Physiology of Urogenital system

Potassium

*As we know that the intracellular K+ is high and extracellular K+ is low.

* The normal K+ concentration in the extracellular matrix is **3.5 to 5.5 mEq/L**, if the concentration goes below 3.5 then we call this situation (**Hypokalemia**) , and if it was above 5.5 we call it (**Hyperkalemia**) .

Remember: The equilibrium potential of potassium ions (using Nernst equation) approximately equals -90 mV (at equilibrium there is no net movement of K+ across the membrane).

*Potassium is the main ion that determines the **resting membrane potential (RMP)** , the permeability of the membrane for the K+ is the highest compared with other ions . So the RMP in many cells is around the K+ equilibrium potential. The K+ outside the cell is what we care about because it is the one that affect the resting membrane potential, **when potassium increases outside the cell, the RMP becomes less negative** which means two things:

1- The RMP will become **closer to the threshold.**

2-Shifting the permeability of membrane from (**fast response action potential**) to (**slow response action potential**) , this is because the fast Na+ channels works only when action potential started from very negative RMP so when the RMP is less negative , then the action potential will depends mainly on the **slow Na+ channels**.

Clinically

Hypokalemia (below 3.5) makes the RMP more negative (hyperpolarization) so the depolarization will be harder, so the muscles cannot form action potential which means **Muscle Paralysis**.

Hyperkalemia (above 5.5) mainly affects the heart causing **Arrhythmias**.

*As we said, the normal K+ concentration is 3.5-5.5 mEq/L , on average 4 mEq/L in plasma or interstitial fluid . So if we know that the volume of our extracellular fluid is 14 L then (14 L x 4 mEq/L = 56 mEq) which is the total amount of K+ outside the cells.

If we ingest one single meal that contains 50 mEq of K+ , so (50 mEq / 14 L = 3.5 mEq / L) which is the increase in the K+ concentration caused by that meal , so the total concentration will become around 7.5 mEq/L .

In the case of Acute renal failure, there will be an increase in the urea , creatinine, uric acid in the blood , but the most important is the K+ concentration which also increases , so if the K+ reaches more than 7 mEq/L with the specific ECG changes we should take the patient directly to the **dialysis** (**hemodialysis** or **peritoneal dialysis** in which we put the fluid inside the abdominal cavity (2 L) and use the peritoneum as an exchange membrane , after few hours we flush out the fluid, we keep doing this procedure during the period of 24-48 hours) .

* After we eat a meal, the pancreas will secrete more **insulin**, because the main function of insulin is to push the K+ inside the cells (which is a big reservoir for K+), in the next few hours it will be released slowly and excreted through the kidneys outside the body. So in the case of **diabetes mellitus we expect hyperkalemia** because of insulin depletion .But when we start treating the patient with insulin, the K+ will be pushed inside the cells in a great manner so we will end up with Hypokalemia , because of that, usually the doctors give the patient potassium with every dose of insulin , even though he started with hyperkalemia .

*Also in the case of **acidosis** there will be accumulation of H+ that will cause **hyperkalemia** by 2 ways:

1 - The accumulated H+ will be **exchanged with the K+** through the membrane: In the case of acidosis the cells of the blood (RBCs) will push the H+ inside and the K+ outside causing hyperkalemia.

2 - It will **impede the potassium excretion** by the kidneys, How? Acidosis inhibits Na+/K+ pump which prevent secretion of K+ outside the body.

Note 1: each 0.1 decrease in pH will increase the K+ concentration between 0.2-1.7 mEq.
For each 10 mOsm increase in osmalrity, this will make 0.4-0.8 mEqv increase in potassium extracellular concentration.

Note 2: chronic acidosis might do the opposite of acute acidosis, because it inhibits Na+ reabsorption so there will be more Na+ delivered to distal tubules, more water, more washing out, loss of K+, hypokalemia .

Note 3: 7 In the case of **alkalosis**; there will be increase in K+ excretion so we expect the patient to have **hypokalemia**

*K+ input must equal K+ output , K+ input per day equals around 100 mEq so it's the same amount of K+ output , 92% of them will excreted by the kidney through the urine and the other 8% by other types of excretion like the GI . So the major K+ regulator is the kidneys , we start with filtration , the filtered load of k+ per day is equal to (GFR x Concentration of K+ extracellularly) which equals (180 L/day x 4mEq/L= 720 mEq/day) , 65 % is reabsorbed in proximal tubules and 25% reabsorbed in the thick ascending loop of Henle , the rest is 10% which equals 72 mEq .

*Potassium in the urine **, two-thirds of it comes from the filtered and not reabsorbed K+** and **one-third from the secretion** , if you eat too much K+ (200 mEq for example) the additional amount will excreted by secretion , so **most of the K+ in the urine comes from the secretion** .

* Talking about the cells of renal tubules , the K+ outside the cells (in the ECM) equals 4 mEq/L , and inside it 150 mEq/L , in the membrane we have **Na+/K+ pump** and **K+ channels** , there is a gradient

between K+ inside the cells (high) and K+ in the lumen (low) , if we keep these gradient high then we can keep a constant K+ excretion , and one way to do this is to **increase the flow and wash out the K+ in the lumen** , this is done by giving the patient a **diuretic** , this condition may end up by having hypokalemia because of over-washing out .

Note: Anyone taking potassium – wasting diuretics like Lasix and Thiazide should make sure that the lost potassium is replaced by eating bananas, drinking juice or taking potassium pills. And it is recommended to do tests during the treatment period and check the potassium level in order to avoid ending up with hypokalemia.

So to increase potassium secretion we have 3 ways:

1- activate **Na+/K+ pump**.

2- Insert an activator in the **K+ Channel**.

3- **Keep the gradient** for K+ secretion high by more flow (diuretics).

* if we eat a meal with low K+ , the kidney will secrete part of these low K+ so there will be hypokalemia , but In the case of Na+ the kidney can handle more efficiently .

*Other factors that affect K+**: Aldosterone** activates the enzymes that makes ATP that activates Na+/K+ pump, and reabsorbs Na+ so it will increases the K+ excretion.

Exercise increases K+ extracellularly.

Beta receptors induce the entry of K+ to the cell, so **Beta-blockers** (like Atenolo) also increase K+ concentration. Thus, those who take beta-blockers and do severe exercise might suffer from severe hyperkalemia.

Increased osmolarity increases K+ outside the cells (the doctor said that the most important number about K+ metabolism is the normal extracellular concentration 3.5-5.5 mEq/L).

So let's summarize, the factors that may affect K+ homeostasis:

1-Insulin **2-Acid-Base balance** **3-Diuretics** **4-Aldosterone**
5-Exercise **6-Beta-Blockers** **7-Osmolarity**

Calcium

*Most of the kidney stones composed of calcium oxalate, so a patient with hypercalciuria is exposed to have a stones.

*Hypercalciuria : the calcium the urine is **more than 4 mg/kg body weight/day**.

*Ca++ concentration outside the cells = 10 mg/dl, 50% is bound to protein we don't care about it and the other 50 % (5 mg/dl or 50 mg/L) is free which is the one that is going to be filtered. The filtered load of Ca 2+ = 180 x 50 = 9 g or 9-10 g/day.

*99% of Ca++ is in the bone, 1% in the extracellular space, extremely small portion inside the cells.

*Around 10g of calcium filtered per day, 99% of the filtered calcium will be reabsorbed, 1% is excreted, **most of the reabsorption in the proximal tubule, smaller in the distal tubule**.

If you reabsorb Ca++ you will decrease its amount in the tubular fluid, thus overcoming the hypercalciuria.

There are two types of diuretics:

Furosemide (lasix) , decreases Ca++ reabsorbtion , shouldn't be given to a patient with hypercalciuria .

Thiazide , increases Ca++ reabsorption , so it can be given to a patient with hypercalciuria but it might causes hypercalcemia .

* The Ca++ enters the proximal tubular cells by **simple diffusion** (from high to low). And leaves actively; either primary active by **Ca++ pump** or secondary active by **Na+/Ca++ exchanger**.

*If a patient eats **salt-rich diet** (NaCl) ,then there will be too much Na+ delivered to the distal tubule , too much water with it , expansion of fluid in this area , dilution of Ca++ , **decreased reabsorption** .

* Increase fluid intake → dilution of Ca++ in the urine and inhibition of the crystals formation.

*Calcium is under the control of **3 hormones** (Vitamin D , PTH , Calcitonin)in **3 organs** (Bone , GI tract , Kidneys) .

PTH increases Ca++ reabsorption from the kidneys , the kidneys activate Vitamin D that causes more Ca++ absorption from the GI tract . So in the renal failure, no vitamin D, hypocalcemia , increases PTH , secondary hyperparathyroidism (most common cause of it is the renal failure) , PTH will take Ca++ from the bones causing Osteoporosis.

Water Reabsorption

Where water is reabsorbed in the nephron?

*65% in the proximal tubule , 15% in the descending loop of Henley , 0% in the ascending loop of Henle (important) , 10 % in the distal tubule , more than 9% in the collecting duct. So we **excrete less than 1%** of the water, from 125 ml of water we excrete 1 ml.

In the **collecting duct, the water reaborption if under the effect of ADH** that opens water channels **enhancing the reabsorption** , with no ADH the volume of urine may reach 20 liters/ day instead of 1.5 liters/day in the normal situation, which expose the patient to dehydration . Why we need to drink water?

* Water is a **solvent** that carries urea, creatinine , K+ , Na+ .. etc. Our body makes at minimum 700 milliOsm that must be removed from our body per day (at the bed rest) , but the average is 1000 milliOsm , osmolarity of urine is (1000 milliOsm / 1.5 L = 650 osmolarity) so the urine is kind of osmolar compared to the plasma (300) , but with too much water the urine will be hypoosmolar .

*Our kidneys can make the concentration of urine maximally **1400 milliOsm/L** , so to get rid of 700 milliOsm you need to make 0.5 L of urine and this is the minimum daily obligatory volume of urine (MDOVU) .

*So if you drink a salty water with an osmolarity of 2800 (double the concentrating ability of the kidneys), then your body should add an extra 1 liter (to make the osmolarity 1400), so you become thirsty.

***Oliguria**: In this case, the urine output is less than 0.5 liter daily, there no specific amount of minimum urine output per day and it has different values when comparing infants to adults, but the doctor believes that it is actually **300 ml / m square body surface area / day,** if the urine output below this number then we call this situation **oliguria.**

Note: Acute renal failure is characterized by two things:

1- Increase in urea and creatinine.

2- Decrease urine output (Oliguria) .

Good Luck =)