Potassium regulation

-Kidney is a **major** regulator for potassium balance.

The kidney cannot reduce K^+ excretion to the same low levels as they can for Na^+. Therefore hypokalemia can develop in individuals placed on a K+ deficient diet (less than 10-15 mEq intake per day). In case of K+ depletion, intercalated cells can also reabsorb K+ in.

K^+-Reabsorption

- Potassium concentration in the plasma equals 4 mEq/L (3.5-5.5 mEq/l)
- Hyperkalemia >5.5 Hypokalemia <3.5
- When K^+ reaches 7-8mEq\L plus ECG changes → top emergency that requires dialysis (hemo-or peritoneal)
- K^+-balance :

  K^+ intake=K^+ output= from 50-200mEqv (Avg 100Eqv\day). (92-95 mEq) through the kidneys and the rest is removed by other routes
- Renal Failure→ hyperkalemia

Renal Failure does not cause hypernatrimea because when Na increases H_2O increases too thus Na+ remains relatively constant or slightly decreased.

K^+ - Reabsorption

- K contributes to RMP (increase or decrease in K_o affects RMP and thus membrane excitability.
- $\downarrow K^+ \rightarrow$ hyperpolarization and cardiac arrest
- $\uparrow K^+ \rightarrow$ increased excitability and arrhythmia.
- "K^+ Clearance"

$$C_{K^+} = \frac{60 \text{ mEq/L}}{4 \text{ mEq}} * 1 \text{ ml/min}$$

= 15 ml/min

Which is much more than that for C_{Na+}

Potassium regulation

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- Potassium is found mainly as INTRACELLULAR ion in a concentration of 150 mEq\L
- If we want to calculate how much the total potassium inside the cell, we simply multiply 28L (the intracellular volume) by 150mEq/l
- To calculate the extracellular total potassium we multiply 4mEq\L by 14L(the extracellular volume) which is equal about 56 mEq (generally speaking =60mEqv)

Potassium regulation

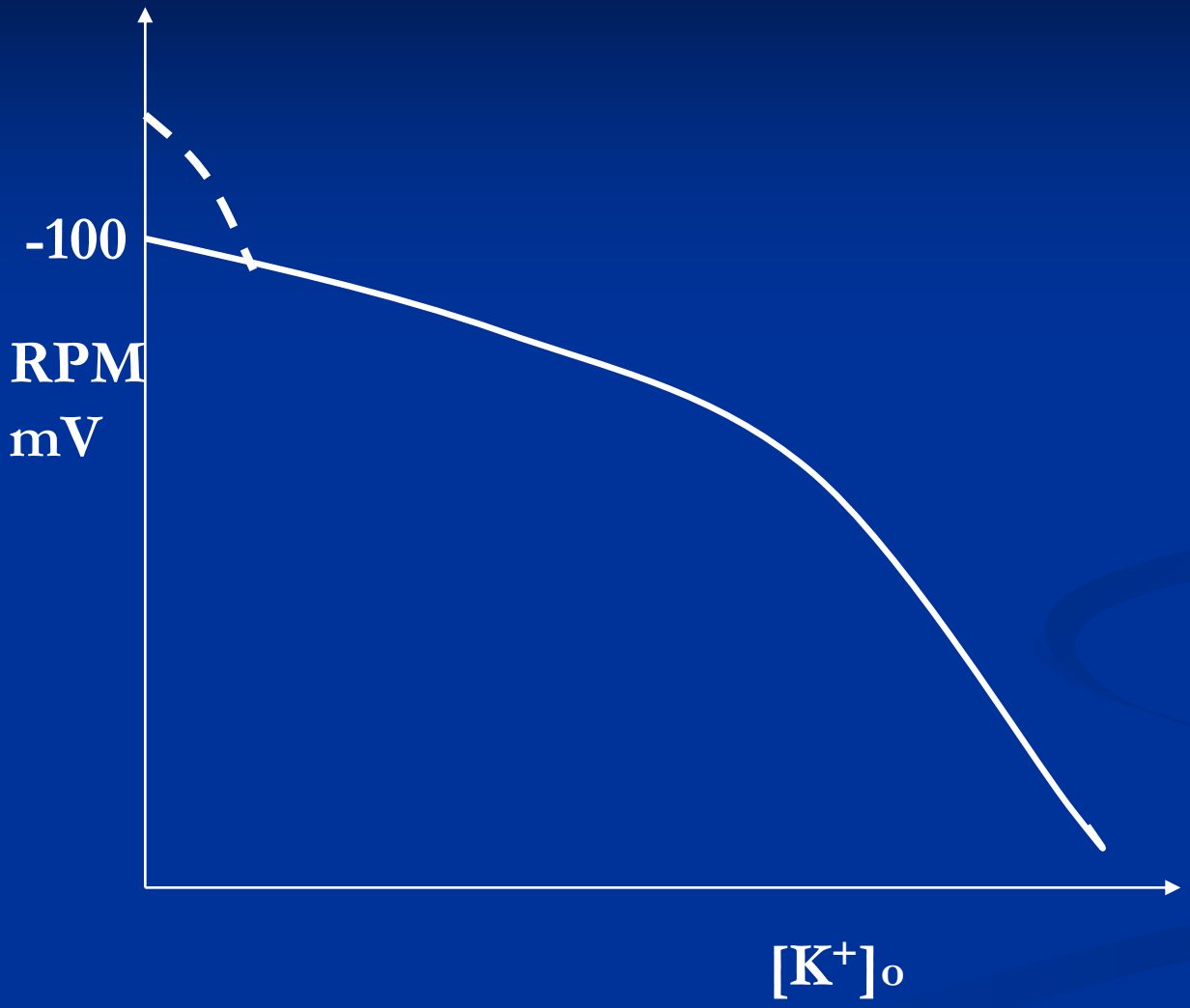
- In each large meal we ingest 50 mM of K^+.
- Suppose that you ingest 50 mM of K^+ in one meal, which are going to be distributed in the 14L of the ECF…this will increase plasma K^+ by 3.6mEqv/L (this is above normal…this example is very hypothetical). It makes potassium of extracellular concentration to reach 7.6 mM/l!! Very high and dangerous level…we cannot withstand!

Potassium regulation

- After the meal: **K^+ does not remain in the ECF. In the contrary, after each meal we push the ingested K^+ inside the cell which acts as a BANK for potassium…this is the function of insulin which is secreted immediately after we start eating the meal. Note that the increase in intracellular concentration of potassium is harmless…*Remember Nernst Equation***

Look at the figure next slide and notice the following:

- **This resembles the relationship between potassium outside the cell and the resting membrane potential RMP given by Nernst's Equation.**
- **The more the $[K^+]_o$, the less the negativity (less –ve RMP)…This affect the voltage sensitive channels…it cancel the FRAP (fast response action potential).**


-100
RPM
mV
[K+]o

Clinical note:

- A patient with Diabetic Ketoacidosis (a life-threatening complication in patients with untreated diabetes mellitus especially type 1 DM) came to your clinic with hyperkalemia, how you manage him/her?
- We know that deficiency of insulin will cause hyperkalemia when the body ingests a meal containing potassium.
- When insulin is given → hypokalemia
- We must give K^+ supplement with insulin infusion.
- Management of diabetic ketoacidosis is by giving INSULIN and POTASSIUM

Potassium regulation

- 2) kidney management

remember that clearance of potassium is *about* 15 ml\min

(depends on the K^+ intake)

- Potassium is FREELY filtered. Filtered load equals 180L\day* 4 mEq/l= 720 mEq per day.
- Now how much is excreted??
- As I mentioned earlier, 92-95 mEq will be excreted by the kidney if the intake was 100 mEq.
- Where reabsorption takes place ?

a)2/3 of total filtered potassium is absorbed in proximal tubules (65%)

b)25% from thick ascending part of Henle's loop

Potassium regulation

- note that 10% of fraction filtered has NOT been reabsorbed …this is equal to 72 mEq….but 92 mEq must be excreted/D. …where the additional 20 mEq comes from?
- So the amount of potassium in the urine has 2 sources:
- (1) filtered NOT reabsorbed (2\3)
- (2) secreted (1\3)
- -We have a type of cells called principal cells found in late distal tubules and collecting ducts, these cells will secrete potassium by the following mechanism:

- increased sodium entry into the cell across the luminal side will activate Na^+-K^+ pump at the basolateral side which will increase the intracellular concentration of K^+ $\rightarrow$ increasing a driving force for K^+ secretion

Potassium regulation

- How can we increase the K^+ secretion?? By:
- 1)activating Na^+-K^+ pump
- 2)make more K^+ channels at the luminal side
- 3)keep the gradient by removing the luminal K^+…through increasing TF flow rate…this what diuretics do…they increase flow rate.
- These are the 3 mechanisms by which potassium secretion is altered.

Potassium regulation

- When you eat too much potassium, most of the additional execreted potassium in the urine comes from secretion. The filtered not reabsorbed part is almos tconstant regardless the alteration in K^+ intake.
- Back to our example of eating a meal containing K^+ which will have a potential of increasing ECF-K^+ …remember that the first mechanism was to push K^+ inside the cell with the help of insulin …now comes the role of the kidney!!
- -Increase K^+ in ECF will activate Na^+-K^+ pump and will activate aldosterone secretion which in turn increases potassium secretion

Potassium regulation

- **How does aldosterone works?**
- Simply it **enhances sodium entry** (reabsorption) to the principal cell initiating the steps for increasing potassium secretion as mentioned earlier.

Clinical notes:

- Acute Acidosis inhibit potassium secretion causing hyperkalemia
- H^+ exchanges with K^+ so hydrogen ions will enter the cell and potassium ions will exit through the basolateral membrane causing hyperkalemia.
- For every ↓ in pH of 0.1 unit→↑ K. 0.2 to 1.7 mEq/L.

Note that the term hyperkalemia may not mean a total increase in the K^+ in the body… *it means an increase in blood K^+*

- Chronic acidosis: it inhibits *sodium-chloride reabsorption* which will inhibit water absorption indeed…leading to an increase in flow rate and thus, washing out K+(the same effect as diuretics) resulting in hypokalemia
- Addison's disease which means insufficient amount of adrenal gland secretions including aldosterone will induce hyperkalemia

Clinical notes:

- Conn syndrome which is characterized by increase amount of aldosterone will cause hypertension and hypokalemia
- Hyperosmolirity will drive water outside the cells and that's make the potassium concentration inside the cell higher (the cell actually will shrink), therefore, driving potassium outside the cell causing hyperkalemia
- *For each 10 mOsm increase in osmolarity, this will make 0.4-0.8 mEq increase in extracellular potassium concentration*
- Remember that the normal osmolarity in the plasma is 284mOsm (285-310)
- Epinephrine (through β-receptor) pushes potassium inside the cells, so giving beta blocker as propranolol will cause hyperkalemia.
- Exercise through α-receptors causes hyperkalemia. Thus, Those who take beta-blockers and do severe exercise might suffer from serious hyperkalemia.
- Burns and cell lysis would increase K_o

Calcium		Increase Ca^{++} Reabsorption	Decrease Ca^{++} Reabsorption
Proximal	65%	Volume Contraction	Volume Expansion
TAL	25%	PTH, Clacitonin	Furosemide
DCT	8%	PTH VitD AVP (ADH) Alkalosis Thiazide	Phosphate depletion
Coll Ducts	1%	Amiloride	

Ca^{++} Homeostasis

- *PTH is the most important hormone for regulating Ca^{++} reabsorption
- *Most of the Ca^{++} is in the bone which serve as a reservoir (98%) and 2%in the plasma. Of the 2% of the plasma almost 50%bound and 50%free. We care about the free portion.
- The free part of which 99% is reabsorbed and 1% is excreted