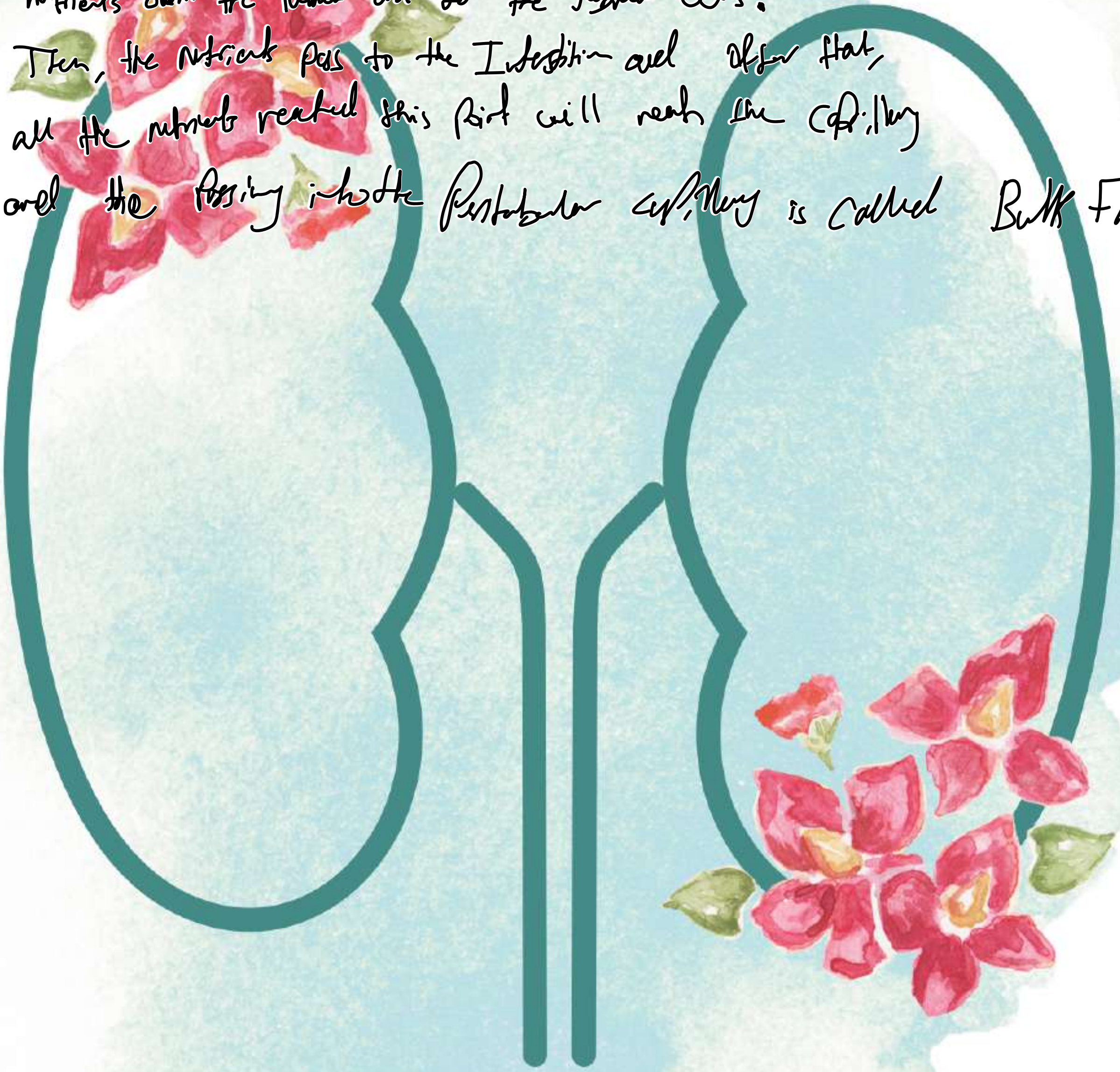
Recap ⇒ we said that the Tubular Reabsorption mechanism is the transport of desired nutrients from the lumen and to the Tubular Cells.
Then, the nutrients pass to the Interstitium and after that, all the nutrients reached this point will reach the capillary and the passing into the Peritubular capillary is called Bulk Flow



PHYSIOLOGY

- SHEET NO. 6
- WRITER : Dentistry
- CORRECTOR : Lina Albayati
- DOCTOR : Eba'a M alzayadneh

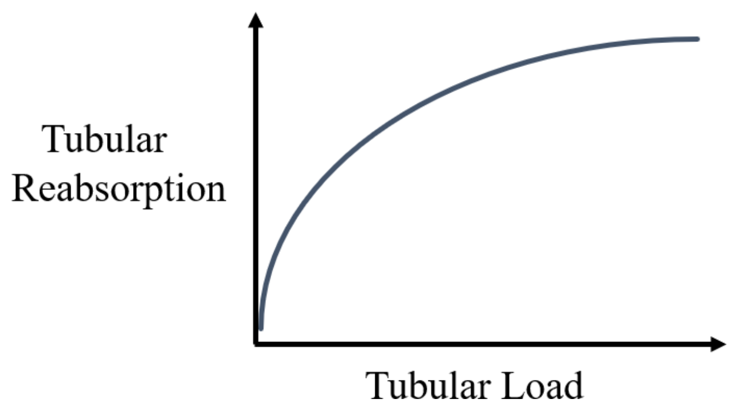
Recap ➡️ we said that the tubular reabsorption mechanism is the transport of the desired nutrients from the tubular lumen into the tubular cells. Then, the nutrients pass to the Interstitium and complete passing until reaching the the peritubular capillaries And the nutritional passage into the peritubular capillaries is called BULK FLOW, which depends on:

- **The Tubular Reabsorption Regulatory Mechanisms include:**

Tubular Reabsorption Regulatory Mechanisms	
	1- Glomerulotubular Balance
	2- Peritubular Physical Forces
	3- Hormones (aldosterone, angiotensin II, antidiuretic hormone (ADH), natriuretic hormones (ANF), parathyroid hormone)
	4- Sympathetic Nervous System
	5- Arterial Pressure (pressure natriuresis)
	6- Osmotic factors

- The graph on the right depicts the relationship between **Tubular load** and **Tubular Reabsorption.**

- **Tubular load** Filtered amount of the Renal Plasma fluid



- From the figure, we can notice that **as the concentration of the substance that has been filtered (the higher the Filter/ Tubular Load) increases, the tubular reabsorption also increases** up to a limit "reaching Plateau at the end" in an attempt to adjust the tubular reabsorption to an extent to become compatible with the increase in the Tubular load that was due to the increase in the filtration load.

The importance of Glomerulotubular balance in minimizing the changes that can take place in urine volume due to changes in the Glomerular Filtration Rate.

- In the previous lectures, we discussed the importance of Tubuloglomerular feedback/Balance.

- **The tubuloglomerular feedback is the feedback that can change/ modify glomerular filtration rate** while **the Glomerulotubular balance is the balance that takes place between the GFR and tubular reabsorption** (notice that **reabsorption** is the thing that is going to be modified here)

Extra Note: Kidneys regulate this salt excretion by modulating the rapport between glomeruli and tubules. The tubules respond to glomeruli with **Glomerulotubular balance**, whereas glomeruli respond to tubules through **tubuloglomerular feedback**.

GFR	Reabsorption	% Reabsorption	Urine Volume
	no Glomerulotubular balance		
125	124	99.2	1.0
150	124	82.7	26.0
	"perfect" Glomerulotubular balance		
150	148.8	99.2	1.2

Glomerulotubular balance absence, means that there is NO change in Reabsorption

Referring to the table above in the case of "No Glomerulotubular Balance":

- If the GFR increased from 125 ml/min (normal value) to 150 ml/min, and reabsorption did not change (stayed as 124), because there was no Glomerulotubular balance → **the urine volume will rise** from 1 to 26 ml/min.
- If we calculate the percentage of reabsorption in the normal case

  124/125 *100 = 99.2 %

- This percentage indicates that from the filtration, 99.2% was reabsorbed back.
- But when there is no Glomerulotubular balance, and the reabsorption is not increased upon the increase in the GFR → **the reabsorption percentage will be reduced** because there is no adjustment or modification for the reabsorption→ 124/150 *100 = 82.7 %

Referring to the previous table in the case of "Perfect Glomerulotubular Balance":

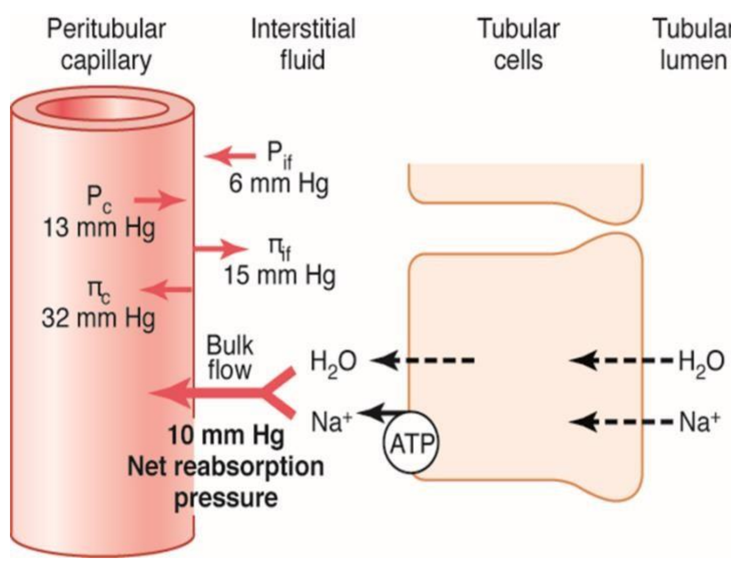
- When the GFR increased from 125 to 150, the reabsorption is also adjusted to increase from 124 to 148.8 → the urine volume will be 1.2 and the percentage of reabsorption equals 99.2%

URINE VOLUME = GFR – REABSORPTION

$$\% \text{ OF REABSORPTION} = \frac{REABSORPTION}{GFR} \times 100$$

- This represents the case of "Perfect Glomerulotubular Balance", meaning that there was an adjustment for the reabsorption, in order to **prevent any changes in the urine volume** (the urine volume stays at the same value present when the GFR and Reabsorption values are normal).

Referring to the Figure on the right:



- **<u>Remember:</u>** we have talked previously about the forces that govern the glomerular filtration.
- NOW, we will discuss the forces thar govern the **Peritubular Capillary Reabsorption**.
- The type of forces is the same, but here we are talking about **tubular cells** (that form the wall of the tubules) and peritubular capillaries.
- The forces are:
  1- **Capillary Hydrostatic Pressure** = 13 mmHg, and the direction of this pressure is **to the outside** of the capillary.
  2- **Interstitial Hydrostatic Pressure** = 6 mmHg, it is found in the hydrostatic fluid and it is directed **into the capillaries.**
  3- **Capillary Oncotic Pressure** = 32 mmHg, it is directed **toward the inside** of the capillary.
  4- **Interstitial Fluid Oncotic Pressure** = 15 mmHg, and it is directed **toward the outside** of the capillary

forces above govern the bulk flow

After reablsorption and transport take place, all absorbed water and solutes will flow from interstitium to capillaries as bulk flow

- **Notice that the values of the forces here are different from that of the glomeruli or Bowman's Capsule, BUT the direction of the forces are the same.**

- Since the processes occurring in the Peritubular capillaries are **reabsorption processes NOT filtration process** (as in the glomeruli), and therefore when we want to calculate the **Net Reabsorption Pressure**, we consider that **any force toward reabsorption is POSITIVE**, and any force against reabsorption is NEGATIVE.

any decrease in the Net absorptive force leads to less fluids entering the Peritubular capillaries and accumulate in the interstitium then will leak back to the tubular lumen causing (P) and dilution of tubular

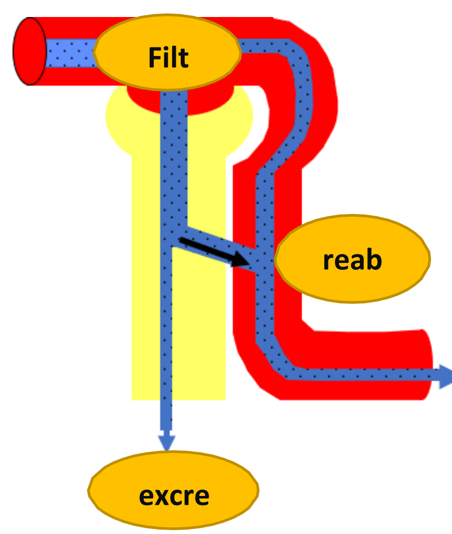
  - By this we consider the **Capillary Hydrostatic Pressure** and the **Interstitial Fluid Oncotic Pressure** as **NEGATIVE** pressures
  - The **Interstitial Hydrostatic Pressure** and **Capillary Oncotic Pressure** are **POSITIVE** pressures.

The NET REABSORBTION PRESSURE = +6 +32 -13 -15 = 10 mmHg

  - The net reabsorption pressure is the process of water and sodium reabsorption represented by the **BULK FLOW** or diffusion into the peritubular capillaries.

Calculating the Rate of Tubular Reabsorption

- **When Excretion is less than Filtration (Excret s < Filt s)**
  - Having the Excretion less than the filtration means that part of the substance is reabsorbed.
  - Referring to the figure on the right:



Excretion = Filtration – Reabsorption

Reabsorption = Filtration – Excretion

- In order to calculate the **reabsorption**, we need to know the **filtration rate** and the **excretion rate.** Amount filtered per min
- We can calculate the **Filtration Rate [filtered load] for a particular substance** by multiplying the **GFR** (Glomerular Filtration Rate) by the **concentration of the substance** in plasma.

Filt s = GFR x Ps

(Ps = Plasma conc of s)

Note: ***The Glomerular Filtration Rate is a function in the Glomeruli that does not depend on the type of the substance*** = **125 ml/min**

The concentration of the substance is measured in mg/ml.

The Filtration rate is measured in mg/min.

Excret s = Us x V

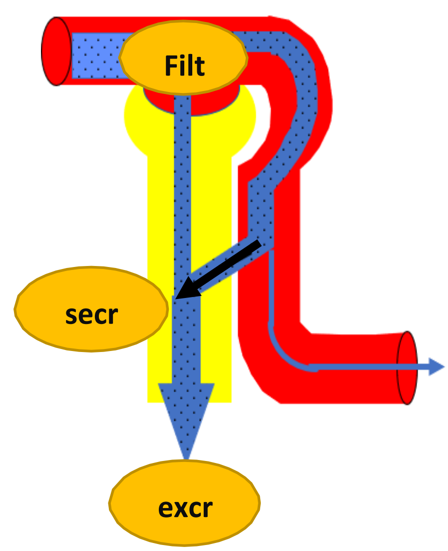
Us = Urine conc of s

V = urine flow rate

- Now, we want to calculate the **Excretion Rate** of a substance.
- In order to calculate the excretion rate, multiply the **concentration of the substance** (that we are measuring its reabsorption) in the urine by the **urine flow rate**.
- The **Urine concentration of a substance** is measured in **mg/ml.**
- The **urine flow rate** is measured in **ml/min**.
- Therefore, the **excretion rate** is measured in **mg/min.**

After calculating the filtration and excretion rates we can easily get the Reabsorption rate using the equation: **Reabsorption = Filtration – Excretion**

- **When Excretion is more than Filtration (Excret s > Filt s)**
  - When the excretion is more than the filtration, this means that the substance had undergone a **Net Secretion**.
  - In this case, we are measuring the **Tubular Secretion Rate.**



Secretion = Excretion - Filtration

- We use the same equations discussed previously to get the excretion and filtration and then we can calculate the secretion.

> **Remember:**
>
> **Filt s = GFR x Ps**
>
> **Excret s = Us x V**

- **<u>Example:</u> Given the following data, calculate the rate of Na^+ filtration, excretion, reabsorption, and secretion**

  GFR =100 ml/min (0.1 L/min)
  P_{Na} = 140 mEq/L
  urine flow = 1 ml/min (.001 L/min)
  urine Na conc = 100 mEq/L

  - **Answer:** we know that the Na is reabsorbed, but in case we don't know, we first need to calculate the filtration and excretion, then we see which one is higher in order to decide whether absorption or secretion occurred.

Filtration Na = GFR x PNa

= 0.1 L/min x 140 mEq/L

= **14 mEq/min**

Excretion Na = Urine flow rate x Urine Na conc

= 0.001 L/min x 100 mEq/L

= **0.1 mEq/min**

Be careful to the units while solving.

Now, we can see that the filtration is much higher than the excretion → ***Reabsorption*** occurs.

Reabsorption Na = Filtration Na - Excretion Na

= 14.0 - 0.1 = **13.9 mEq/min**

Secretion Na = There is no net secretion of Na since Excret Na < Filt Na

The Concept of Transport Maximum

- As we mentioned earlier when we discussed glucose transport, **some substances have a maximum rate of tubular transport due to saturation of carriers, limited ATP, etc.**

- ***Transport Maximum:*** Once the transport maximum is reached for all nephrons (the transporters are saturated with the substance), **further increases** in tubular load (concentration of this substance in the tubular fluid) is not going to be reabsorbed instead they are going to be **excreted** through urine.

Transport maximum is the maximum amount of substance that can be reabsorbed based on the number of transport proteins available.

- ***Threshold:*** is the tubular load (concentration of the substance) at which transport maximum is exceeded in some nephrons. This is not exactly the same as the transport maximum of the whole kidney because some nephrons have lower transport max's than others.
- In other words, there might be a certain concentration of a substance in the tubular fluid, and some nephrons reach their transport maximum at this concentration, but the rest of the nephrons are still not reaching their transport maximum.
- At the threshold we notice an increase in the excretion of a certain substance, but some other nephrons can still reabsorb this substance.

- **Transport maximum and Threshold are related terms, but they are not the same**.
- The following are examples of **substances having a transport maximum and a threshold:** ***glucose, amino acids, phosphate, sulphate.***

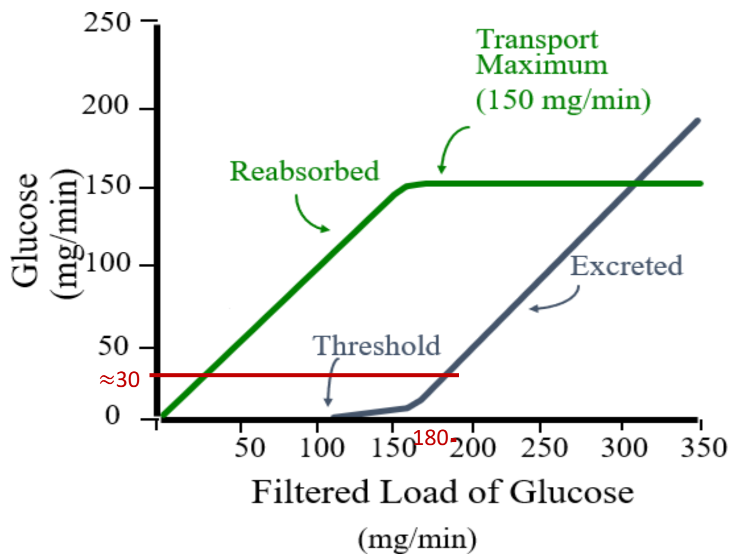
The graph on the right, helps in understanding the previous concepts (Threshold and Transport Maximum)

MCQ QUESTION: A uninephrectomized patient (having one kidney) with uncontrolled diabetes has a GFR of **90 ml/min**, a plasma glucose of 200 mg% (2mg/ml), and a transport max (Tm) shown in the figure. What is the glucose excretion for this patient?

A. 0 mg/min B. 30 mg/min C. 60 mg/min D. 90 mg/min E. 120 mg/min

Answer:

- From the figure we can see that the Transport maximum equals 150 mg/min
- We first calculate the tubular load/ filtered load of the patient using the GFR and the plasma glucose level.



GFR = 90 ml/min
Plasma Glucose = 2 mg/ml
The tubular load/ filtered load = 2 x 90 = 180 mg/min
The excreted = 180 – 50 = **30**

Notice that the transport maximum is 150 mg/min, meaning that the transporters found in the kidney can only transport 150 mg/min, but the tubular load is 180 mg/min → so there will be a remaining of 30 mg/min that are going to be excreted.

Referring to the figure, we can notice that at a filtered load of 180, the transport maximum was already achieved, and that's why the remaining 30 mg/ml are going to be excreted.

Therefore, the answer is **B.**

- Notice that **from the previous figure**, we can see that at the threshold, we did not reach the transport maximum for all the nephrons. And since the 150 mg/min is the transport maximum for all the nephrons, at this level of glucose filtered load, all the nephrons are saturated, and the excess is excreted.
- At the threshold, some nephrons reached their transport maximum before the other nephrons, and that is why we can notice the excretion after the threshold value at 120 or 130 mg/ml (look at the figure in the previous page) → in other words, at the threshold we start noticing glucose in the urine, although we did not reach the transport maximum in all the nephrons.

- If we want to measure the **peritubular capillary reabsorption**, we multiply the net reabsorption pressure by the peritubular capillary filtration coefficient.

Reabs = Net Reabs Pressure (NRP) x $\boldsymbol{K_f}$
= (10 mmHg) x (12.4 ml/min/mmHg)
= **<u>124 ml/min</u>**

Filtration Coefficient

Reabs = Net Reabs Pressure (NRP) x $\boldsymbol{K_f}$

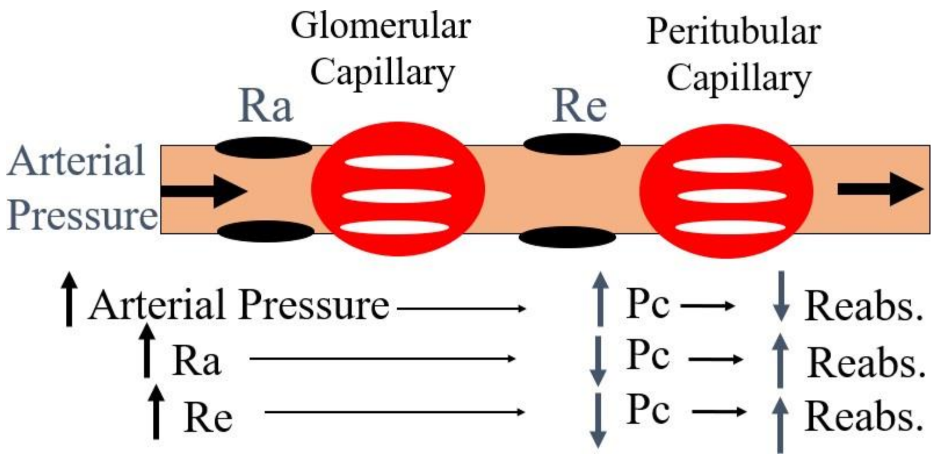
The determinant of peritubular capillary Reabsorption

- As the **peritubular capillary filtration coefficient increases**, the reabsorption rate increases.
- As the **peritubular capillary hydrostatic pressure increases**, the reabsorption rate decreases. (remember that the capillary hydrostatic pressure is negative, in the case of reabsorption)
- As the **peritubular capillary colloid osmotic pressure (Oncotic pressure) increases**, the reabsorption rate increases.

↑ K_f → ↑ Reabsorption
↑ Pc → ↓ Reabsorption
↑ πc → ↑ Reabsorption

Make sure you do not mix between the determinants of reabsorption and filtration, because the two processes are opposite to each other!

*The figure below shows the **afferent** and **efferent** arterioles and between them we can see the **glomerular capillaries** and after the efferent arteriole we can see the **peritubular capillary**.*



- When we study the **reabsorption**, we refer to the **peritubular capillaries**, but we study the **filtration** on the **glomerular capillaries**.

Now we will study the effect of some determinants on both, the glomerular filtration, and the peritubular reabsorption.

> ***Remember:*** the peritubular capillary hydrostatic pressure is **inversely** proportional to the reabsorption.

1- If the **arterial pressure increases** (without any auto-regulation) → the glomerular hydrostatic pressure **increases** and the peritubular capillary hydrostatic pressure **increases** as well → as a result, **the reabsorption decreases.**
2- If the **resistance in the afferent arteriole increases** (by narrowing the arteriole) → the renal blood flow in the glomeruli **decreases** → the glomerular hydrostatic pressure **decreases** → the renal blood in the peritubular capillaries **decreases** → the hydrostatic pressure in the peritubular capillaries **decreases** → as a result, the **reabsorption increases.**
3- If the **resistance in the efferent arteriole increases** → the renal blood flow in the peritubular capillary **decreases** → the hydrostatic pressure in the peritubular capillaries **decreases** → as a result, the **reabsorption increases.**

From this we conclude that an increase in the resistance of the afferent or efferent arteriole, results in an increase in absorption.

Determinants of Peritubular Capillary Colloid Osmotic Pressure

- As the oncotic pressure in the capillaries increase → Reabsorption increases.
- ***What are the factors that increase the oncotic pressure in the peritubular capillaries?***

1- As the **number of plasma proteins increase** → the oncotic pressure in the arterial system increases → oncotic pressure in the capillaries increase → Reabsorption increases.
2- As the **filtration fraction increases** → the oncotic pressure in the capillaries increase → Reabsorption increases.

Remember: there is a **direct** relationship between the filtration fraction and the oncotic pressure.

Filtration Fraction = GFR / RPF

GFR: Glomerular Filtration Rate **RPF:** renal plasma flow

$\uparrow \pi c \rightarrow \uparrow$ **Reabsorption**

$\uparrow$ **Plasma Proteins** $\rightarrow \uparrow \pi a \rightarrow \uparrow$ **Reabsorption**

$\uparrow$ **Filtration Fraction** $\rightarrow \uparrow \pi c \rightarrow \uparrow$ **Reabsorption**

- ***When does the Filtration Fraction increase?***

1- When the renal plasma flow decreases.
2- Or the Glomerular Filtration Rate increases

Summary for all the Factors that influence Peritubular Capillary Reabsorption

1. ↑K_f → ↑ hydraulic conductivity & surface area → t Reabsorption
   (the coefficient depends on the permeability of the membranes)
2. ↑Pc → ↓ Reabsorption
3. ↑πc → ↑ Reabsorption
4. ↑ Ra → ↓ Pc → ↑ Reabsorption
5. ↑ Re → ↓ Pc → ↑ Reabsorption
6. ↑ Arterial Pressure → ↑ Pc → ↓ Reabsorption
7. ↑ arterial oncotic pressure (in plasma and blood) → ↑ πc → ↑ Reabsorption
8. ↑ Filtration Fraction → ↑πc → ↑ Reabsorption
9. ↓ RPF → ↑ Filtration Fraction → ↑πc → ↑ Reabsorption.
10. ↑ GFR → ↑ Filtration Fraction → ↑πc → ↑ Reabsorption.

وَ تَعاوَنُوا عَلَى الْبِرِّ وَ التَّقْوى وَ لا تَعاوَنُوا عَلَى الْإِثْمِ وَ الْعُدْوانِ وَ اتَّقُوا اللَّهَ إِنَّ اللَّهَ شَدِيدُ الْعِقاب