Homeostasis of electrolytes (k+)

- A 26-year-old woman recently adopted a healthier diet to eat more fruits and vegetables. As a result, her potassium intake increased from 80 to 160 mmol/day. Which of the following conditions would you expect to find 2 weeks after she increased her potassium intake, compared with before the increase?

	Potassium Excretion Rate	Sodium Excretion Rate	Plasma Aldosterone Concentration	Plasma Potassium Concentration
A)	↔	↔	↑	Large increase (>1 mmol/l)
B)	↔	↓	↑	Small increase (<1 mmol/l)
C)	↑ 2×	↔	↑	Small increase (<1 mmol/l)
D)	↑ 2×	↑	↓	Large increase (>1 mmol/l)
E)	↑ 2×	↑	↔	Large increase (>1 mmol/l)

-mechanisms of regulating k+ is mainly about aldosterone, Aldosterone increases the amount of k+ excretion when its concentration is increased.

-the low increase in plasma k+ concentration tells us that many things occurred in order to prevent vast changes

Normal potassium intake, distribution, and output from the body

-k+ concentration is higher intracellularly

in a 70kg person the amount of icf is 28l and ecf is 14l

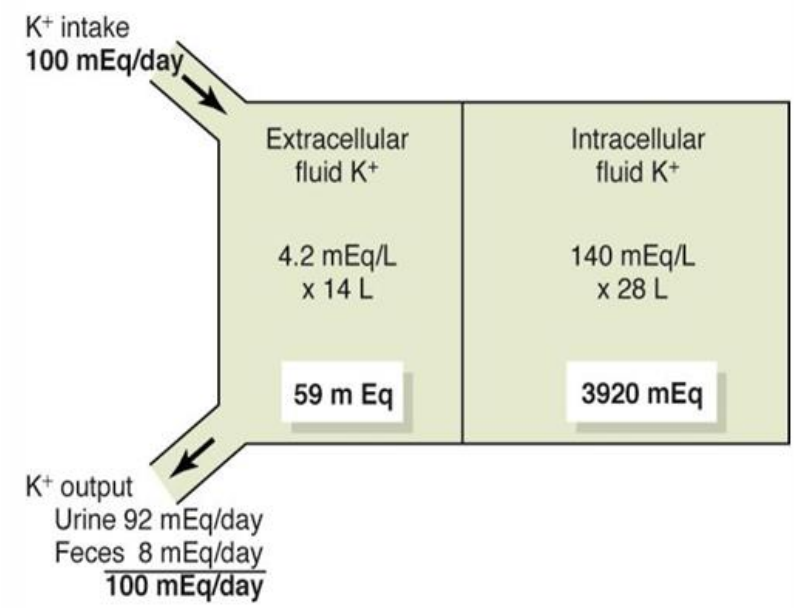
-we normally have :

3920 Meq of k+ per 28l of icf = 140mEq per liter

And 4.2 mEq/l in ecf

-since we have a little amount in ecf, this means that any tiny change in k+ concentration in ecf will make major effects.

-our body's homeostasis depends on having k+ kept within a very narrow window in plasma (only +/- 0.3 fluctuations are allowed)



-the average daily intake of k+ is 100 mEq

-note: in ecf if concentration of k+ is <4.2 mEq/l =hypokalemia and if its higher than that =hyperkalemia

-kidney is the major controller of k+ concentrations; 92mEq of k+ is released in urine daily , while only 8 mEq is released in feces daily.

-two lines of defense against k+ fluctuations :

1-redistribution between inta and extracellular compartments: so if you eat a k+ filled meal , we will have a direct redistribution from the extra to intracellular compartment (intracellular compartment acts as a reservoir of k+) (k+ stays there until kidney excretes the extra amounts).

2- kidney balances between the input and output of k+

Effects of severe hyperkalemia :

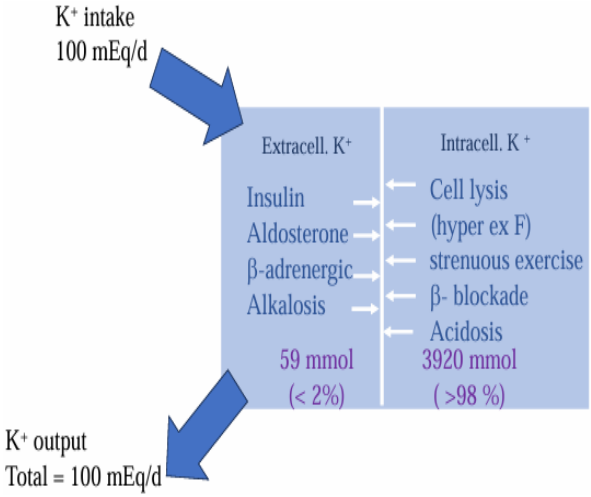
1- Partial depolarization of cell membranes
2- Cardiac toxicity (ventricular fibrillation or asystole)

Effects of severe hypokalemia:

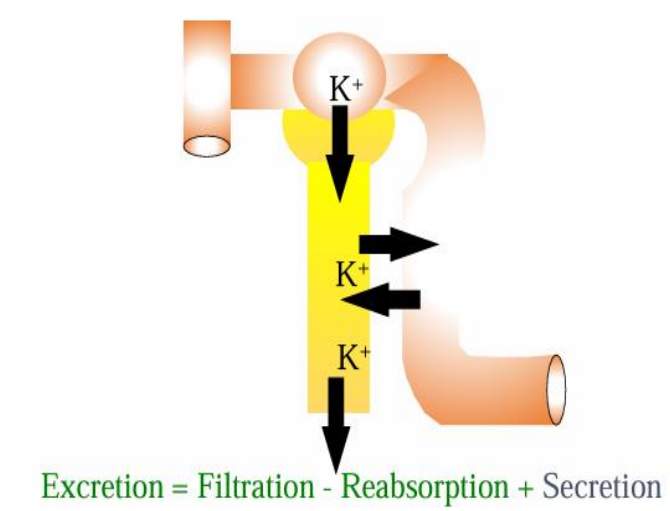
1- Hyperpolarization of cell membranes
2- Fatigue, muscle weakness
3- hypoventilation
4- delayed ventricular repolarization

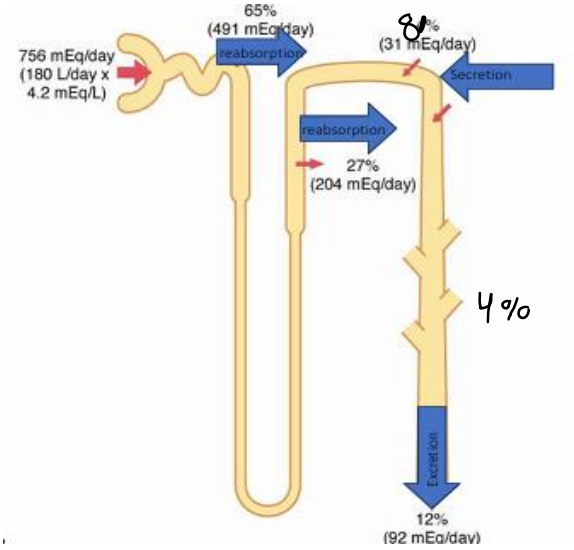
-factors that affect the redistribution of k+ between intra and extracellular fluids:

From extra to intracellular	From intra to extracellular
Insulin: it is secreted after a meal; it increases the uptake of k+ by the cells.	Cell lysis: like in hemolysis
Aldosterone: shifts k+ intracellularly So people with excessive aldosterone like Crohn's syndrome will have hypokalemia And people with Addison's will have hyperkalemia	Increased osmolarity in ecf: fluids will move extracellularly, so concentration of k+ intracellularly increases, so k+ will move extracellularly.
Beta-adrenergic receptors (especially by epinephrine)	Strenuous exercise: it usually only causes mild hyperkalemia, however, it has a big effect in case the person has diabetes of takes beta-adrenergic blockers it causes serious hyperkalemia.
Ph imbalance (alkalosis): more uptake of k+ into cells due to increased activity of Na/k atpase	Beta-blockers
	Acidosis: Na/k atpase activity is inhibited by acidosis



Control of potassium excretion





-filtered load of k+ depends on:

1-its concentration in blood

2-glomerular filtration rate

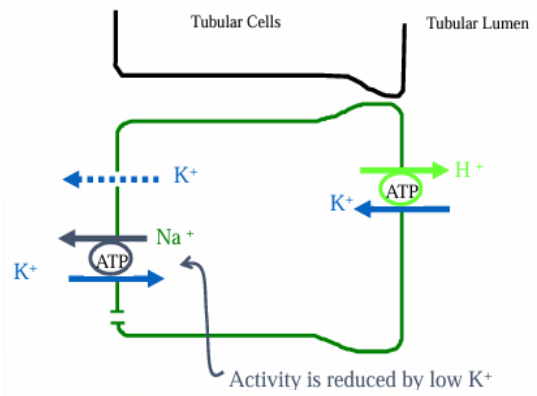
Since gfr is highly regulated, k+'s concentration in blood is the one that has a high impact.

- k+ undergoes reabsorption (in pct and thick ascending limb of Henly),as you can see the % of reabsorption aren't highly variable, which means that the body doesn't apply so much adjustment on it

-the body relies mostly on secretion, which happens in late Dct mainly in principal cells . according to the secretion rate the final excretion of k+ is decided.

Note: secretion 8% on late dct and 4% in the last parts of tubule, so total=12% of secretion and this 12% of secretion is responsible for 12% of excretion. (this isn't a fixed number , because it changes according to k+ intake ,tendency of k+ balance etc)

-in the late DCT we have intercalated cells (especially type a) ,they contain a H+/K+ atpase pump, this pump secretes H+ in exchange of K+ reabsorption. Our body needs this process in the case of hypokalemia.



Imp Note: Na/K+ atpase gets affected by : the amount of k+ in plasma , the more k+ is available in ecf (higher tendency for hyperkalemia), the more active this pump will be and vice versa

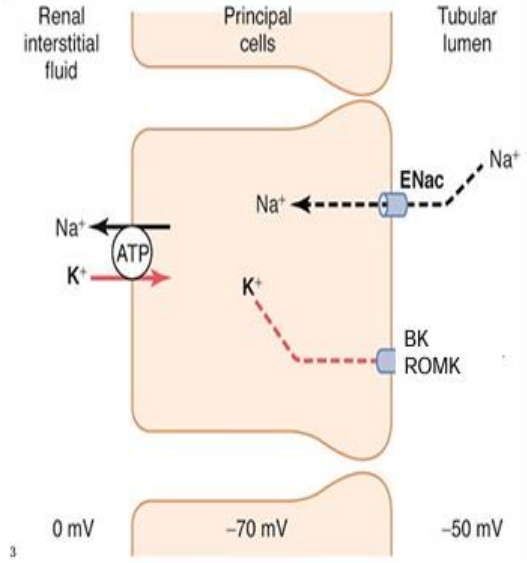
Potassium secretion by principal cells:

- Na/K atpase causes a low gradient in Na and the ENac channel reabsorbs Na in the luminal side,

-the amount Na that enters for exchange to the k+ that exists will increase its concentration intracellularly.

-when there is a high permeability of k+ on the luminal side because of BK (high capacity k+ channel) and ROMK (renal outer medullary k+ channel) channels, secretion of k+ increases.

-when there is a high concentration of aldosterone, BK and ROMK channels become more permeable and the activity of Na/k atpase increases. So more secretion of k+ occurs.



-aldosterone stimuli:

1-hyperkalemia 2-angiotensin 2 in htn

Control of Cortical Collecting Tubule (Principal Cells):

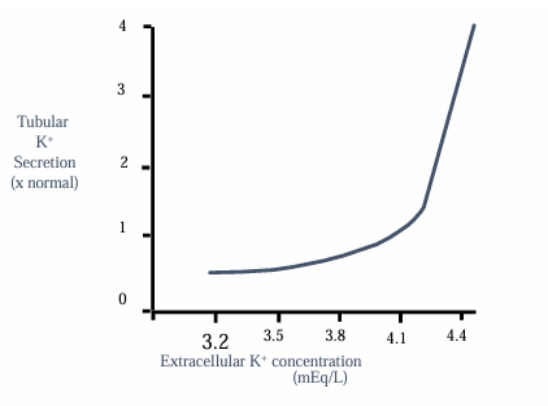
1- K+ Secretion : it is affected by Extracellular K+ concentration (increases K+ secretion, because of Na/k atpase increased activity and because of physical factors that favor excretion due to powers that push k+ to go through secretion)
2- Aldosterone : increases K+ secretion
3- Sodium (volume) delivery: increases K+ secretion (when we have a high salt intake, we will have more fluids filtered , which causes volume expansion in tubules and this increases GFR and therefore there will be increased in flushing (washing out) of the Na that underwent secretion the distal part)
4- Acid-base status:- acidosis :decreases K+ secretion due to reduced activity of Na/K atpase

alkalosis : increases K+ secretion (high activity of Na/k atpase)

relationship between extracellular k+ concentration with tubular k+ secretion:

normal extracellular k+ concentration=4.2mEq/l

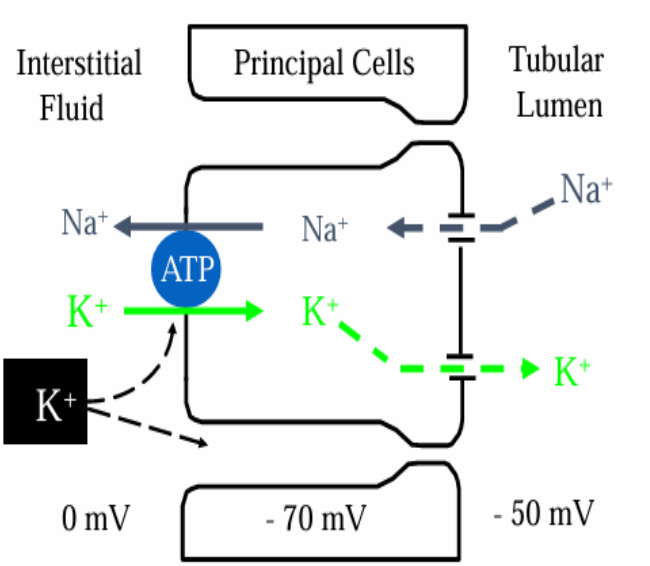
if we noticed the tubular k+ secretion (will become excretion later on) we will see that secretion occurs when k+ concentrations are lower than 4.2 , which means that the system prepares itself for secretion before we reach the ideal concentration, and once we reach it the secretion levels rise quickly.



-on the other hand, as we can notice when the concentration is lower than 4.2 the secretion is very low , this shows that we have a powerful feedback system.

-the system is more robust in the case of hyperkalemia

this image shows the factors that affect the k+ secretion in principal cells and they are:



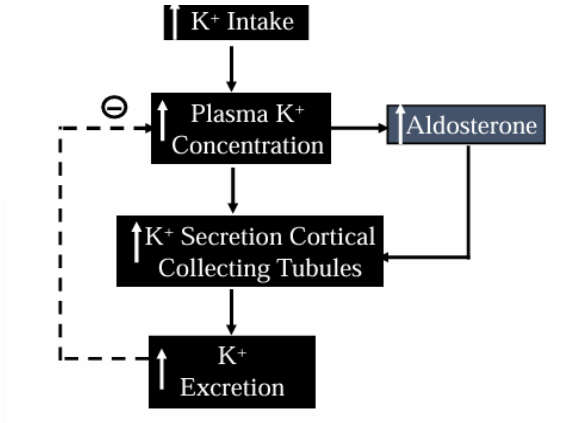
1)Na/k atpase activity which is affected by extracellular k+ level

-When extracellular k+ levels increase : 1- Na/k atpase activity increases 2-gradient favoring secretion increase in paracellular route.

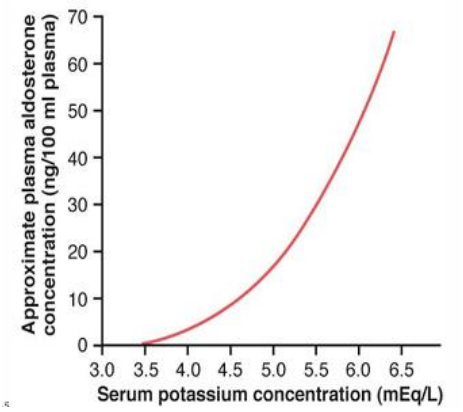
2)when aldosterone is released , activity of Atpase increases

3)tubular flow rate: the higher the flow rate the more washing of k+ happens, so k+ levels in tubular fluid remain low which favors secretion.

what happens when we have a high k+ intake ?



How does aldosterone respond to changes in k+ levels?



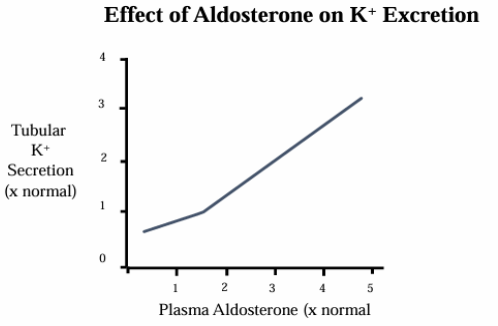
when we have a 4.2 concentration of k+ , the aldosterone concn. =8ng/100ml; even in normal k+ concentrations we have a good amount of aldosterone. The more k+ concentration increases the more aldosterone concentration increases.

This means that aldosterone gets stimulated when k+ concentration increases and at the same time gets inhibited on the lower side of serum potassium concentration.

Direct effect of aldosterone on k+ excretion:

another study to prove the relationship between them.

They realized that the more the aldosterone secretion is increased , the more the k+ secretion increases.



What will happen if we blocked the aldosterone system?

another study

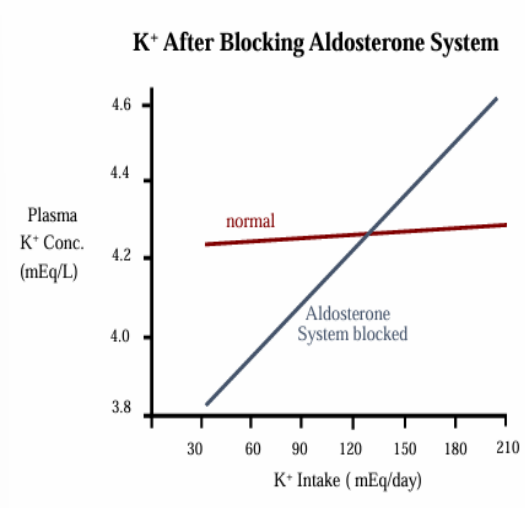
we bring two animals ; one with an intact adrenal cortex (animal A) and one without adrenal cortex (animal b)

we will apply a constant effusion of aldosterone on animal b (so that were able to keep the aldosterone in its body constant and we have the ability to inhibit its feedback system)

They found that whenever we increase its intake of k+ the k+ concentration in plasma stays constant.

When animal b was given an increased amount of k+,the k+ concentration increases.

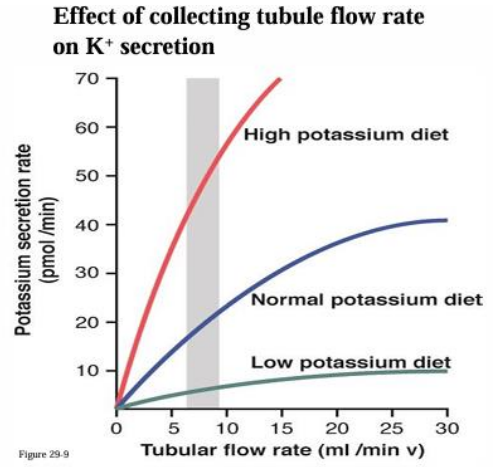
This experiment tells us that there are no other mechanisms that can perform Aldosteron's function . in other words ;aldosterone is the major regulator of k+ in the body.



Tubular flow rate effect on k+ secretion

The more k+ intake someone consumes, the more the effect of tubular flow rate on k+ concentration increases.

So if someone has a low k+ diet and takes a diuretic, they will not get affected in secretion because of tubular flow rate like the people who have a high k+ diet . (the more k+ you take in your diet,the more diuretics can increase your secretion)



diuretics effect:

diuretics decrease water reabsorption; so the expansion in tubules due to fluids increase , so the flow rate increases and flushing and secretion of k+ increases and therefore theses patients have a higher risk of hypokalemia.