PHYSIOLOGY

- SHEET NO. 9
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Homeostasis and Renal Regulation of 1. Potassium,2. Calcium,3. Phosphate, and 4. Magnesium; Integration of Renal Mechanisms for Control of Blood Volume and Extracellular Fluid Volume:

1.Potassium

Potassium is not considered to be the major electrolyte/cation/component in the extracellular compartment; however, it is so in the intracellular compartment, and as it is very easy for us to understand how the kidney makes adjustments to the extracellular fluid electrolytes, with intracellular ones like potassium we expect a slightly different scenario:

Our daily intake of K^+ (from meals, fruits and vegetables) is roughly 100mEq/day, and one meal can actually provide us with half of these which directly plays with the level of K^+ in the extracellular fluid changing it significantly.

What is the concentration of K^+ extracellularly? 4.2 mEq/L

What is the concentration of K^+ intracellularly? 140 mEq/L

Volume of extracellular fluid? 14 L Volume of intracellular fluid? 28 L

volume*concentration

Extracellularly: 4.2 mEq/L*14 L = 59 mEq

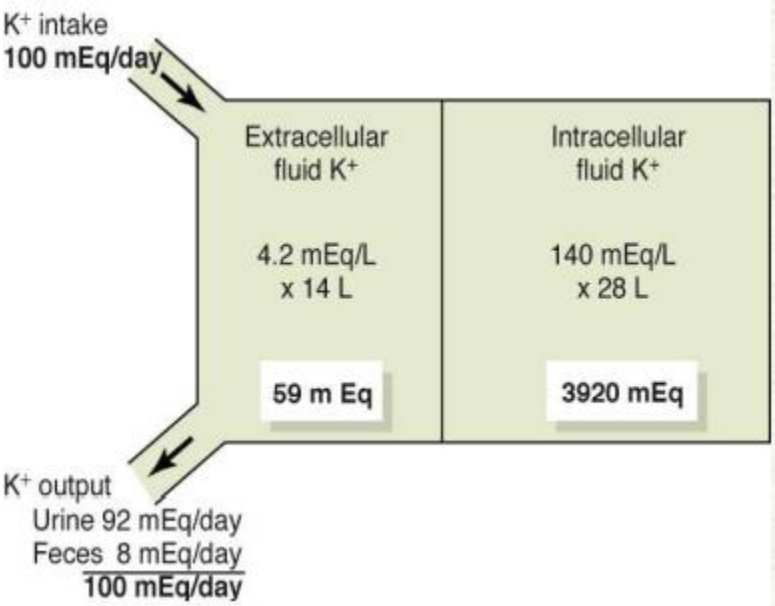
Intracellularly: 140 mEq/L *28 L = 3920 mEq

Now in order to maintain these 59 mEq(4.2 mEq/L), the intake of potassium should equal the output of potassium to guarantee that it doesn't increase nor decrease (if the output exceeds the intake it'll start pulling(draining) potassium from extracellular fluid and vice versa) as it is very important to keep K^+ concentration in the blood/plasma/extracellular fluid regulated within a very narrow window because keep in mind that bold fluctuations in K^+ affect the activity of the heart(conductive system) , neural activity and has various other adverse effects.

***How do we lose K^+?** by **urinary excretion(kidney)** 92 mEq/day and through the GIT **(feces)** 8 mEq/day (and this is usually fixed and not regulated).

- If we increase the input by 50mEq by eating vegetables- por ejemplo (cells are rich with K^+),the extracellular concentration of potassium will overshoot (La Professora said double) which is incompatible with life, and will cause hyperkalaemia, or might result in serious side effects especially if followed by the consumption of another potassium rich meal Orrr

Exercise(physical activity) during that day to the point of causing a Heart Attack (two Somali bananas then ascending the stairs is a deadly combination) and this is where urinary regulation comes to the rescue (and is helpful even when extracellular K^+ is not too high).



Mira la figura 9.1: Normal potassium intake, distribution, and output from the body.

Effects of severe Hyperkalaemia: ↑

1. Partial depolarization of cell membranes (no matter how much Na^+ influx is, the overwhelming extracellular concentration of positive ions (k^+) is holding back full depolarization from happening).

2.Cardiac toxicity (ventricular fibrillation or asystole)→can't fully contract

*in the last 2 points I added the clues to help you digest the effects and they were not mentioned by the Prof.

Effects of severe Hypokalaemia: ↓

1. Hyperpolarization of cell membranes: hard to develop action potential

2. Fatigue, muscle weakness

3. Hypoventilation

4. Delayed ventricular repolarization

*Even though there are barriers between the different compartments of the body, yet still any change in one compartment will affect the other compartment.

Factors that cause K^+ to move from ECF to ICF (decrease in plasma):

1.Insulin: insulin promotes entry of both glucose and K^+ into cells, so when insulin is high or when you give an insulin injection to a patient to lower their high blood sugar one of the major consequences that might happen is hypokalaemia.

2.Aldosterone: mainly by increasing the activity of the (Na+/K+-ATPase) pump, as it pumps Na^+ out and K^+ in, reducing K^+ extracellularly (we'll see how).

3.Sympathetic System: when catecholamines are released they bind to **Beta2-adrenergic** receptors increasing potassium entry into cells and reducing K+ extracellularly.

4.PH(Alkalosis): increases tendency to hypokalaemia (we'll see how).

Factors that cause K^+ to move from ICF to ECF (increase in plasma):

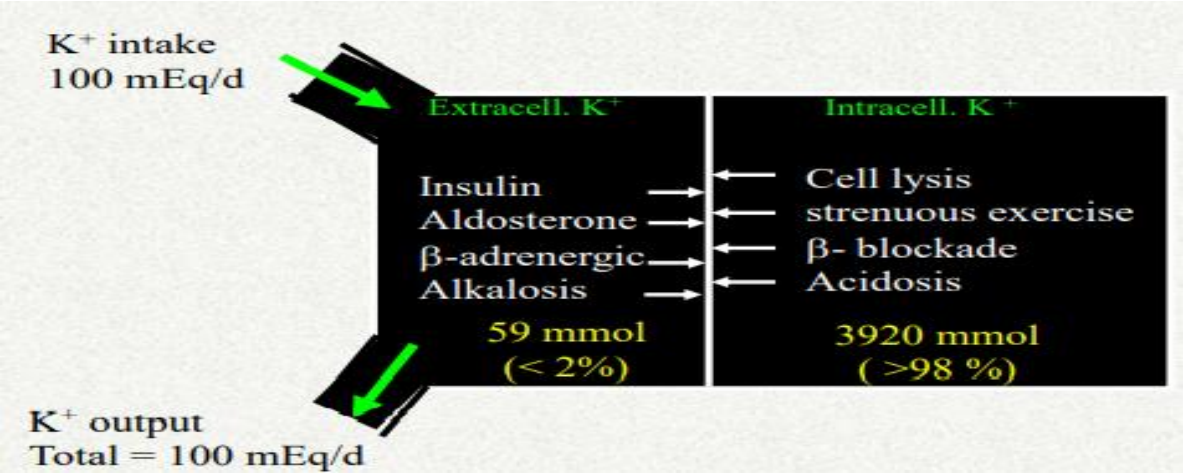
1.Cell lysis : -very logical- when we have haemolysis, or when cells lyse because of the infusion of a hypotonic fluid, their high content of K^+ will pour into the ECF.

2.Strenuous Exercise

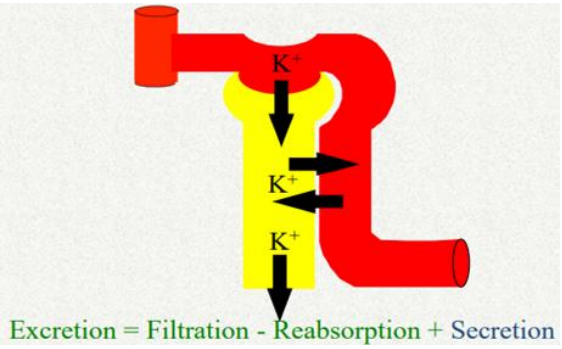
3.ß2-blockade

4.PH(Acidosis): the theory behind this is that protons inhibit the sodium potassium pump (Na+/K+-ATPase), which causes potassium to accumulate extracellularly (hyperkalaemia), the opposite happens in alkalosis(hypokalaemia).

5.High osmolarity in interstitial fluid: cells shrink as fluid leaves the cell to the extracellular compartment, and thus intracellular potassium concentration relatively increases, a gradient develops, and potassium starts to leak through leak channels, consequently, we get hyperkalaemia. Mira la figura 9.2: Potassium Regulation: Internal and External



-> Potassium (homeostasis) is controlled through the three processes of urine formation (GFR~Filtration, rate of reabsorption, secretion (mainly by principal cells and intercalated cells from peritubular capillaries into filtered fluid)).Mira la figura 9.3 : Control of Potassium Excretion

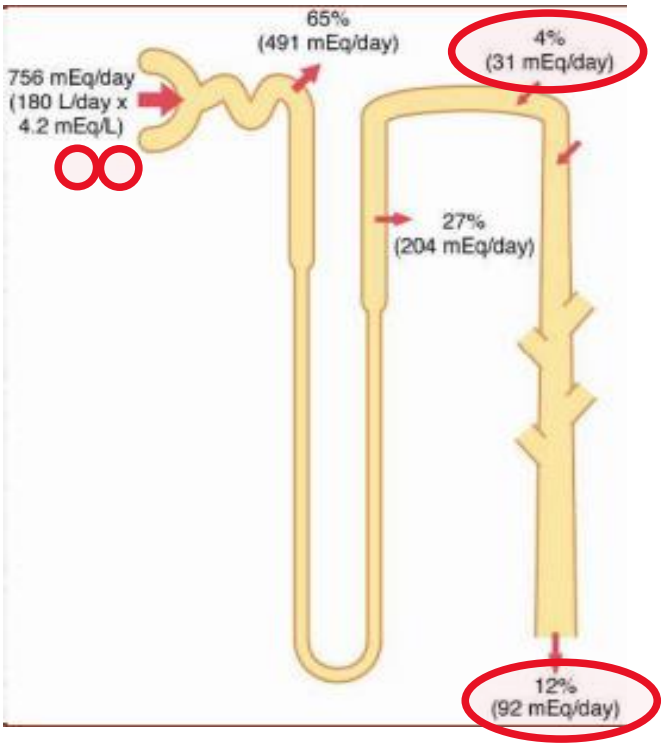


Potassium filtration load= GFR x plasma concentration of potassium

= 180L/day x 4.2 mEq/L = 756 mEq/day

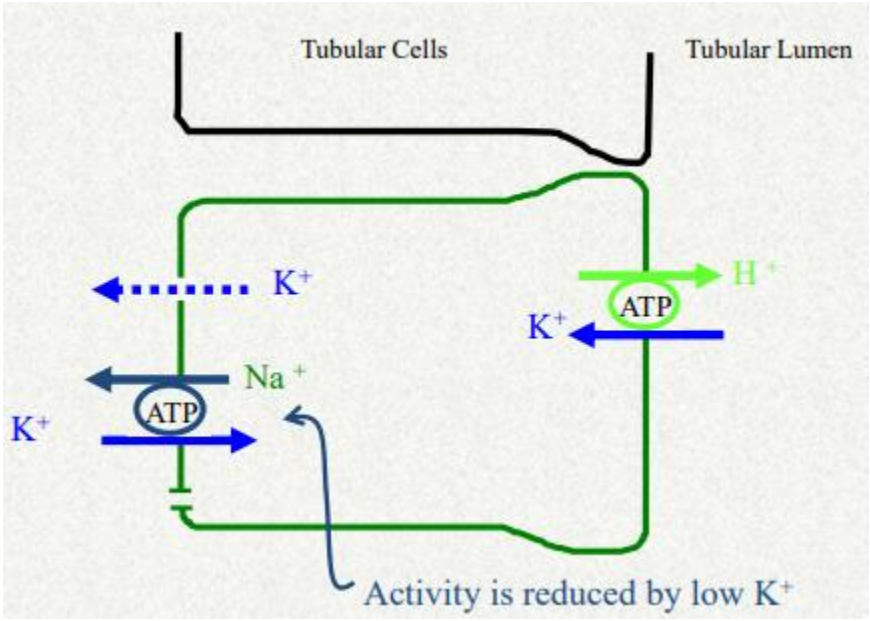
In the **proximal convoluted tubule 65% of not only sodium but also potassium and water will be absorbed, which is equivalent to 491 mEq/day of potassium, then nothing significant happens to potassium **until** we reach the **thick ascending loop of Henle** **active** reabsorption of potassium occurs through the **sodium potassium chloride channel** 27% (204 mEq/L), in the **late distal convoluted and collecting tubules** potassium gets reabsorbed indirectly by the action of ENaC by Na+/K+ ATPase, but because there are potassium channels(more permeability to potassium) and as a result of the reabsorption of sodium, potassium gets secreted to the luminal side by principal cells.

The first 65%+27%= 92% of reabsorption that happens in the PCT and the thick ascending loop of Henle are fixed, however, in the late distal and collecting tubules there are adjustments, these adjustments depend on our daily intake (fine- tuning) and **this toning happens through secretion**, so secretion increases when the diet is rich in potassium, and decreases when it's deficient in potassium or when potassium plasma levels are low. Mira la figura 9.4: Renal tubular sites of potassium reabsorption and secretion



*Regulation of potassium secretion in intercalated cells and principal cells:

Intercalated cells are important in the acid/base balance, and they have H^+/ K^+ ATPase on the luminal surface and Na^+/K^+ ATPase on the basal surface, if we increase the activity of the H^+/K^+ ATPase, potassium reabsorption increases, and we need the net reabsorption of potassium when it's depleted in the body(hypokalaemia), the sodium potassium pump is mainly affected by levels of potassium in blood. Mira la figura 9.5: Late Distal and Cortical Collecting Tubules Intercalated Cells –Reabsorb K+



Hyperkalemia increases the activity of the sodium potassium pump so that it creates an intracellular gradient and gets secreted while its reabsorption decreases (the activity of H^+/K^+ ATPase is decreased).

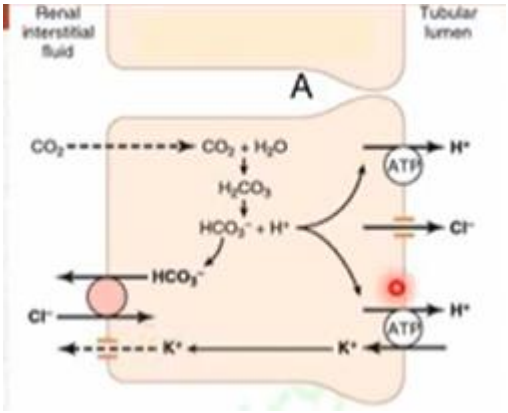
Acidosis causes H^+ to be secreted and so it encourages potassium to be reabsorbed, the opposite happens in alkalosis.

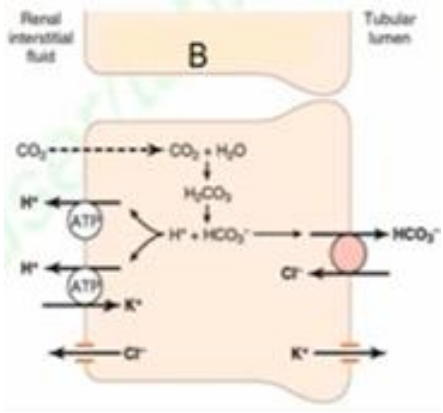
There are two types of intercalated cells: Type A, Type B

In both A and B we don't rely on Na+ /K+ ATPase but rather on ATPase activity of the proton pumps themselves

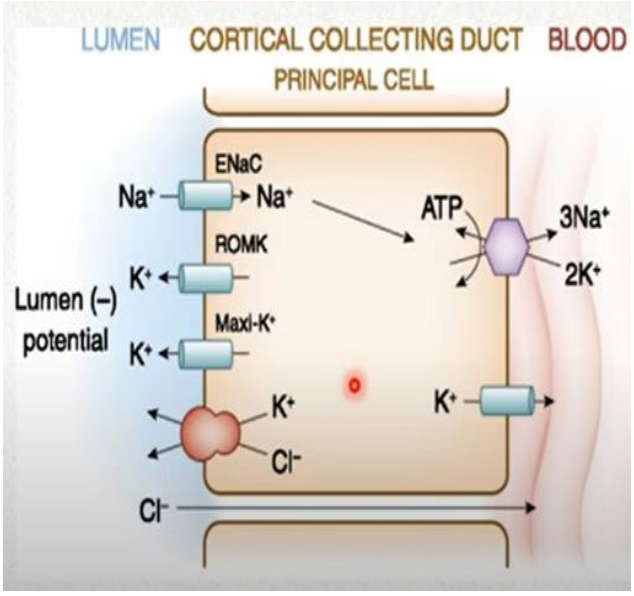
In type A: the H^+ ATPase and the H^+/K^+ ATPase are facing the tubular lumen and we expect to have H^+ secretion and potassium reabsorption, it is active mainly when the body is short on potassium-keep in mind that the sodium potassium pump is responsible for the gradient even though it's not showing on the figure.

In type B: the H^+/K^+ ATPase is on the basal surface (facing the capillaries) whilst the Cl^-/HCO_3^- is on the apical/ tubular lumen. Mira las figuras 9.6,9.7





Generally, in the DC an collecting tubules potassium is secreted unless the body is hypokalaemic we'll have net reabsorption, in case of hyperkalaemia we'll have secretion by principal cells (look at the Aldosterone sites/ENaC channels), the more the sodium potassium pump works, the more sodium gets reabsorbed by ENaC channels, K^+ accumulates in cells and gets secreted by ROMK and big or Maxi-K^+ (leak channels), keep in mind that Aldosterone is the major regulator of potassium secretion and potassium levels. Mira la figura 9.8: Potassium Secretion by Principal Cells



Maxi has high conductance for potassium

Control of cortical collecting tubule (principal cells) K^+ secretion:

1.Extracellular K^+ concentration: as it increases it increases K^+ secretion-by the work of gradient (concentration and electrochemical), sodium potassium pump, direct effect on adrenal gland to increase aldosterone secretion.

2.Aldosteron: increases K^+ secretion in principle cells (pump+perm).

3. Sodium(volume delivery) or tubular flow rate: when we have extracellular fluid volume expansion as a result of sodium, when GFR is high, tubular flow rate increases(ml of tubular fluid passing a segment/min) like blood flow rate, when sodium levels are high in tubules this will cause volume expansion(same effect with diuretics),this will have a flushing or washing effect on potassium in tubules ,and as potassium is being secreted there will still be a difference in gradient(increased gradient) because the cell will start from zero more often! مش عم بلحق أسكر فجوة الفرق بتركيز البوتاسيوم بيني كخلية و بين المي بالأنبوب لأنه زي النهر الجاري بضل يتجدد و عم بضل أبلش من أول و جديد

*if the tubular flow rate is low the cell will be able to alleviate the gradient and so potassium secretion will be limited.

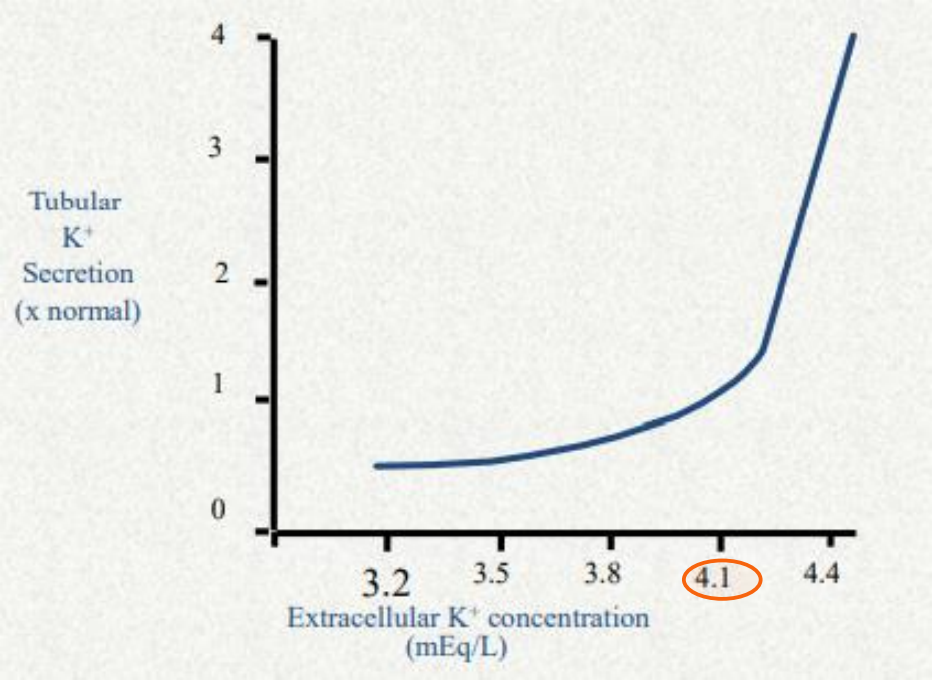
The more flow rate the more flushing of potassium and the more secretion of potassium.

4. Acid - base status:

acidosis: decreases K+ secretion ***less sodium potassium ATPase action***

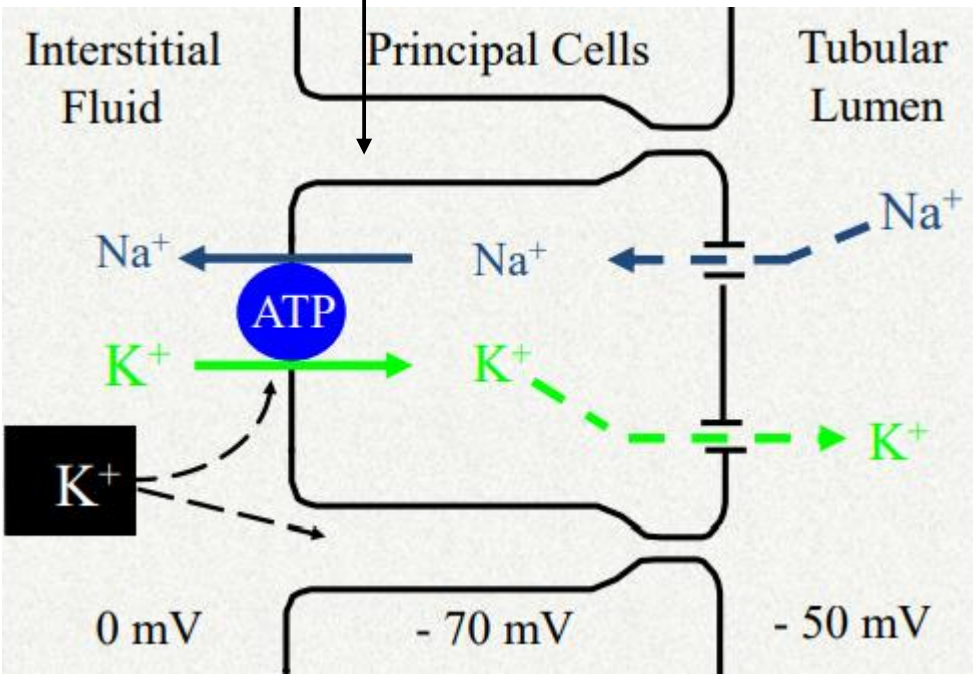
- alkalosis: increases K+ secretion ***vice versa***

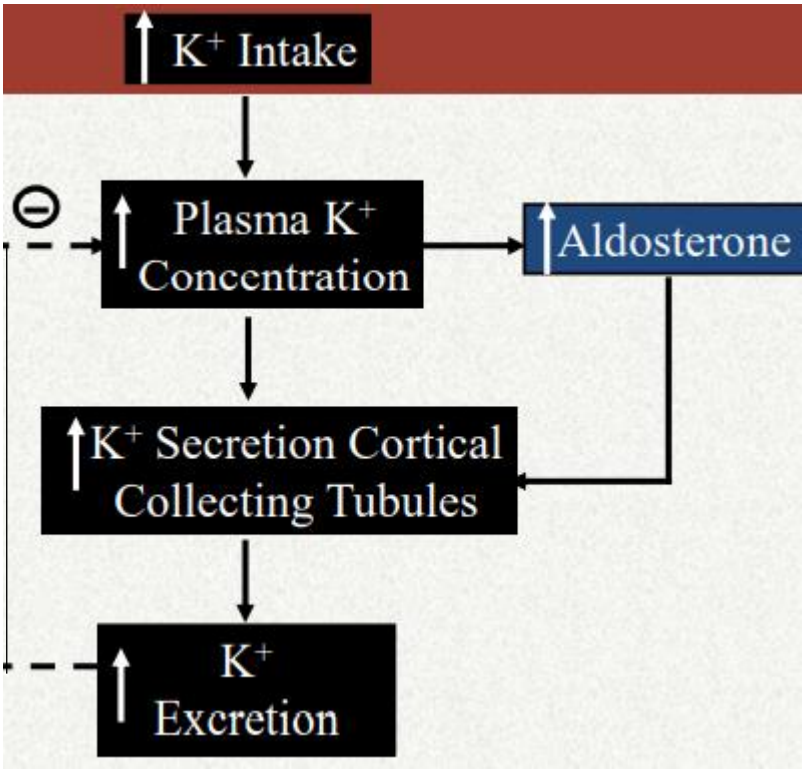
Effect of extracellular potassium on secretion of potassium: Mira la figura 9.9



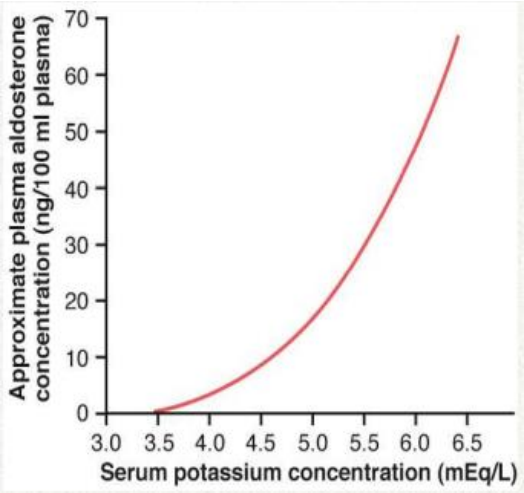
Once extracellular potassium concentration exceeds the normal (4.1) any increase in concentration highly increases tubular potassium secretion (very potent through the mechanisms previously mentioned).

Mira la figura 9.10

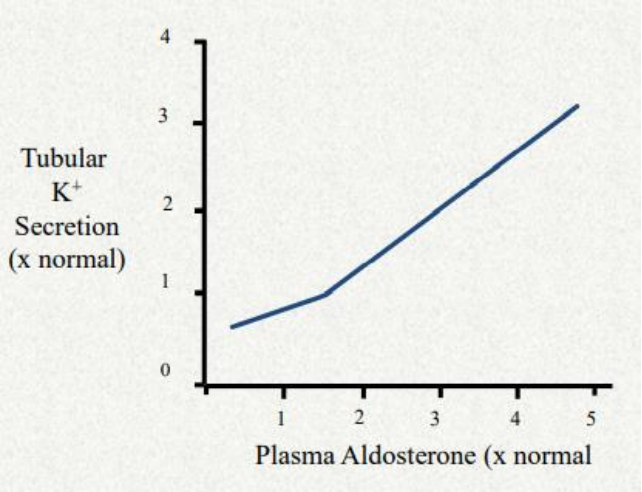




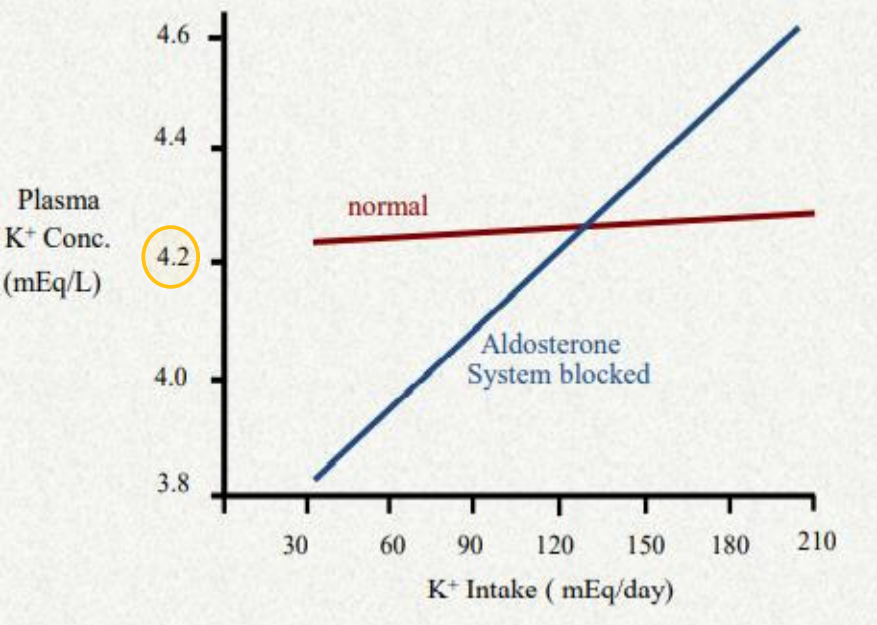
Normally, if you double or even triple your potassium intake, its extracellular concentration will increase, and the potent mechanism of secretion will counterbalance all of that, so you can eat 3 bananas and not worry because secretion and excretion will efficiently increase and prevent hyperkalemia.



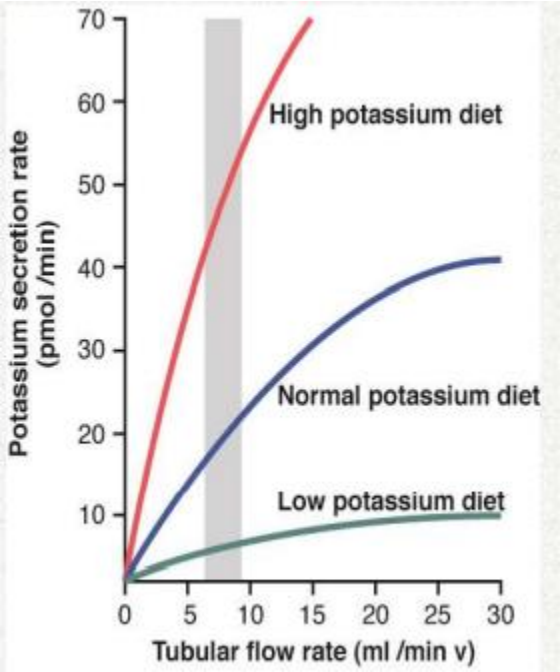
Increased serum K^+ stimulates aldosterone secretion (direct relationship).



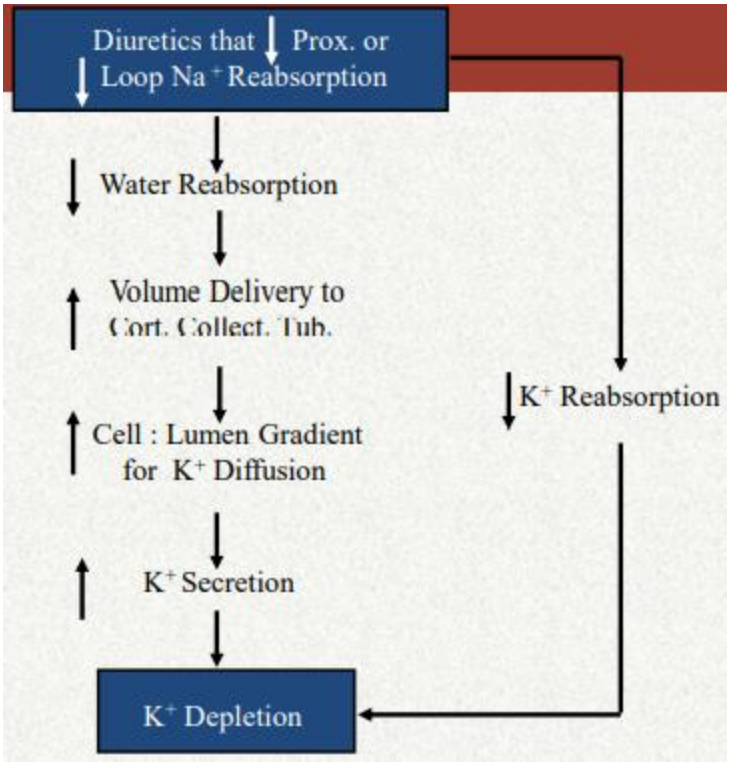
Effect of aldosterone on K^+ secretion.



Effect of changes in K^+ intake on plasma K+ conc. after blocking the aldosterone system-when there are many factors affecting a subject of study, we eliminate one of them to have a better understanding of its contribution- so when we block aldosterone by removing the adrenal gland and infuse it at a constant rate meaning that it no longer responds to feedback many fluctuations happen and this is not compatible with life.



Effect of collecting tubular flow rate on K+ secretion: tubular flow rate affects potassium secretion and shines best when potassium intake is normal or high, more GFR,more filtration load, more tubular potassium, clearer observation of flow rate effect.



Same principle of flow rate and potassium washing seen with diuretics (high flow rate due to decreased reabsorption of water)

The diuretic after a while reduces blood pressure and thus increase aldosterone → increase secretion of k resulting more depletion of potassium in blood

https://www.youtube.com/watch?v=khdoXB5PtpQ