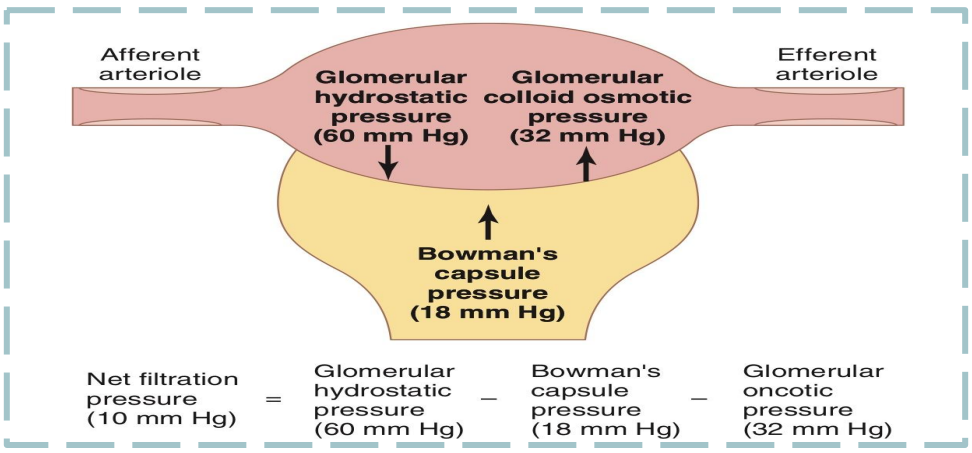
❖ The GFR can therefore be expressed as **GFR= Kf × (PG –PB –πG +πB)**

❖ Any factor that affect the parameters in the equation will affect the GFR.

❖ However, Physiologic regulation of the GFR involves mechanism that affect mainly the PG (hydrostatic pressure in glomerular capillaries).

❖ **PG Depends on:** Arterial BP, Afferent arterioles resistance and Efferent arteriole resistance.

❖ Kf, πG and PB can all get affected in disease conditions causing changes in GFR.



Physiological regulation of GFR

Constriction of Afferent arteriole

↓ Renal Blood flow

↓ PG

↓ GFR

Constriction of Efferent arteriole

Moderate

↓ Renal Blood flow

↓ PG

↑ GFR

It abstract the arteriole completely leading to accumulation of blood in Glomerulus so filtration will increase first and then declining due to Increased FF = proteins

Severe

↓ Renal Blood flow

↓ PG

↓ GFR

Factors that constrict the Afferent:

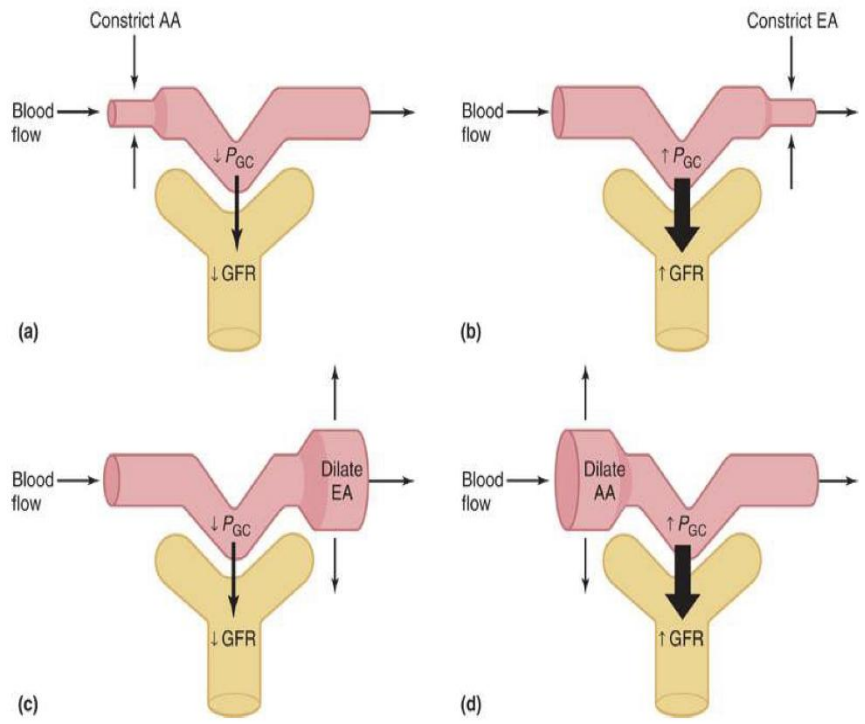
- ❏ Sympathetic stimulation, which will decrease GFR and RBF.
- ❏ Epinephrine
- ❏ Norepinephrine, will decrease GFR and RBF
- ❏ Endothelin
- ❏ (It cosnsrticts the A.arteriole because it has more alpha receptor + explained later)

Other factors affecting Renal blood flow and GFR:

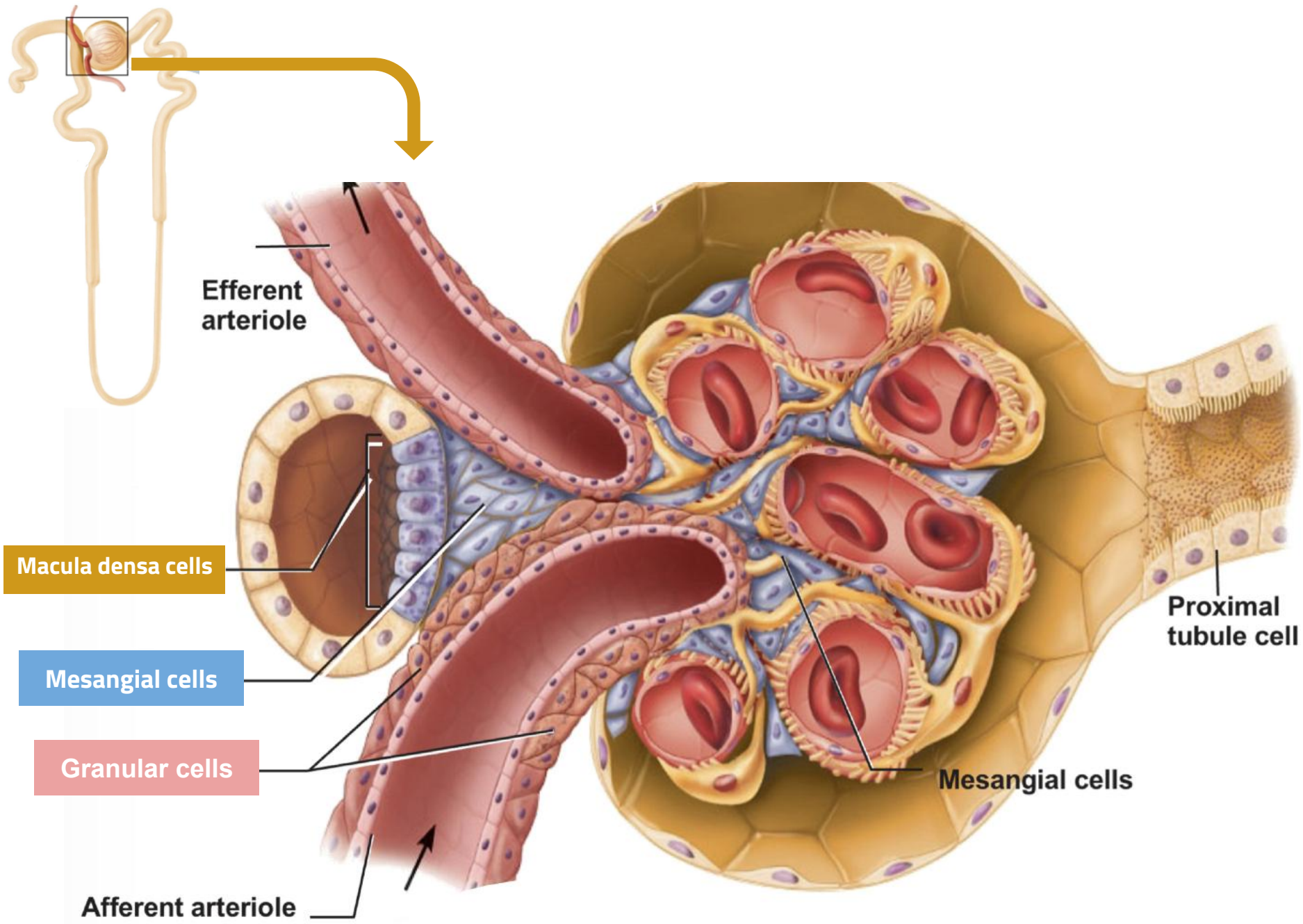
- ❏ High protein diet increases GFR. because πB has increased.
- ❏ Hyperglycemia increases GFR and RBF.
- ❏ Fever increases GFR and RBF.
- ❏ Aging decreases RBF and GFR.

Factors that constrict the Efferent:

- ❏ Angiotensin II,It will constrict Efferent (more sensitive) more than Afferent, and it will decrease RBF.



juxtaglomerular Apparatus (JGA)



Macula densa cells
-Tubular cells
-**Chemoreceptors (Na,K and Cl)**

Granular cells
-Smooth muscles.
-Secrete Renin.
-Mechanoreceptors

Mesangial cells
-Contractile properties.
-Capillary filtration

(it will be discussed in the next lecture)

Summary

- Enumerate general functions of the kidney.
- Synthetic, Excretory, and Regulatory Functions.
- The nephron is the structural and functional unit of the kidney.
- Explain glomerular filtration membrane & filtration forces.
- Filter that lies between the blood and the interior of the glomerular capsule.
- The filtration or the passages through the Glomerular membrane depend on the Charge, if it's -ve it won't pass,+ve will pass and the size if it's Small it passes easily.
- Describe mechanism of filtration & composition of the glomerular filtrate.
- Glomerular filtration,Tubular reabsorption, Tubular secretion and Excretion.
- Composition:
  - **Organic molecules:** Glucose, Amino acids. (but not proteins)
  - **Nitrogenous waste:** Urea, Uric acid, Creatinine.
  - **Ions:** Sodium, Potassium, Chloride.
  - **Water.**
- Calculate the net filtration pressure using parameters of Starling forces.
- Net filtration pressure = 60 – 18 – 32 = +10 mm Hg

Click here to see Dr.Manan notes as a summary of the lecture

MCQ & SAQ

Q1: Bundles of Collecting tubules

A. Medulla
B. Cortex
C. Pyramids
D. Renal Pelvis

Q2: Delivers blood from glomeruli to peritubular capillaries

A. Afferent Arteriole
B. Efferent Arteriole
C. Vasa Recta
D. Loop of Henle

Q3: Originates in the Inner ⅓ of cortex

A. Juxtamedullary nephrons
B. Loop of henle
C. Collecting Tubule
D. Cortical Nephrons

Q4: If there is a moderat constriction of the efferent arteriole, which of the following will occur?
A. Decrease in GFR
B. Decrease in PG
C. Increase in renal blood flow
D. Decrease in renal blood flow

Q5: The PG depends on:

A. Arterial BP
B. Afferent arterioles resistance
C. Efferent arteriole resistance
D. all of the above.

Q6: Which of the following can't pass the gumelur capillary?

A. NA+
B. K+
C. Amino acids
D. Proteins

answer key:
1: C
2: B
3: A
4: D
5: D
6: D

1- Name some substances synthesized by the Kidney

2- What are the two capillary beds found in Renal Circulation

3- What are the steps for urine formation?

4- What is GFR determined by?

A1: Glucose (Gluconeogenesis), Erythropoietin, 1,25-dihydroxy Vitamin D (calcitriol), Renin

A2: Glomerular & Peritubular

A3: Glomerular filtration,Tubular reabsorption, Tubular secretion and Excretion.

A4: Net filtration pressure (NFP), Capillary filtration coefficient (Kf)

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