UGS

Physiology

Doctor 2021

Sheet (3)

Name: Tasneem Alremawi

Corrector:

Doctor: Ebaa Alzayadneh

بِسْمِ ٱللَّهِ ٱلرَّحْمَٰنِ ٱلرَّحِيمِ بِسْمِ ٱللَّهِ ٱلرَّحْمَٰنِ ٱلرَّحِيمِ

Regulation of Glomerular Filtration

- **Homeostasis of body fluids** and electrolytes level **require 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.** It could be from low and inefficient elimination or very high absorption, higher than the filtration.

Please watch this video demonstrating mechanisms of renal regulation for this lec and the following one:
https://www.youtube.com/watch?v=dFnLbgPjiUw

Determinants of Glomerular Filtration Rate

Normal Values:

- **GFR = 125 ml/min**
  (Although there are some differences in the value between individuals e.g. gender, BMI, age..., but for now we will only use this number.)
- **Net Filtration Pressure = 10 mmHg**
  (The pressure needed to have 125ml/min filtration.)

  The relationship between glomerular filtration rate and the net filtration pressure is **DIRECT** and **CONSTANT**, if we increase the net filtration pressure, the glomerular filtration rate will increase and vice versa. And if we divide the GFR over the net filtration pressure the result will ba a constant (**filtration coefficient** or **Kf**), which also have in different capillary bed systems in different tissues with different values.
- **Kf = 12.5 ml/min per mmHg** (for the two kidneys ≈300mg), **or 4.2 ml/min per mmHg/ 100gm** (we use to compare it with other tissues (unify the weight unite)) **(400 x greater than in many tissues** e.g. .01 ml/min per mmHg/ 100gm).

Kidneys have a high filtration coefficient that serves the function of filtering the blood.

Glmeuli in the two kidneys have membrane hydrolic conductivity

Glomerular Capillary, Filtration Coefficient (Kf)

• **Kf =** membrane **hydraulic conductivity x surface area** of all glomeruli in the kidneys, but it is impossible to do that, so we use the next equation to calculate Kf:

- **Kf = GFR/net filtration pressure**

• **Normally <u>not</u> highly variable** (not changing from day to day for the same person).

• **Disease that can reduce Kf and GFR:**

- Damage of capillaries (loss of surface area for the filtration process)

- Basement Membrane thickens (by deposition of matrix proteins for example which decreases the hydraulic conductivity)

- Chronic hypertension

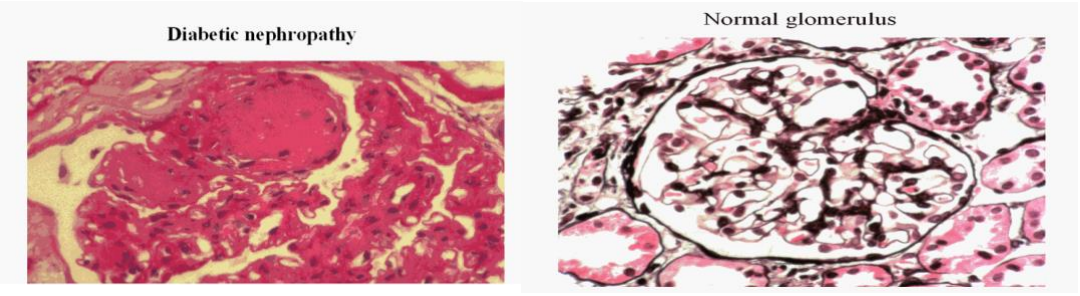
- Obesity / diabetes mellitus (in late diabetic nephropathy)

- Glomerulonephritis

The relationship between the Kf and GFS is direct; factors that reduce Kf (pathological), will cause GFR to be reduced too.

The kidney has physiological regulators or tools that it uses to keep the GFR constant, and they should be changeable to do this job. Kf is NOT one of them because it is constant in normal humans and can only change in diseases.

Glomerular Injury in Chronic Diabetes:



Bowman's Capsule hydrostatic Pressure (PB)

In the last lec we said that the bowman's capsule hydrostatic pressure is related negatively to the filtration,

- **Normally changes as a function of GFR** (happens as a consequence after the filtration), **not a physiological regulator of GFR** منطق .

If the GFR was high, the PB will be high, and if the GFR was low, the PB will be low منطق برضو .

- **PB increases with Tubular Obstruction** (In pathological cases, because the urine flow decreases and it will accumulate in bowman's capsule)
    - **Kidney stones** or tumers
    - **Tubular necrosis** or calcification
    - **Urinary tract obstruction**
    - **Prostate hypertrophy/cancer**

- Increasing PB (more than 15) ⟶ **Reduces GFR.**

Factors Influencing Glomerular Capillary Oncotic Pressure (πG):

- **Arterial Plasma Oncotic Pressure (πA)**

    ↑ πA ⟶ ↑ πG

The blood in the glomerulus originally came from the arterial blood, so the oncotic arterial pressure reflects the glomerular capillary oncotic pressure. The arterial oncotic pressure cannot be modulated by the body, so it is not a physiological regulator of GFR.

- **Filtration Fraction (FF)**

    ↑FF ⟶ ↑ πG

FF = GFR / Renal plasma flow

= 125 / 650 ~ 0.2 (or 20%)

We said before that the filtration fraction in the body is constant, however here we said that the afferent end has a higher net filtration pressure and the efferent end has a lower net filtration pressure. How is that?

FF = GFR / Renal plasma flow, from this relationship we can say that the FF can increase when the GFR increases or when the renal plasma flow decreases.

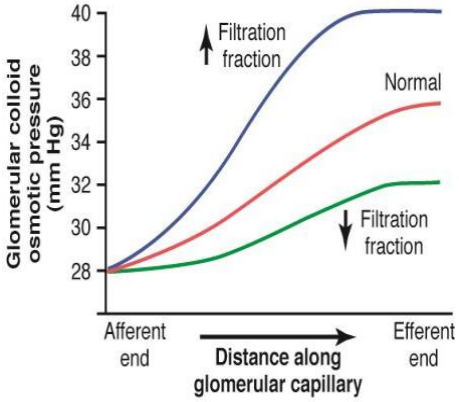
بالمنطق If the FF increased (more than 20%), more fluid would come out of the glomerulus and the oncotic pressure will increase (proteins will be more concentrated), direct relationship.

♛ If there have been an <u>initial</u> **increase in the GFR**, how would that affect oncotic pressure?
Increased GFR would increase the FF and the oncotic pressure would also increase and this will decrease the net filtration pressure afterwords the **GFR will decrease**☉

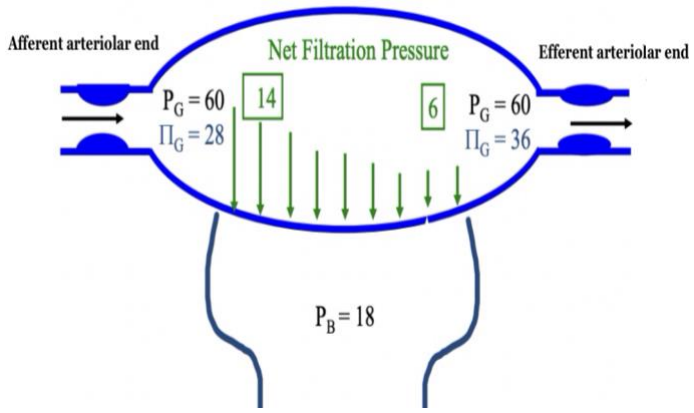
♛ Another scenario, if the **renal plasma flow was decreased**, how would that affect GFR?
The FF would increase and the oncotic pressure will increase, as a result the net filtration pressure will decrease and the **GFR will decrease.**

In this experiment measured the oncotic pressure from the afferent to the efferent end of the glomerulus in different filtration fractions.

1. In the normal red polt, as we go from the sffeerent to the efferent, the oncotic pressure increases because the filtered fluid increases.
2. When fltration fraction was more than normal (more than 20%), this increase will shift the plot upwards, increasing the scale of oncotic pressure for both afferent and effent ends.



3. If the fltration fraction less than normal, all the plot will be shifted downwards, meaning that the oncotic pressure will still be increasing from the afferent to the efferent but in a much lower scale.



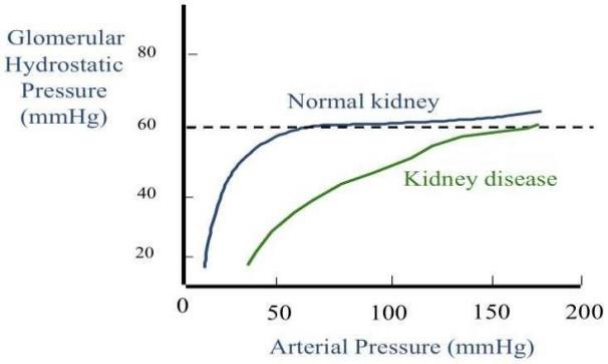
In this image you can see that the amount of filtered fluid **decreases** as we go distally, this causes the oncotic pressure (πG) to **increase** as we go to the efferent end (from 28 to 36mmHg, the average is used to calculate the net filtration pressure). This makes the glomerular hydrostatic pressure remains **unchanged** (PG=60), like a ballon the pressure inside it is distributed, and that is because on the two ends (afferent and efferent) there are constraints (see the pic) making the overall hydrostatic pressure almost constant from a physical view☉

Because the oncotic pressure is increasing and the hydrostatic pressure is constant, the net filtration pressure will **decrease** along the way.

Glomerular Hydrostatic Pressure (PG) is a physiological regulator of GFR.

- **Is the determinant of GFR most subject to physiological control,** the kidney can adjust It.
- **Factors that influence PG:**
  - **arterial pressure (effect is buffered by autoregulation).**
  - **afferent arteriolar resistance**
  - **efferent arteriolar resistance**

Glomerular Hydrostatic Pressure (mmHg)



This pic shows the relationship between the arterial pressure and PG, and it was found that Glomerular hydrostatic pressure remains **constant** within a range of 60-180 mmHg of Mean Arterial Pressure (MAP)! This means that the kidney **buffers** the fluctuations of arterial pressure in a wide range to keep the PG constant, this is called the **renal autoregulation.** So, that whenever the BP is increased or decreased, the function of the kidney won't be affected.

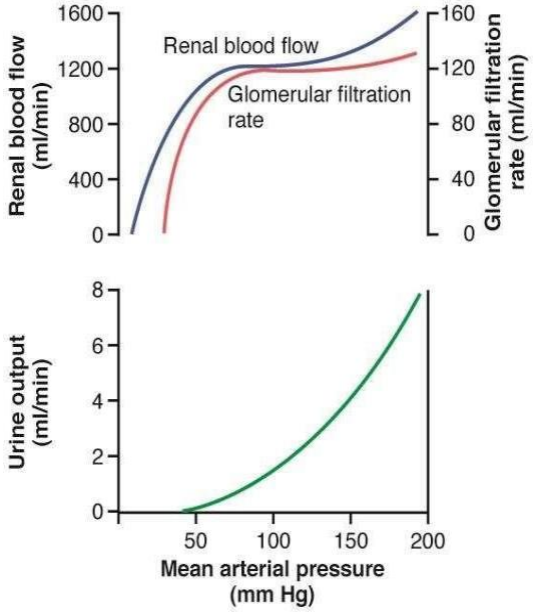
In renal diseases, the autoregutation is impaired.

In extremes (less than 60 and higher than 200) the PG is affected by the arterial pressure in a direct relationship as expected.

Autoregulation of renal blood flow and GFR but not urine flow

In the first figure you can see that the renal blood flow and GFR are subjected to autoregulation (from 60 to 180).

While urinary output (urinary flow rate) isn't subjected to autoregulation (the higher the MAP, the higher the urinary output), and this is needed as a mechanism to lower the blood pressure, it is done by a process called pressure natriuresis (increased secretion of sodium) and pressure diuresis (increased secretion of water) to decrease the ECF and pressure.

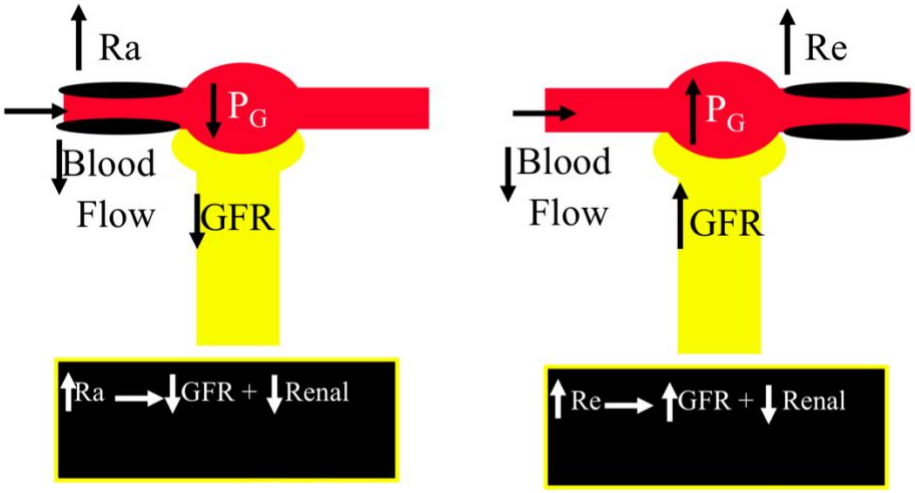


Point is NOT all kidney's functions are subjected to autoregulation.

We said before that when the arterial pressure increases, the filtration won't be affected and yet the urinary output would increase, how come?

Because the urine isn't made only by the filtration, reabsorbtion also has a role and we will take about it later.

Effect of afferent and efferent arteriolar constriction on glomerular pressure



Both ends are arteriloes and have resistance (sphincters) which can vasoconstrict or vasodilate depending on the resistance.

If the resistance in the **afferent** arteriole was increased, the **renal blood flow would decrease** to the glomerulus. If the resistance in the afferent arteriole wase increased, the **glomerular hydrostatic pressures would <u>decrease</u>** because the amount of entering fluid would decrease., this would decrease GFR. This shows that the afferent arteriole can be used as a **tool to regulate GFR.**

And if we increase the resistance in the **efferent** arteriole (constricting the sphincter), this will **decrease the renal blood flow** (same as the afferent)

(في سيارة صافة بآخر الشارع فالسيارات يلي قبلها بمشوا ببطىء) , This **<u>increases</u> the glomerular hydrostatic** pressure because the glomerulus will be filled with more fluid as it's not going out properly (opposite to what happens when the afferent is constricted), as a result GFR will increase.

Constricting the afferent and efferent arterioles has a differential affect on hydrostatic pressure and GFR, and the kidney adjusts them to keep GFR constant (renal autoregulation).

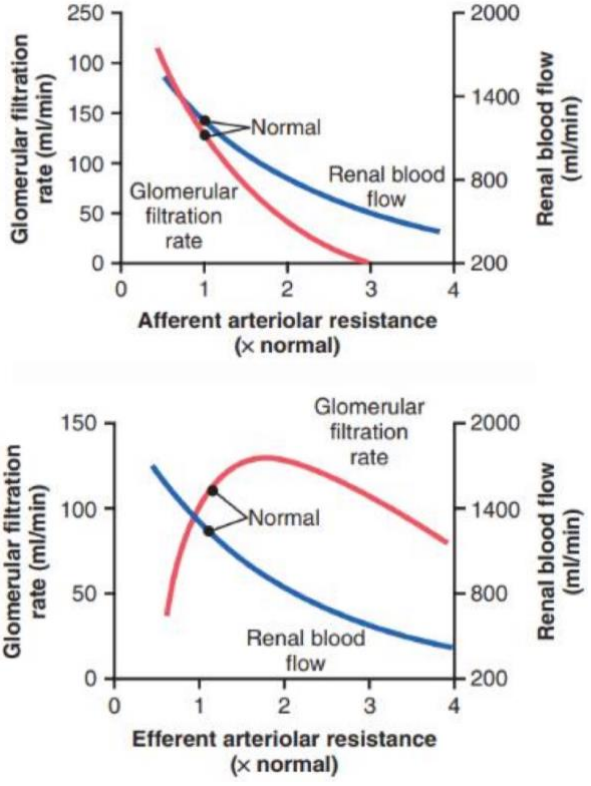
Glomerular hydrostatic pressure is determined by three variables, each of which is under physiological control:

1. arterial pressure
2. afferent arteriolar resistance
3. efferent arteriolar resistance

Effect of changes in afferent arteriolar or efferent arteriolar resistance (Biphasic)

Changing the resistance of afferent and efferent arterioles have different consequences:

1. Increasing the **afferent** arteriolar resistance to 2x (double), the renal blood flow will decrease and GFR will also decrease, in 3x they decrease even more. (Both have a liner inverse relationship).
2. Increasing the **efferent** arteriolar resistance to 2x, the renal blood flow will decrease, and in 3x it decreases even more (it declines progressively as the resistance increases, liner).



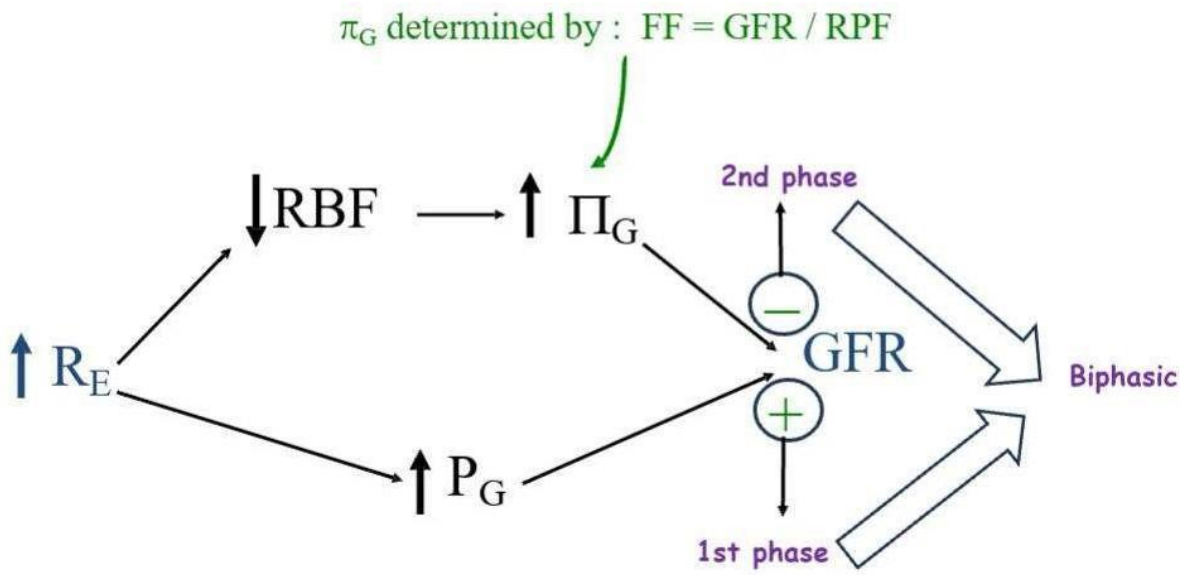
On the other hand, see the glomerular filtration rate have a **biphasic** behaviour; at first it increases as the resistance increases, then when it reaches more than 3x the GFR decreases as the resistance increases (non linear).

All have liner relationship, the exception is the GFR in response to increasing the resistance in the efferent arteriole for more than 2x (which decrease after it was increasing, biphasic).

The reason is because that when the resistance increases for more than 3x the renal blood flow will decrease drastically to the point where it will cause a huge increase the filtration fraction, this will increase the oncotic pressure hugely making the proteins repel from each other increasing the oncotic pressure even further, this is called the **donann effect,** it will then **decrease the GFR**, (the effect of the oncotic pressure overrides the effect of the hydroststic pressure).

Increasing resistance of efferent arterioles leads to:

1. Increase glomerular hydrostatic pressure ⟶ increase GFR (the main effect when the increase in the resistance is up to 2x)
2. Decrease renal blood flow ⟶ increase the oncotic pressure ⟶ decrease GFR (the main effect in more than 3x).



↑GFR If → ↑ K_f

↑GFR If → ↓ P_B

↑GFR If → ↓ Π_G

↑ Π_G If → ↑ Π_A → ↓GFR

↑ Π_G If → ↑FF

↑GFR If → ↑ P_G

↑ P_G If → ↓ R_A → ↑ GFR

↑ P_G If → ↑ R_E → ↑ GFR

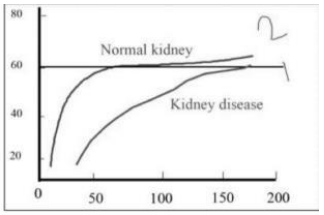
(as long as ↑ R_E < 3-4 x normal)

Physical Determinants*	Physiological/Pathophysiological Causes
$\downarrow K_f \rightarrow \downarrow$GFR	Renal disease, diabetes mellitus, hypertension
$\uparrow P_B \rightarrow \downarrow$GFR	Urinary tract obstruction (e.g., kidney stones)
$\uparrow \pi_G \rightarrow \downarrow$GFR	↓ Renal blood flow, increased plasma proteins
$\downarrow P_G \rightarrow \downarrow$GFR $\downarrow A_P \rightarrow \downarrow P_G$	↓ Arterial pressure (has only a small effect because of autoregulation)
$\downarrow R_E \rightarrow \downarrow P_G$	↓ Angiotensin II (drugs that block angiotensin II formation)
$\uparrow R_A \rightarrow \downarrow P_G$	↑ Sympathetic activity, vasoconstrictor hormones (e.g., norepinephrine, endothelin)

*Opposite changes in the determinants usually increase GFR.
A_P, systemic arterial pressure; GFR, glomerular filtration rate; K_f, glomerular filtration coefficient; P_B, Bowman's capsule hydrostatic pressure; π_G, glomerular capillary colloid osmotic pressure; P_G, glomerular capillary hydrostatic pressure; R_A, afferent arteriolar resistance; R_E, efferent arteriolar resistance.

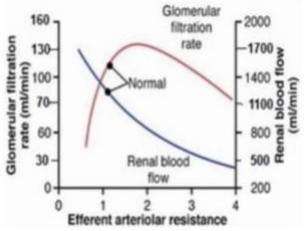
Past papers:

What is true regarding this graph?



Answer: renal autoregulation is impaired in 1.

Which statement is true about this curve:



Answer: when resistance increases 3 folds, GFR decreases.

What happen when FF increase?

Answer: GFR increase from afferent to efferent.

Glomerular filtration rate (GFR) when efferent (e) arteriolar resistance is 2X, is higher than GFR when resistance is 4X due to the following:

a. Glomerular capillaries oncotic pressure is lower at 4X (e) resistance due to decreased renal blood flow.

b. Glomerular capillaries oncotic pressure is higher at 4X (e) resistance due to decreased renal blood flow.

c. Glomerular hydrostatic pressure is higher at 2X (e) resistance than 4x (e).

d. Capsular hydrostatic pressure is higher at 4X (e) resistance than 2X (e).

e. Capsular oncotic pressure is higher at 4X (e) resistance than 2X (e).

Answer: B