PHYSIO

MODIFIED NO.3

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Welcome to the 3rd physiology lecture

This lecture is very important for understanding how our kidney function

You will enjoy it, say بسم الله and let's start

Color code

- Slides
- Doctor
- Additional info
- Important

Renal Physiology Lect-3
Guyton chapter 28

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Control of GFR and renal blood flow

- Neurohumoral
- Local (Intrinsic)

- We've talked about the main functions of the UG system and also we talked about the histology of the filtration membrane
- Also, filtration function is very important for the function of the kidney in forming urine and if anything went wrong with the filtration function For example, loss of the negative charges of the basement membrane or loss of podocytes, this leads to leakage of proteins to the urine.

- one of the early signs is microalbuminuria, it is when albumin is excreted in the urine between 30 and 150 mg/ day.

•This is very important for early detection , it’s an early sign for renal diseases specially for DM pt. & hypertension, patients with glomelular hyper filtration.

•These patients may progress into more progressive form of the renal disease. They may come later, having proteinuria (more excretion of albumin).

Microalbuminuria

- Definition: urine excretion of > 30 but < 150 mg albumin per day

- Causes: early diabetes, hypertension, glomerular hyperfiltration

Prognostic Value: diabetic patients with microalbuminuria are 10-20 fold more likely to develop persistent proteinuria

Clinical Significance of Detection of Proteinuria

- Early detection of renal disease in at-risk patients
  - hypertension: hypertensive renal disease
  - diabetes: diabetic nephropathy
  - pregnancy: gestational proteinuric hypertension (pre-eclampsia)
  - annual "check-up": renal disease can be silent
- Assessment and monitoring of known renal disease

- Also it is important during pregnancy if she have preeclampsia or before it proteinuria or Albuminuria

Glomerular Filtration

GFR = 125 ml/min = 180 liters/day

- Plasma volume is filtered 60 times per day
- Glomerular filtrate composition is about the same as plasma, except for large proteins
- Filtration fraction (GFR / Renal Plasma Flow) = 0.2 (i.e. 20% of plasma is filtered)

- we will discuss glomerular filtration function and what determines it (GFR = filtration rate)

- As we said, rate of filtration is 180 L/day => don't panic, yes we have 3L in our body but how they become 180L? By being filtered 60 times (سبحان الله العظيم) ،why??

  1- To remove wastes efficiently
  2- For regulation & monitoring of plasma all the time (faster response to changes)

- filtration rate of kidney **is higher** than other organs filtration rate => why this?

  1- high hydrostatic pressure
  2- special filtration membranes with high filterability (fenestrations)
  3- high renal plasma flow (20% of Cardiac Output)

- If we look at kidney mass, it receives blood amounts that are higher than it should be (this isn't because of its metabolic demand but for its function, recall RS physio)

- Glomerular filtrate composition is about the same as plasma except for large plasma proteins **mainly albumin** ,which is the major protein of plasma, **because** of the structure of the filtration membrane, barriers, the charge, pore size & the slits

- There's **almost a constant fraction** of filtration:
  Filtration fraction= GFR/ (renal plasma flow) = 20% of plasma filtered

Just before starting a new topic, let's remember the types of pressure:

Hydrostatic => exerted by the fluids

Oncotic (colloid) => exerted by proteins

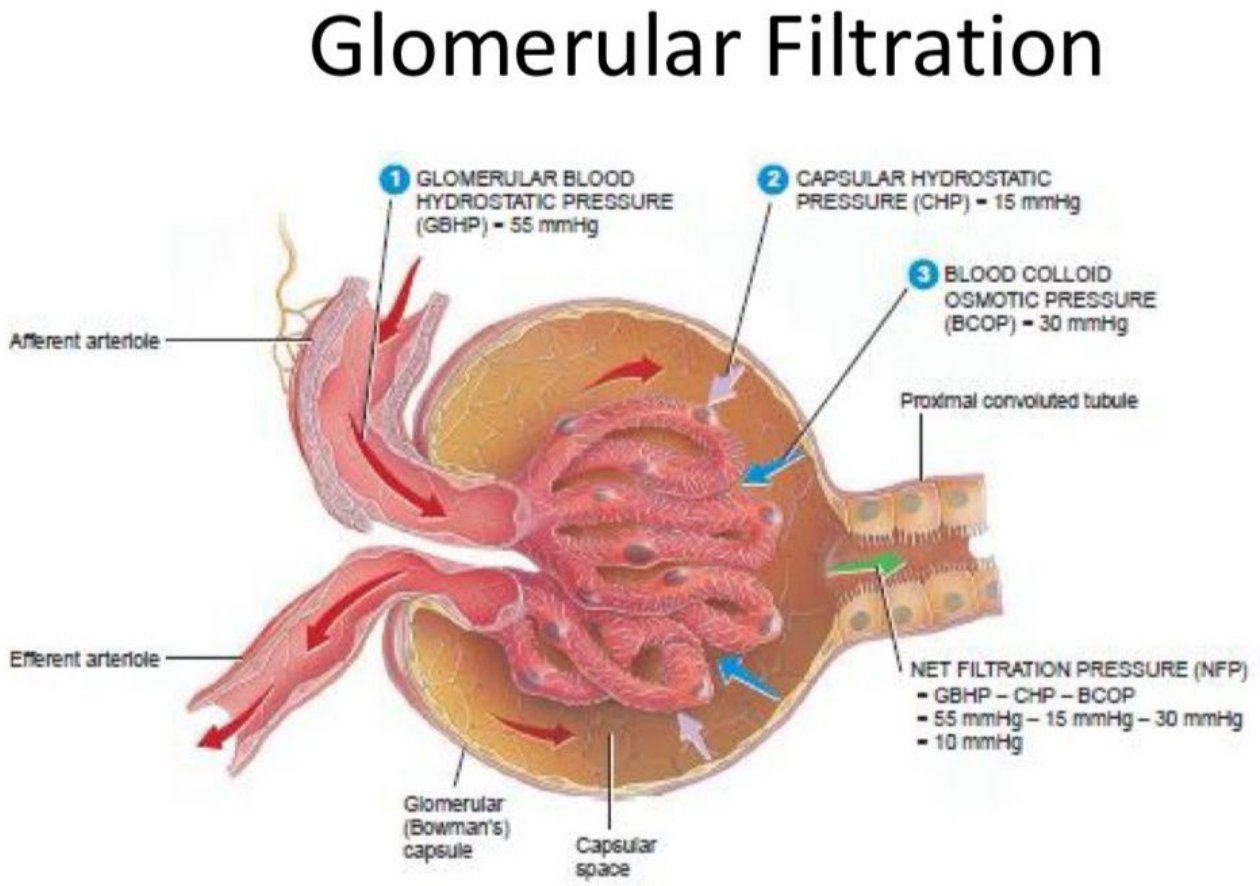
- let's start discussing the determinants of filtration:

=> look here, blood comes from renal artery (with certain hydrostatic pressure- which is originated from the pumping of the heart)

From renal artery to the **afferent arterioles** where pressure value decreases **(55 / 60 mmHg)**

=> this pressure will be exerted on the wall of the glomeruli (which is high for the capillaries in kidney)

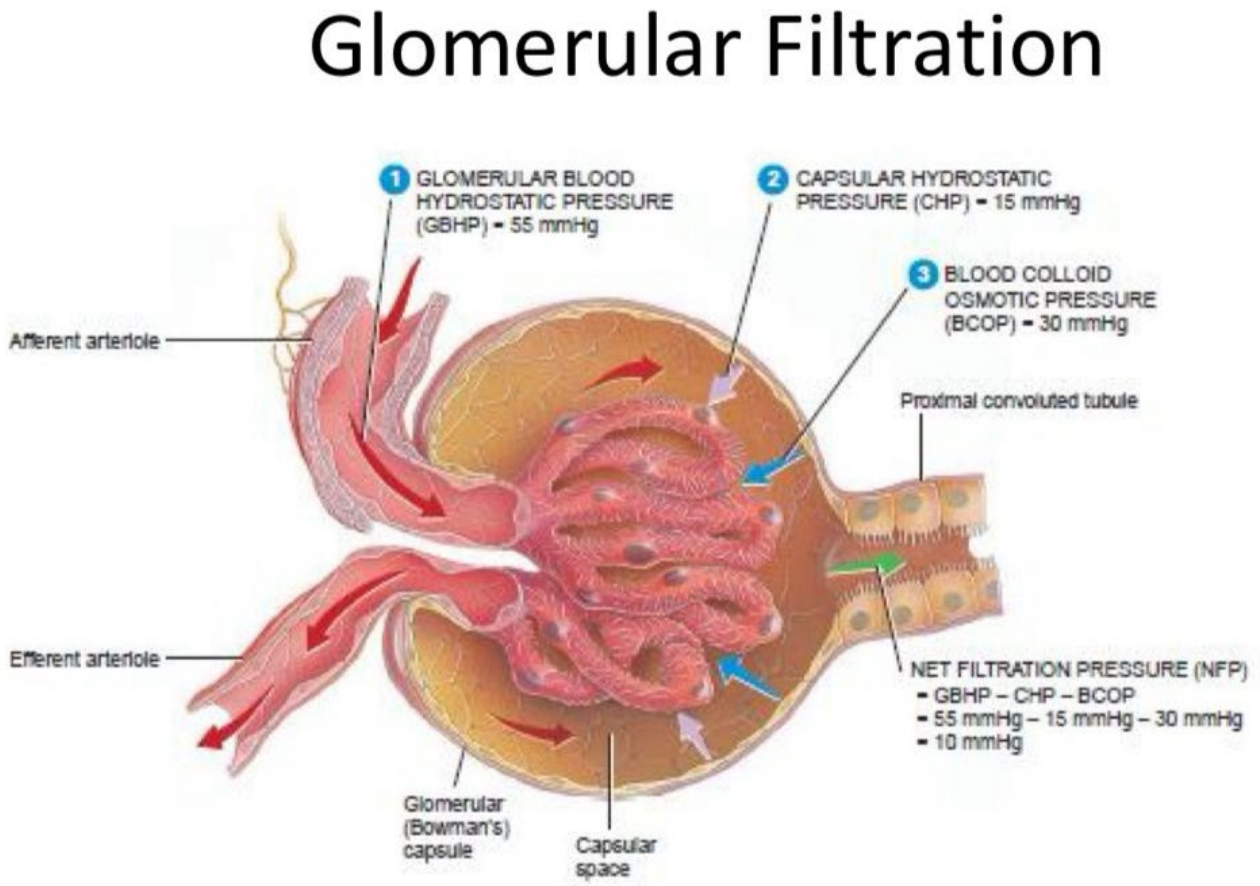
This pressure will push fluids outside the capillaries through the pores to the Bowman's capsule

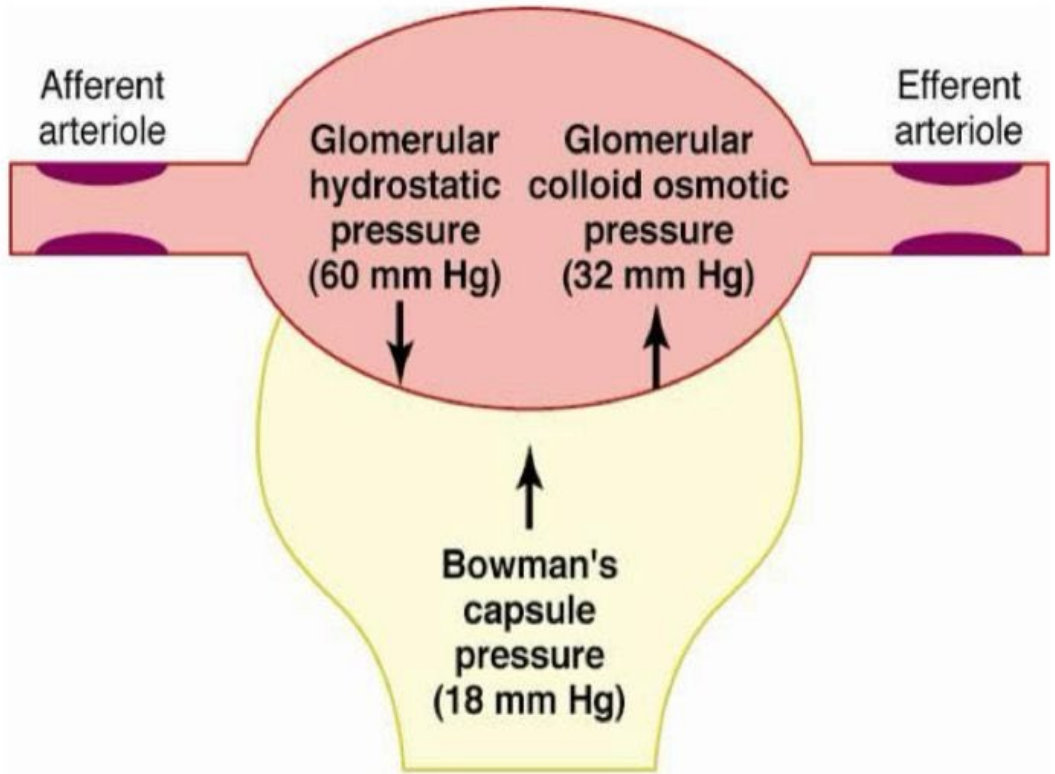


The fluid in the capsular space will also exert pressure on the walls but this is against filtration (**15/18 mmHg**)

=> there's another type of pressure: **colloid pressure (oncotic pressure)** due to filtration of fluids leaving proteins in the glomeruli, so that will Build up the oncotic pressure pulling fluids **inside the glomeruli against filtration** (**30/32mm Hg**)

=> **oncotic colloid pressure inside bowman capsule** is negligible when compared with the oncotic pressure in glomeruli (**0 mmHg**)





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)

+ colloid capsular pressure (0)

Figure 26-13

=> so we have to calculate the Net. Filtration pressure, there are 2 ways:

1- we sum the pressures that favor outward movement of fluid - pressures that favor inward movement of the fluid)

Net. Filtration= (Hydrostatic glomerular P.+ Bowman oncotic P.)-(capsular hydrostatic P. + glomerular oncotic P.)

= (60 + 0) - (18 +32) = 10 mmHg (toward filtration, capillary --> bowman's capsule)

2- we say net. Filtration is (anything favoring filtration is positive, anything opposite to that is negative and then sum all of them)

Net. filtration = +55 –15 –30 = +10 (toward filtration).

These 10mmHg are the driving forces for fluids to be filtered (filtration is directly proportional to it, meaning if this net. Filtration pressure increased the filtered fluid will increase and so on).

=> so the balance of the hemodynamics forces to give us net. Filtration pressure is very important to have glomerular filtration.

Glomerular Filtration Rate (GFR)

- **Filtration Fraction (FF)= Fraction** of blood plasma in the afferent arterioles that becomes filtrate= 16-20%.
- **GFR** =The volume (ml) of fluid filtered through all the corpuscles of both kidneys per minute.
- The volume of fluid filtered daily through all the corpuscles of both kidneys per day = 180 L
- **Hence, GFR**= 180 L/24hours * (1000 ml/ L)*(1hour/60 min)= **125 ml/min (Males)**
- For 125ml/min; renal plasma flow = 625ml/min

FF * PF=GFR, PF= 125/(20%)=625 ml/min

- 55% of blood is plasma, so blood flow = 1140ml/min

55% * BF= PF; BF= 625ml/min/ (55%)=1140 ml/min

- Renal Blood Flow of 1140 ml/min = (22.8 % of 5 liters) is required to have GFR of 125ml/min.

- GFR could vary based on age, hight, gender ,etc.

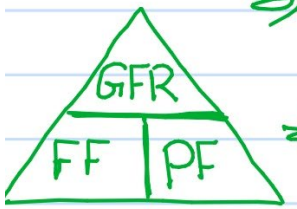
Kindly check the image here then read the box

Now the value we have calculated the **plasma** flow but to calculate **blood flow** we have to remember this note :
Plasma form 55% of the blood so if I want the renal blood flow :

PF = 55% x **BF** => **BF**= **PF**/ 55% = 625/55% =1140 ml/min

Now if we say => BF/BV (BV:blood volume) = 1140/Bv = 20% of CO

Kidney receive 20% of CO to achieve normal GFR & this percentage is considered high but why it take it ? Because it is a requirement to have normal GFR



⇒ FF is constant = 20%

⇒ GFR normally = 125 mL/min

⇒ So, we can calculate plasma flow

⇒ $PF^{*} = \frac{125}{20\%} = 625 mL/min$

⇒ then how much blood reach the kidney from Cardiac output (CO)

⇒ $\frac{625}{CO} = 20\%$

!! so 20% of Cardic output should go to the kidneys

* keep in mind here plasma Not Blood

Regulation of Glomerular Filtration

- Homeostasis of body fluids requires constant GFR by kidneys.
- If the GFR is too high, needed substances cannot be reabsorbed quickly enough and are lost in the urine.
- If the GFR is too low -everything is reabsorbed, including wastes that are normally disposed of.

Did you ask yourself **why all the body homeostasis depends on normal GFR**??

1 => because this filtration function affects the composition and the volume of our fluids
If GFR is **high** => a great amount of the needed substances will be filtered (including H2O) & **kidney will not be able to preserve them**

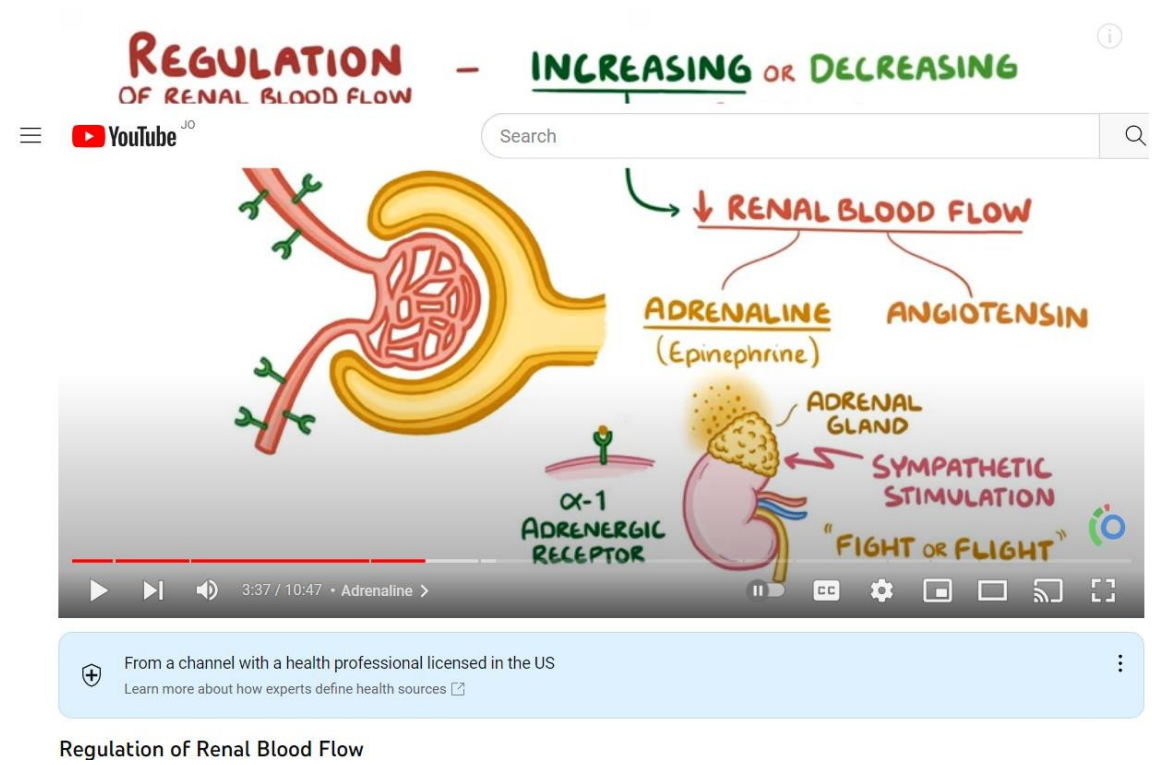
=> this loss leads to imbalance in homeostasis of fluids and electrolytes
& kidney will not be able to reabsorb due to high filtration

2 => if GFR is **low**, wastes will stay for a longer time in our body and **will not be efficiently eliminated** & **more reabsorption of some wastes** due to low GFR

So, we don't want GFR to be neither lower or higher than normal.

Audio-visual Aid

[Regulation of Renal Blood Flow - YouTube]



- The first determinant of GFR is : **Net filtration pressure**
- There is a **direct relationship** between GFR & Net Filt. Pressure
- **GFR = Net filtration pressure X Kf (constant)**
- Kf : coefficient of filtration
- It is hard to calculate Kf from its formula (Kf = hydrolytic pressure X surface area) , so by knowing the **GFR and the Net filt. Pressure, we can calculate Kf from the above formula**
- Kf in kidneys = **12.5 ml / min per mmHg .**

To accurately compare the filtration coefficient (Kf) of kidneys with other organs of varying weights, values are normalized per 100 grams of tissue.
The Kf in classical capillary beds and tissues is approximately 0.01 per 100 g, whereas the Kf of the kidneys is about 4.2 per 100 g — making it roughly 400 times greater

- and this maybe due to:
- 1. **the characteristics of the filtration membrane (surface area and permeability)**
- 2. **Net filtration forces**
- 3. **the high renal blood flow that comes to the tissues.**
- **Kf can't be a physiological regulator that the body can use to fix GFR (it's not variable)**
- But it can be changed in pathological conditions , for example : thickening of the basement membrane or damage to the capillaries (reducing the surface area) **this can reduce GFR** (but only in pathological conditions) .
- These pathological conditions might occur in diabetes, hypertension or glomerulonephritis.

Determinants of Glomerular Filtration Rate

Normal Values:

GFR = 125 ml/min

Net Filt. Press = 10 mmHg

K_f = 12.5 ml/min per mmHg, or 4.2 ml/min per mmHg/ 100gm

(400 x greater than in many tissues)

Glomerular Capillary Filtration Coefficient (K_f)

- K_f = hydraulic conductivity x surface area
  - Kf can't be directly measured through this formula

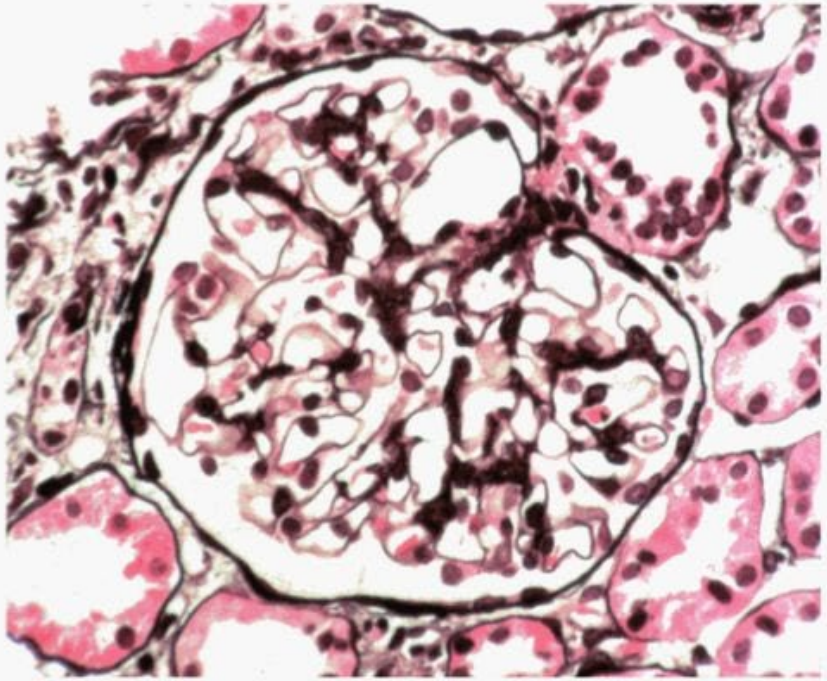
K_f = GFR/net filt pressure

- Normally not highly variable
- Disease that can reduce K_f and GFR
- Damage of capillaries, Basement Membrane thickens,
  - chronic hypertension
  - obesity / diabetes mellitus
  - glomerulonephritis

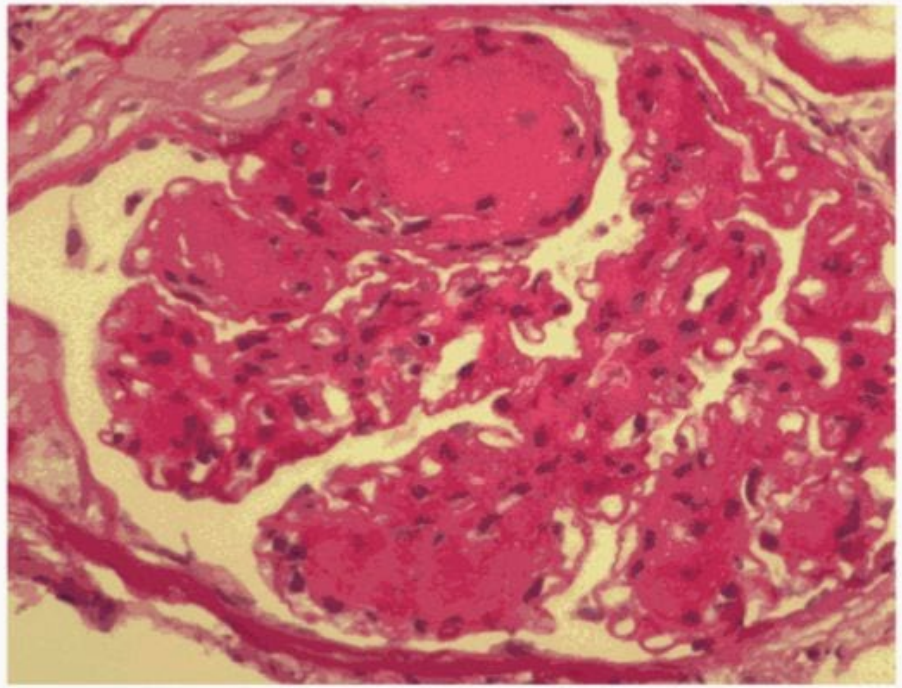
Glomerular Injury in Chronic Diabetes

- This is an example on how filtration membrane can change in diabetes

Normal glomerulus



Diabetic nephropathy



- **Bowman's capsule hydrostatic pressure**
- **It depends on GFR , so it <u>can't</u> be a physiological regulator for GFR**
- As for Kf , bowman's capsule hydrostatic pressure may change in **pathological conditions,** like any obstruction in the tubules (due to stones or tumors for example) this will lead to **accumulation of fluids in bowman's capsule leading to an increase in bowman's capsule hydrostatic pressure** >> reduced Net filtration pressure >> reduced GFR.
- So it can affect GFR only in pathological conditions and not physiologically (because actually it depends on GFR)

Bowman's Capsule hydrostatic Pressure (P_B)

- Normally changes as a function of GFR, not a physiological regulator of GFR
- Increases with Tubular Obstruction
  kidney stones
  tubular necrosis
  Reducing GFR

- Urinary tract obstruction
  Prostate hypertrophy/cancer

- **Glomerular capillary oncotic pressure**
- Factors affecting oncotic pressure:

1. **Arterial oncotic pressure** (oncotic pressure depends on **Albumin** which is originally from The arterial circulation)
2. **Oncotic pressure will build up as long as we go from the afferent end of the glomeruli to the efferent end** (more filtration more build up of proteins in the glomeruli)

- Remember FF = GFR/ RPF
- **So FF increases if GFR has increased or RPF has decreased**
- FF affects the oncotic pressure, as **FF increases > oncotic pressure increases**
- Oncotic pressure **can't** be a physiological regulator of GFR
- It depends on GFR , like bowman's capsule hydrostatic pressure

Factors Influencing Glomerular Capillary Oncotic Pressure (Π_G)

- Arterial Plasma Oncotic Pressure (π_A)

$\uparrow \pi_A \longrightarrow \uparrow \pi_G$

- Filtration Fraction (FF)

$\uparrow$ FF $\longrightarrow$ $\uparrow \pi_G$

FF = GFR / Renal plasma flow

= 125 / 650 ~ 0.2 (or 20%)

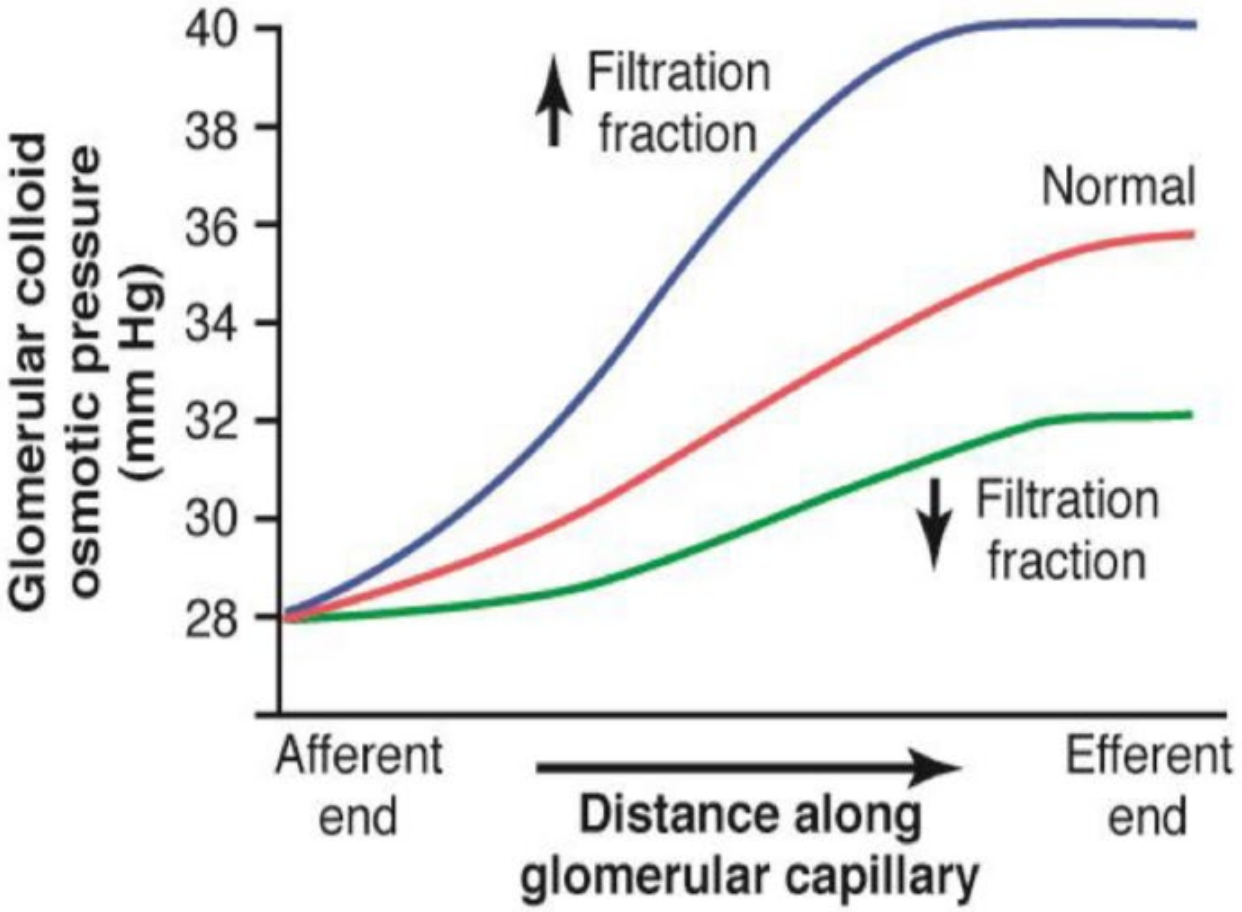
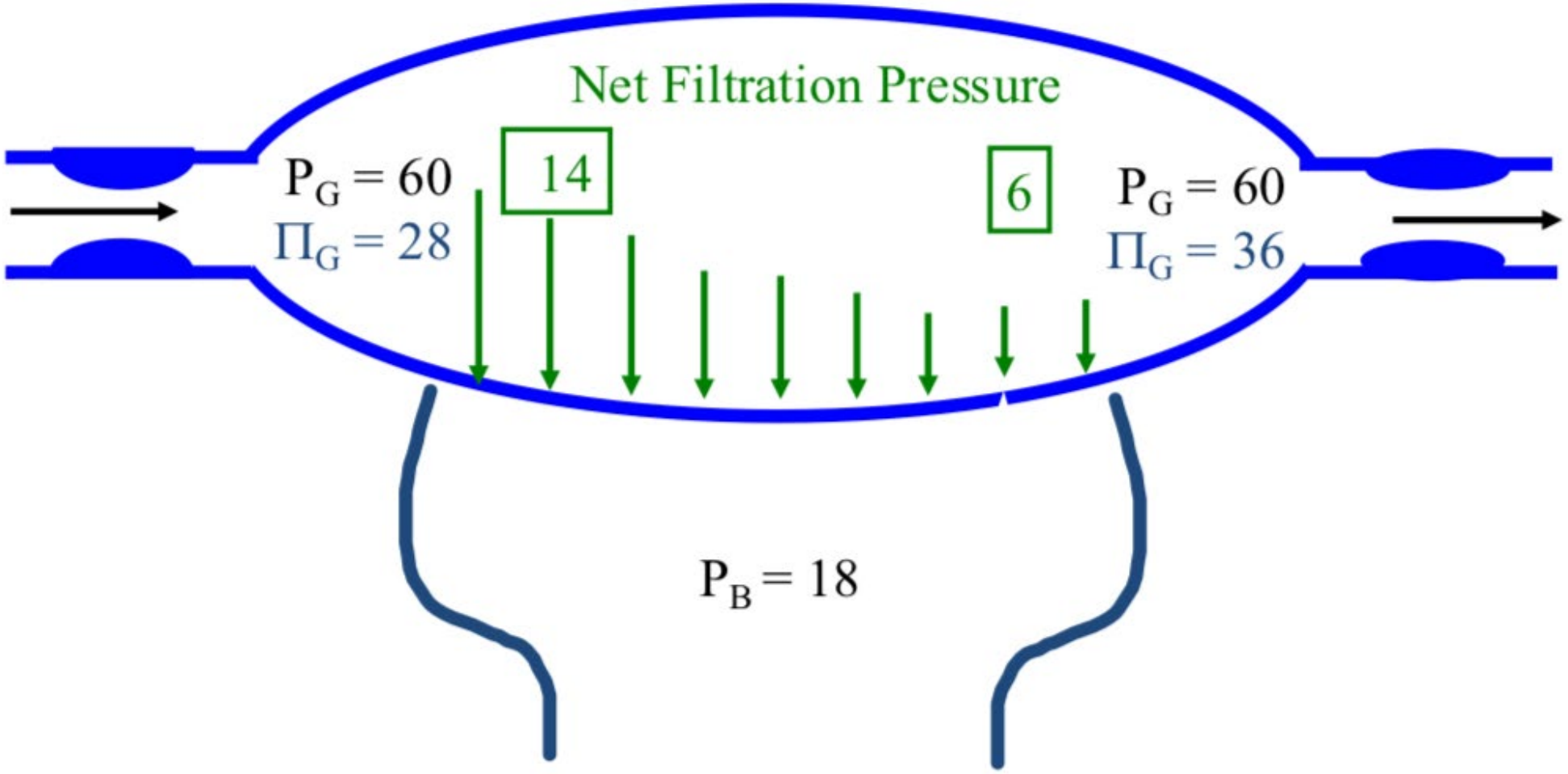


Figure 26-14

- The red curve represents the **normal FF** , oncotic pressure increases as we move from the afferent end to the efferent end (more fluid has been filtered in the efferent end > more build up of the proteins > higher oncotic pressure)
- **If FF is higher than normal (** blue curve) , the curve will be shifted **upward** (higher FF > higher oncotic pressure, plasma proteins got more concentrated)
- **If FF is less than normal** (green curve) , the curve will be shifted **downward** (when does FF decrease? Remember the golden rule, FF= GFR/ RPF , so FF decreases if GFR decreases or RPF increases

- Glomerular hydrostatic pressure **PG doesn't change in both ends** , it remains constant along the length of glomerular capillarie , however, the **oncotic pressure increases** , since PG is constant and the oncotic pressure increases, **The Net filtration pressure will decrease** along the length of the capillary

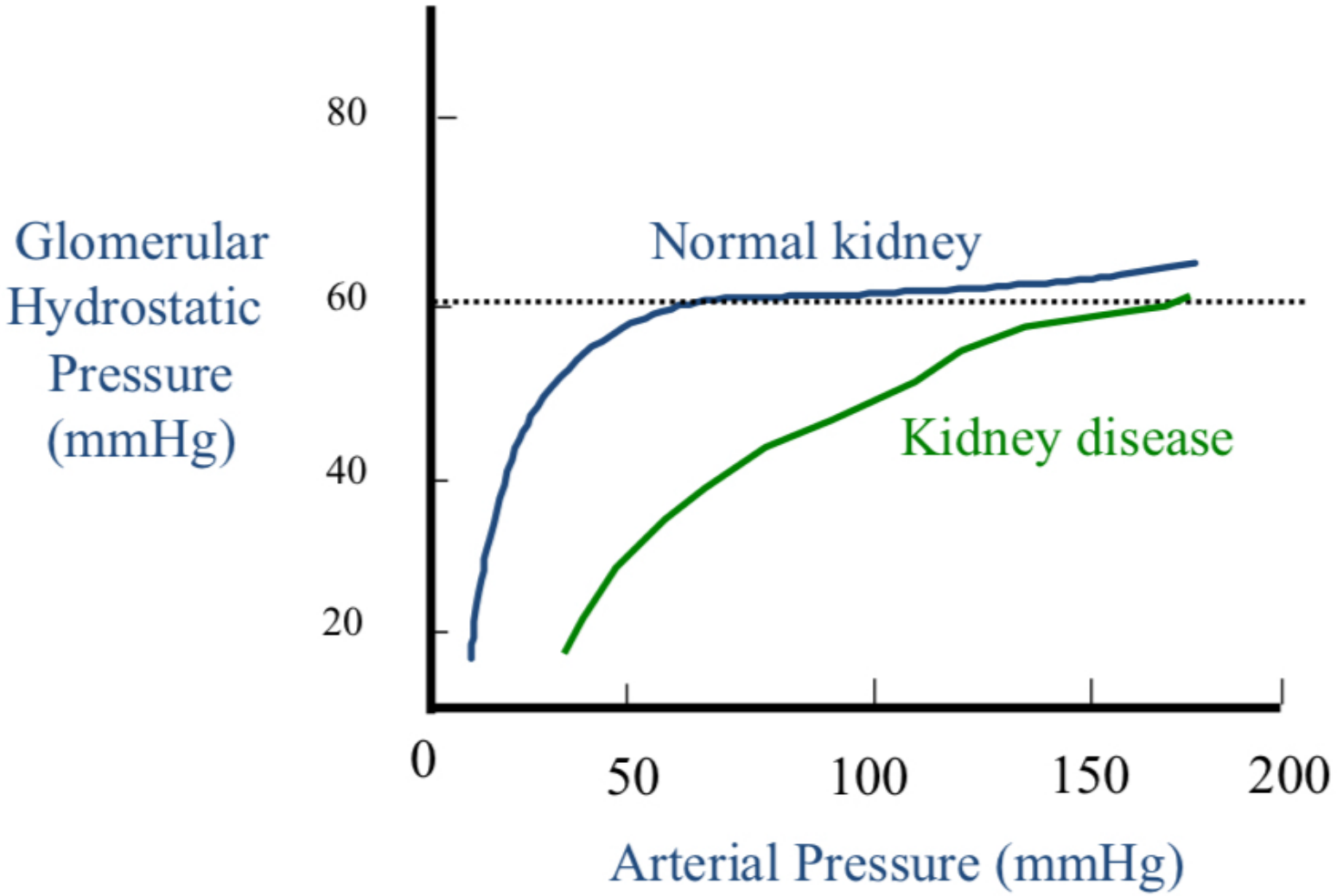


- **Glomerular hydrostatic pressure PG**
- Factors affecting pG : **Mean arterial blood pressure**
- Logically we expect that as blood pressure increases PG increases, however it's was found that **when the blood pressure is between 60 mmHg to 140 mmHg , the PG was nearly constant (platu) , and this due to an auto regulation process in the kidney to resist changes in pressure inside the glomerular capillaries**
- The direct relationship between blood pressure and PG is only true for extreme changes in pressure (lower than 60 mmHg or higher than 140 mmHg) , but in between its buffered by the auto regulation process .
- The auto regulation process is an intrinsic regulation done by the kidney to stabilize PG , so that **changes that affect arterial pressure will not affect GFR .**

Glomerular Hydrostatic Pressure (P_G)

- Is the determinant of GFR most subject to physiological control

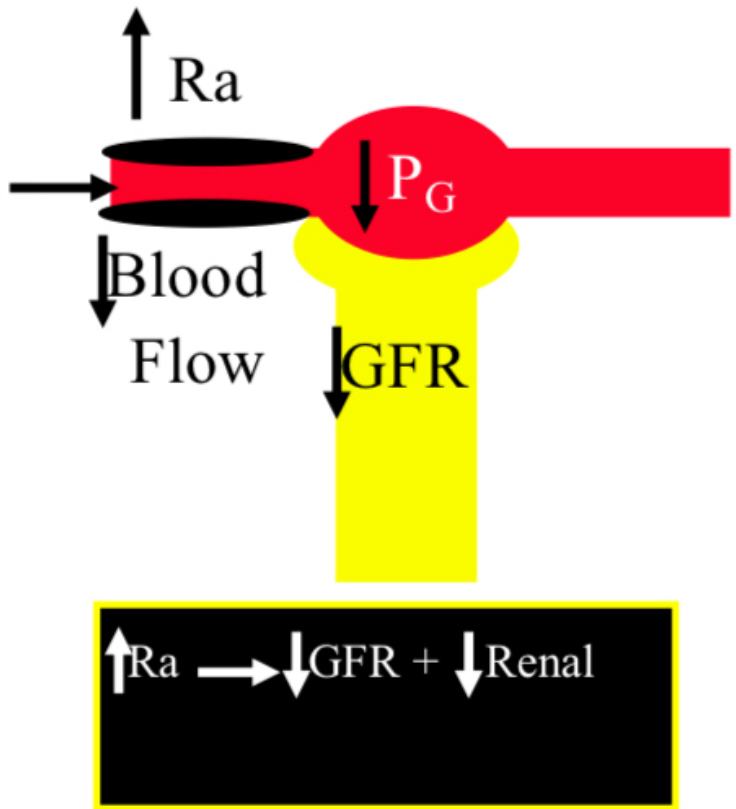
- Factors that influence P_G
  - arterial pressure (effect is buffered by autoregulation)
  - afferent arteriolar resistance
  - efferent arteriolar resistance

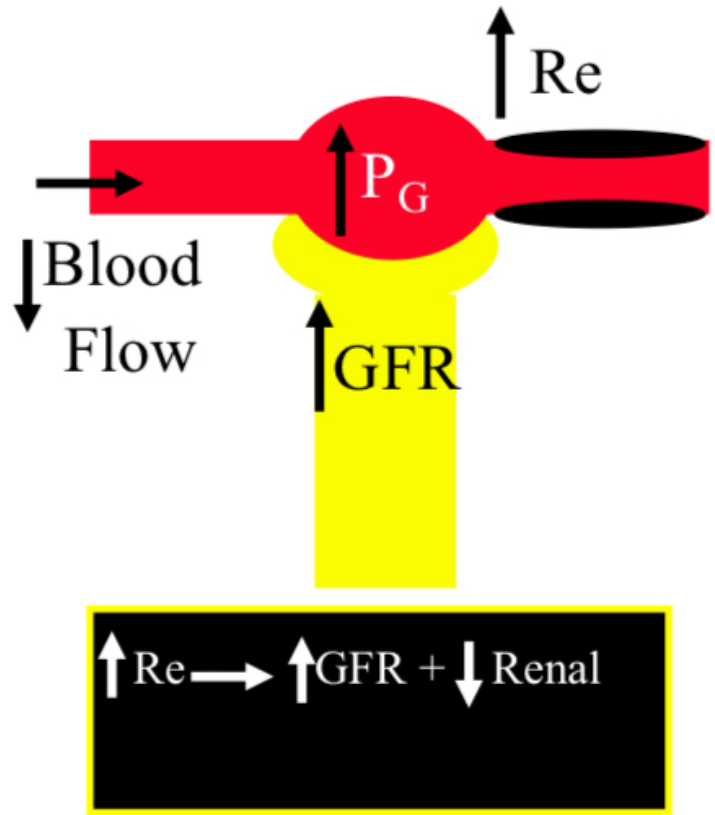


- People with kidney disease don't have an intact auto regulation process, so their PG depends on Arterial pressure , any change in BP will affect PG

- **How does the Resistance in afferent and efferent arterioles affect PG ?**
- If the resistance of **AFFERENT** arteriole has increased the **Renal blood flow inside the glomerulus will be decreased , PG will be decreased** (less blood is flowing inside glomerulus) , **GFR will be decreased**
- If the resistance of **EFFERENT** arteriole has increased , **PG will be increased , renal blood flow will be decreased**
- Renal blood flow is decreased in both cases
- The kidney has the capability in adjusting afferent and efferent resistances , thus adjusting GFR .
- This is the way that our kidney uses in order to fix GFR ," by adjusting the resistances "

Effect of afferent and efferent arteriolar constriction on glomerular pressure





- Notice that when the arterial blood pressure is between 60-140 > platu in both GFR and RBF
- However , if we look at the urine output in the second figure, there is no platu nor auto regulation , which means that as the pressure increases the urine output increases.
- Auto regulation is only to stabilize the filtration process.
- The urine output increased because of the way our body deals with high blood pressure using RAAS, on the reabsorption spicefically (we will discuss later)

Autoregulation of renal blood flow and GFR but not urine flow

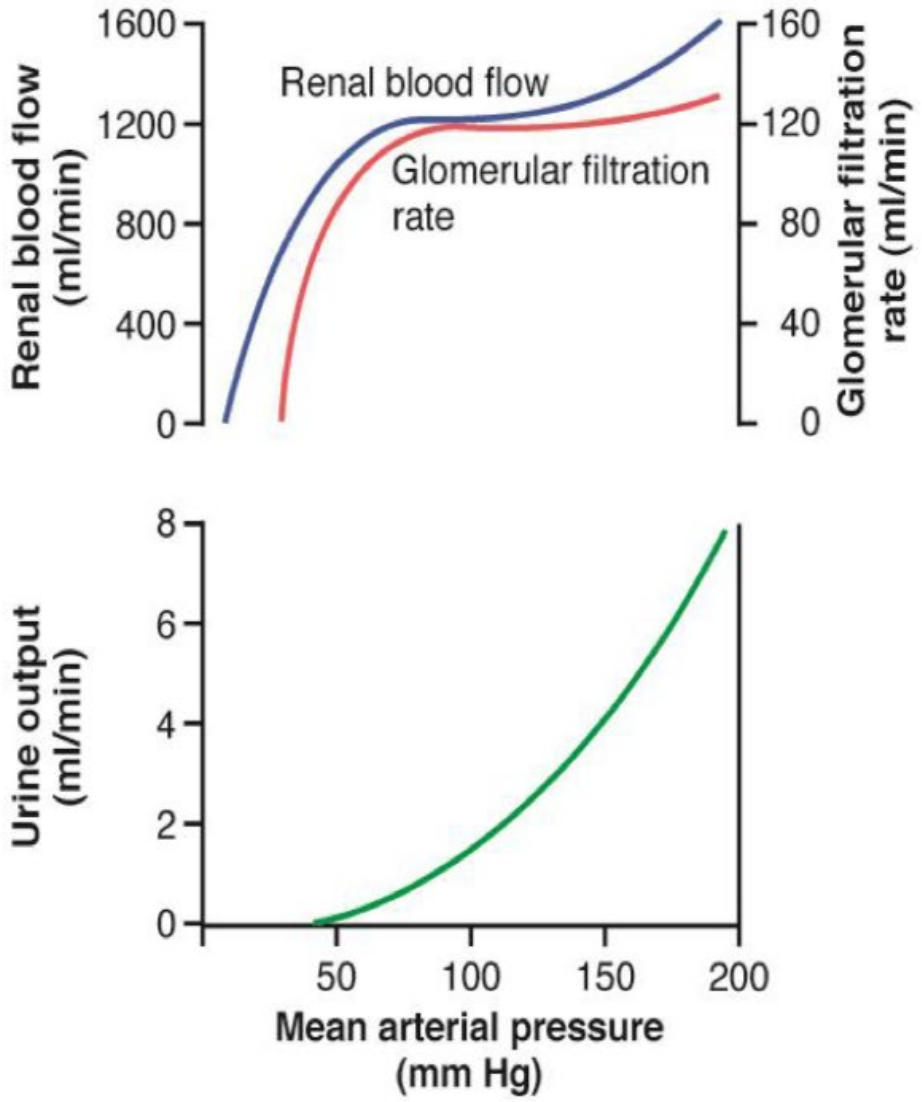


Figure 26-16

Additional sources

1. Book pages
2. Youtube videos
3. Webpages...etc

آية أو حديث شريف دعاء أو نصيحة

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اترك أثر جميل للقارئ

VERSIONS	SLIDE #	BEFORE CORRECTION	AFTER CORRECTION
V1→ V2	26/28	RBF (renal blood flow)	RPF (renal plasma flow)
V2→V3			

امسح الرمز و شاركنا بأفكارك لتحسين أدائنا !!