بسم الله الرحمن الرحيم

1

Physiology sheet

Doctor 2022 -أثر- I medicine I MU

DOCTOR

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Overviews of renal system

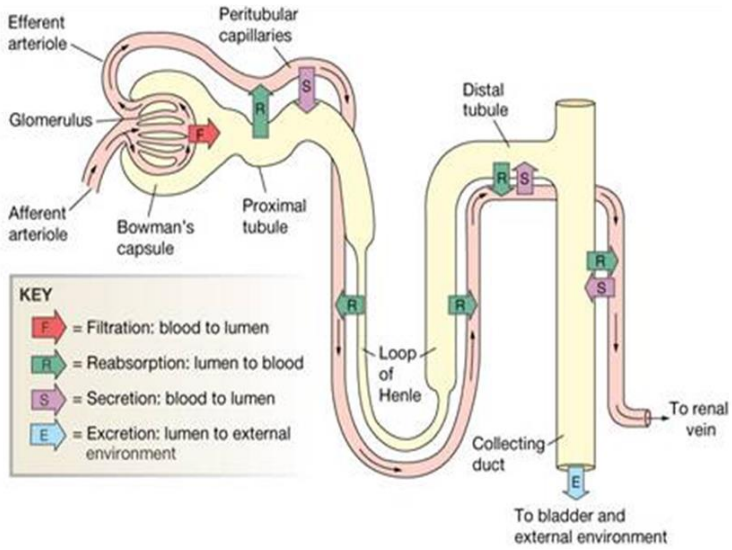
Kindly note that the sheet is arranged in the same order the doctor did and ALL of the slides are included 😊

Function:

Urinary system (renal system) has a very important role in maintaining body homeostasis mostly via: 1. Regulation of water and electrolytes and 2. acid base balance. However, kidneys' other functions include: 3. Secretion of hormones and 4. Metabolism.

Nephrons are the structural and functional units of kidneys.

Urine Formation:



Our hearts pump blood through the aorta to kidneys (descending thoracic aorta → descending abdominal aorta → right& left renal arteries → Afferent arterioles). Blood will then reach a network of capillaries called 1) Glomerulus – a person's head- that is surrounded with a hat-like structure called 2) Bowman's Capsule, then we have 3) Proximal Convoluted Tubule (PCT), followed by a U- shaped tubule called 4) Loop of Henle (LoH), then 5) Distal Convoluted Tubule (DCT), and finally to the 6) Collecting Ducts (CD).

The huge amounts of blood received by glomerulus → high pressure (Hydrostatic Pressure) against the arterial walls compared to a lower pressure in Bowman's capsule → the difference in pressure will result in: Filtration (F): (the 1st process of urine formation). It is directly proportional to renal blood pressure and renal blood flow. Water and solutes is filtered across glomerular capillaries.

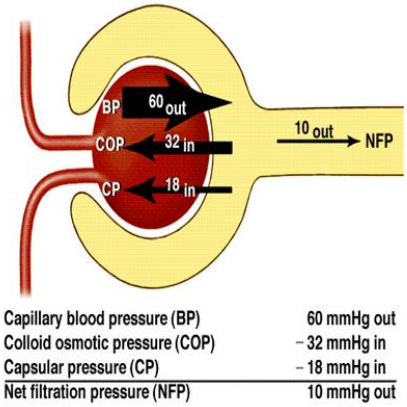
After absorbing a substance from the gut, it will be reabsorbed from the kidneys (from the tubular lumen to the blood, in an opposite direction to filtration process). Reabsorption (R): (the 2nd process) Is the removal of water and solutes from the renal filtrate

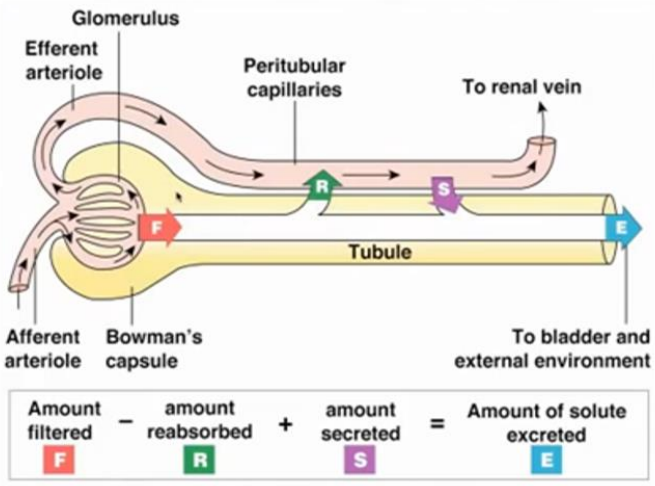
After that comes the 3rd process: **Secretion (S):** where kidneys **Transport of solutes from peritubular fluid into the tubular fluid** (from blood to lumen, similar to filtration direction)

The 4th and final process in urine formation is Excretion (E) where we dispose urine from lumen to external environment (out of the body).

P.S Both R and S occur in PCT and DCT while in LoH only R occur.

Starling Forces

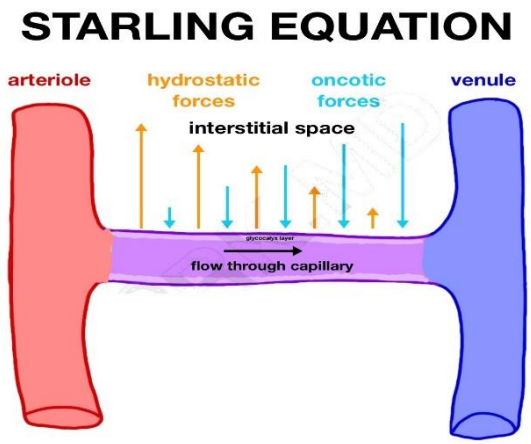




Left figure notes: Capillary blood pressure (hydrostatic pressure) (BP): a pressure exerted by fluid on a wall againt it. Colloid osmotic pressure (COP): an attracting pressure exerted by solutes (proteins mostly) towards it. Capsular Pressure (CP) is the hydrostatic pressure resulted from the fluids inside Bowman's Capsule.

Since Bowman's Capsule doesn't have any proteins NORMALLY, its COP is close to zero.

The following picture is from an external source, however, all of the written notes were explained by the doctor.



The normal flow: arteries (O2 rich) → arterioles → arteriolar end of the capillaries → capillaries → venular end of the capillaries → venules → veins (CO2 rich).

As blood flows, it will be filtered to the interstitium → ↓ in volume → ↓ in BP. Consequently, oncotic forces (COP in this case) will dominate more and more.

COP is constant along all the regions (proteins amount won't be affected), that being said, the Net Balance of Forces will determine the net movement: @Arteriolar End: BP> COP, BP dominates while @ Venular end: COP> BP, COP dominates.

Now back to our specifc case (left figure, page 2), we add the forces in the same direction (60 + 0) together and then we subtract those of opposite directions (32 +18) to yeild Net Filtration Pressure NFP of 10 mmHg out (favoring BP direction → filtration occurs!)

Right Figure Notes (Page 2):

- By the afferent arterioles, the blood arrives to the glomerulus and by efferent arterioles, the blood exits the glomerulus.
- How can we calculate the amount of solute excreted (E)? E= F+ S- R

What are the factors that affect the amounts of filterates being generated? (↑ means direct proportion or increase and ↓ means inverse proportion or decrease).

1. ↑ Amount of blood volume delivered (↑ blood→ ↑BP→ ↑ filtration procces).
2. ↑ Hydrostatic pressure (BP).
3. ↓ Osmotic pressure (COP).

Proximal Convoluted Tubule (PCT):

Reabsorption happens here, where it plays the **(Grandmom roles of handling money)**: she gives a little amount of energy while there is lots of savings. At PCT, 60-65% of sodium (Na) is reabsorbed (Na is considered the most electrolyte reabsorbed and it mainly happens in PCT). PCT has two membranes:

1) **Basolateral membrane** (facing the blood vessels side) where it has: A) **Na+ and K+ ATPase pump** once time energy (as a source of energy: for every 1 ATP molecule used, 3 Na molecules are exported and 2 K molecules are imported→ electrochemical gradient→ change in the electrolytes concentrations). B) **GLUT2** transporter for **Na+ and glucose facilitated diffusion.**

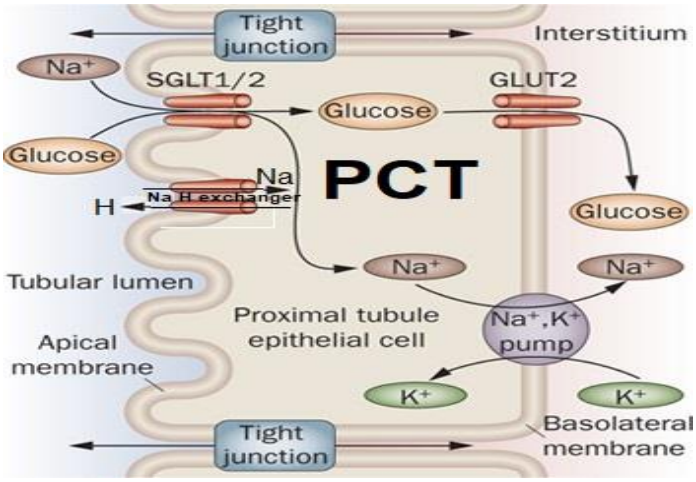
2) **Apical Border** (facing the tubular lumen), where **Na+** enters through **facilitated diffusion?** 1st and then we have a) **SGLT2** transporter for **Na+ and Glucose active transport** (secondary active transport; energy is derived secondarily from energy that has been stored in the form of ionic concentration differences between the two sides of a membrane), where SGLT2 subtype is found in the kidneys (we have two kidneys) and SGLT1 subtype is found in the gut (we only have 1 stomach). Other substances such as **Amino acid, Ca++ and *HCO3*-** are transported too. B) **Na+ and H+ exchanger secondary active transport**: an antiporter: transports Na inside and H outside.

Secretion happens in PCT too for some compounds such as: **Uric acid, Oxalic acid, Bile salts,** protons (H) **and Para aminohippuric acid** (an important amino acid where its levels indicate the renal blood flow in a well-known test).

PCT plays a major role in **Acid base balance** where it helps in **HCO3 reabsorption** and **H+ secretion** by the aid of carbonic anhydrase enzyme that is found in PCT. Taking into account Le Chatelier's principle and this equation: $CO_2 + H_2O \rightleftarrows H_2CO_3 \rightleftarrows HCO_3^- + H^+$,

a group of drugs that does diuresis (increased production of urine) called Carbonic anhydrase inhibiters diuretics, work on PCT. **(the rest of its details are in page #6)**

The following picture is from an external source, it may help in visualizing the whole scene.



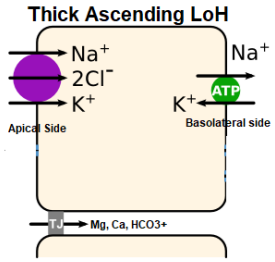
Loop of Henle (LoH):

It starts with a thick Descending limb is only permeable to water concentrated segment and a Thin initially and Thick eventually Ascending limb is permeable to salt and water. The normal tonicity of the filtrate is 300mosm but since the water is constantly reabsorbed into our blood circulation from the descending limb, the tonicity may reach a maximum of 1200mosm. On the other hand, at the ascending limb both NaCl and water will be reabsorbed, with a greater amount of the salt compared to water, and the tonicity may reach in this Diluting segment a minimum of 100mosm then it continues its journey through the other parts of the nephron. (Tonicity= $\frac{Solutes}{Water}$**, when we lose only water the tonicity will ↑, and when we lose MORE solutes than water, the tonicity will ↓).**

The thick ascending part has two membranes:

1) **Basolateral membrane: which has a Na+ K+ pump Once energy.**
2) **Apical surface: Thick segment Na+ K+ 2Cl- secondary (takes energy indirectly from Na K ATPase pump) symport (in the same direction) co-transporter which is a power carrier.**

Moreover, some ions like: Ca+ Mg+ HCO3+ are transferred paracellularly (between the cells not through them [transcellularly]).

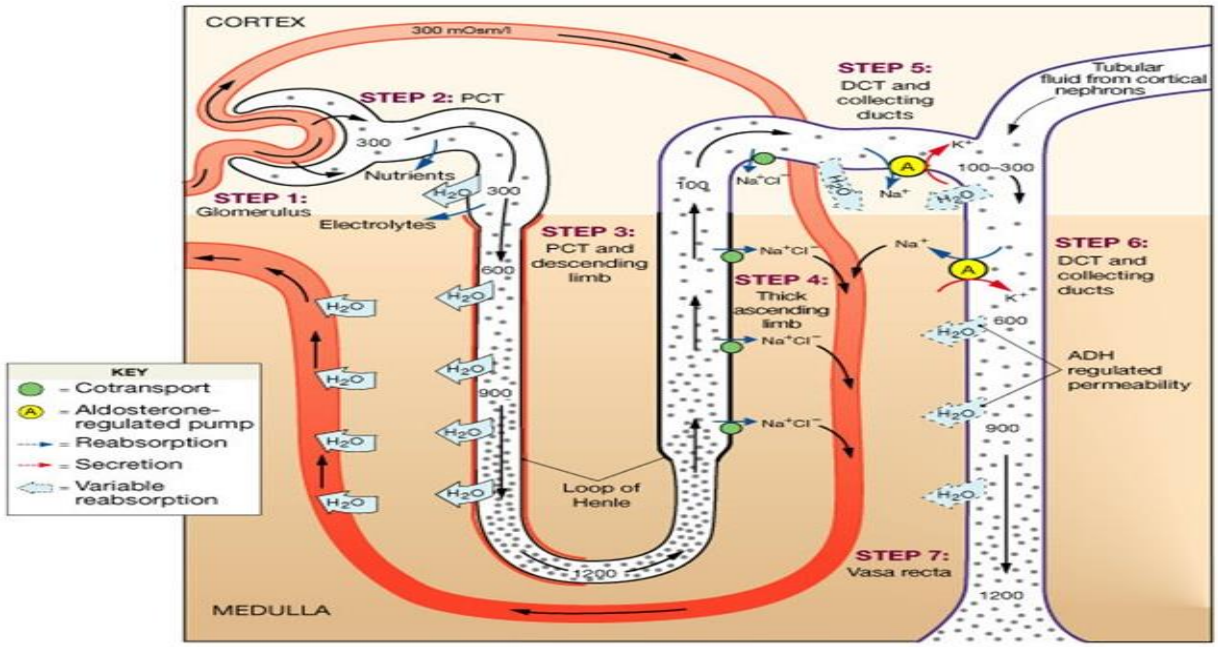


The following picture is from an external source, it may help in visualizing the whole scene

The Counter- Current Mechanism It happens in LoH.

Since the descending LoH's filterate has high osmolality, the water will first diffuse into the renal medulla before it gets into the blood stream, making the osmolality of the media around the descending segement low. On the contrary, a huge amout of salts -with much

less water- will diffuse from the thick ascending LoH making its filterate of a lower osmolarity and the media surrounding it in the medulla of a higher osmolarity. This phenomonon by which one part ↑ the osmolarity and another one ↓it (in opposite directions) is called The Counter- Current Mechanism. It helps in explaining how concentrated urine is formed.



Loop diuretics (the most powerful), work by reducing NaCl reabsorption in the thick ascending limb of LoH where 25% of Na+ is reabsorbed generally. In other words: Na+ K+ 2cl- function is: to modulate Osmolarity of medulla to form less Concentrated urine, by Inhibiting the Na K 2Cl transporter with a drug – loop diuretics for instance- it will shut the pump, more NaCl will be excreted in the urine (no reabsorption happens) and will lead to loss more water in the urine with lost a lot of electrolytes (wherever salt goes, water follows).

- **Uses of Diuretics:**

1. **In hypertension (morbidly high blood pressures): ↑ the water in urine → ↓ the volume of blood → ↓ BP.**
2. **In edema (morbid accumulation of fluids in the interstitium → larger than usual limbs): with the same proposed mechanism.**

Distal convoluted tubule (DCT) and collecting duct (CD):

They both almost have similar functions. There are two main types of cells: 1) Principle cells and 2) alpha intercalated cells.

A simple comparison can be made:

Criterion/ Cell Type:	Principle cells	alpha intercalated cells
Number:	Larger in number	Fewer in number
Length:	Taller	Shorter
Site of action:	Collecting duct	Collecting duct and DCT
Function:	Secrete Aldosterone (Na and H2O reabsorption) and ADH (H2O reabsorption).	H+ secretion by H+ and K+ primary active antiport and HCO3- reabsorption

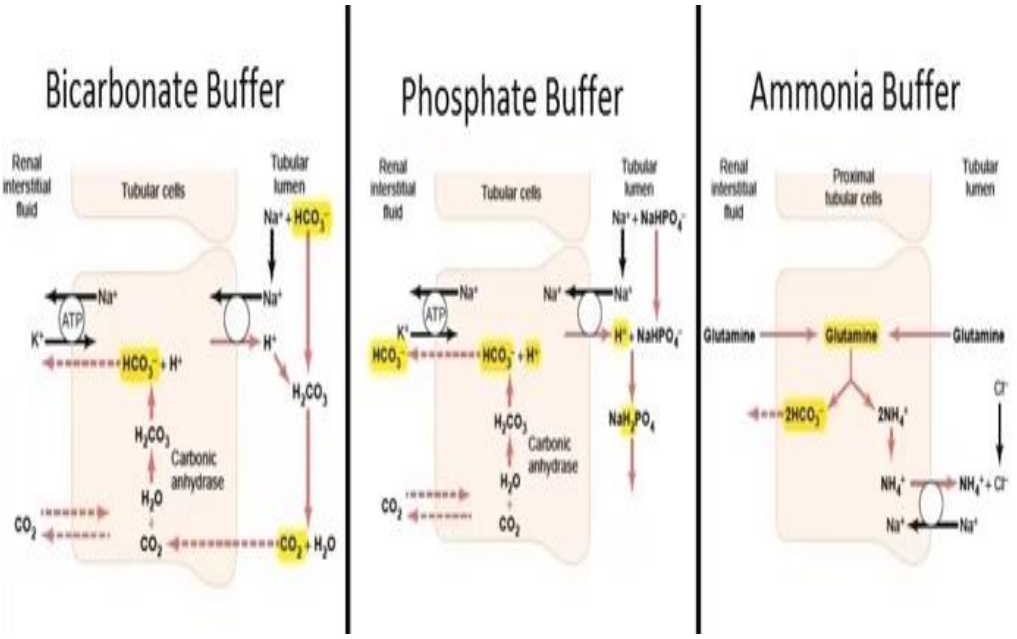
Notes related to the table:

- **Aldosterone ↑ salt and water reabsorption → ↑ Blood volume → ↑BP (used in hypotension). Moreover, it affects the H+ K+ antipump: as aldosterone will cause Na to be reabsorbed and K to be excreted in the filterate [by the prinicple cells], the H+ K+ transporter [in alpha intercalated cells] will use ATP to reabsorb K and excrete H, which will lead to ↑ K concentration ↑ BP. That is why drugs that affect aldosterone should not be given to patients with cardiac or renal problems as it may cause hypokalemia and consequently cardiac arrest, some of these drugs are (carbonic anhydrase inhibitors diuretics and loop diuretics).**
- **Carbonic anhydrase inhibitors will prevent carbonic acid (H2CO3) dissociation → no more bicarbonate (HCO3-) reabsorption and no H+ secretion → Na+ and H+ exchanger secondary active transport won't work→ Na binds HCO3- → secreted as NaHCO3 in the lumen → More Na+ in collecting ducts and Because 60- 70% of Na+ is normally absorbed in PCT, it comes on the expense of K:**
  →1) More salts excreted → more water excreted (diuresis)
  2) Great loss in K+ → hypokalemia → Metabolic acidosis?
- **Accordingly, in patients with heart failure or kidney failure, we <u>don't</u> give carbonic anhydrase inhibitors nor loop diuretics. Instead, we <u>give</u> thiazide diuretics are it will decrease Na and cl reabsorption without affecting K levels. Thiazide diuretics affects mostly the distal tubule and it causes vasodilation so it is generally a safer alternative.**
- **Antidiuretic Hormone (ADH): ↓ urine output by ↑ water reabsorption (works the best in cases of dehydration).**

Concentration of urine: the lowest tolerable pH of urine is 4.4 (Urine limit) if it gets any lower → a critical condition that means kidneys are not working. As we know our blood pH ranges between (7.35- 7.45, more alkaline [as HCO3- is always reabsorbed) and lower pH levels means higher H+ concentrations in the blood, so how can we excrete H+ to avoid such a problem? Especially that H+ is a by- product of many physiological processes→ produced in large amounts! We definitely can use bicarbonate buffering system, however it is not enough! That is why we have many buffering systems.

1) **Bicarbonate Buffer: it is found in PCT, the buffering action of it is very low → just from H2CO3 recycling → limited and not enough. It is considered to be a volatile buffering system (can achieve the same function with the lungs minimum action).**
2) **Phosphate Buffer: hydrogen phosphate (HPO4--) is found on our filtrate, it binds Na in the lumen to form NaHPO4- which binds the H+ coming from Na+ H+ antiporter, which will eventually be excreted outside the body. We consider HPO4- - a Titratable acid (an acid we can determine its concentration via titrating it with a base) and a non-volatile buffering system (can't be achieved by lungs, only by kidneys). Note that this system only gives 1 bicarbonate molecule (even if it did not really have any role in binding H+).**
3) **Ammonia Buffer: the most powerful buffer, it forms new 2 HCO3- molecules, contrary to the previous two systems that generate only 1 HCO3- molecule and from recycling. In the system, Glutamine amino acid metabolism will result in 2 HCO3- and 2 ammonia (NH4) molecules:**
   - ➔ **HCO3- will be reabsorbed to the blood for further action and NH4 will be secreted in exchange to Na then excreted as NH4Cl in urine.**

Ammonia buffering system is considered the last resort for chronic respiratory acidosis compensation.



Filtration:

Our bodies have 5L/min of Cardiac output, 25% goes to kidneys (1.25 L/min) and the rest to other organs. Since 55% of blood is plasma, the plasma of the 25%= 600ml/min (this resembles the plasma flow rate to kidneys). Only 20% Renal plasma flow will go from the afferent arteriole to the glomerulus =120ml/min reabsorbed most which is known as GFR (glomerular filtration rate) that is only 20% the remaining 80% go to efferent arterioles. Since we have 24 hours a day and 60 minutes an hour: 120*60*24=180L/day is the GFR per day. Since we have 3L plasma in the blood (55% of 5 L), then our kidneys need 60 times/day (180 L/day ÷ 3L) to filter our plasma fully. Patients who require hemodialysis – as in those with renal failure- needs 2-3 sessions a week, with a machine filtration rate of 200- 400 mL/ min for 4 hours!

صوتك الذي تظن أنه لن يتجاوز سقف غرفتك، يتجاوز سبع سماوات!

"وَمَا كَانَ رَبُّكَ نَسِيًّا" .

- د/ مصطفى محمود .

فاستَعِن بالله يا صاحِبي واعلَم أنّ لكلّ ساعٍ ما سعَى وأنّ الله لا يُكلّف نفسًا إلا وُسعها، والذّي كلّفك هذا قدِير أن يُعينَك عليه؛ فلا تيأس وحاوِل حتّى تَصِل.

مع تمنياتنا بالتوفيق والنجاح

لا تنسونا من صالح دعائكم

#لجنة_الطب_والجراحة