URO-GENITAL SYSTEM

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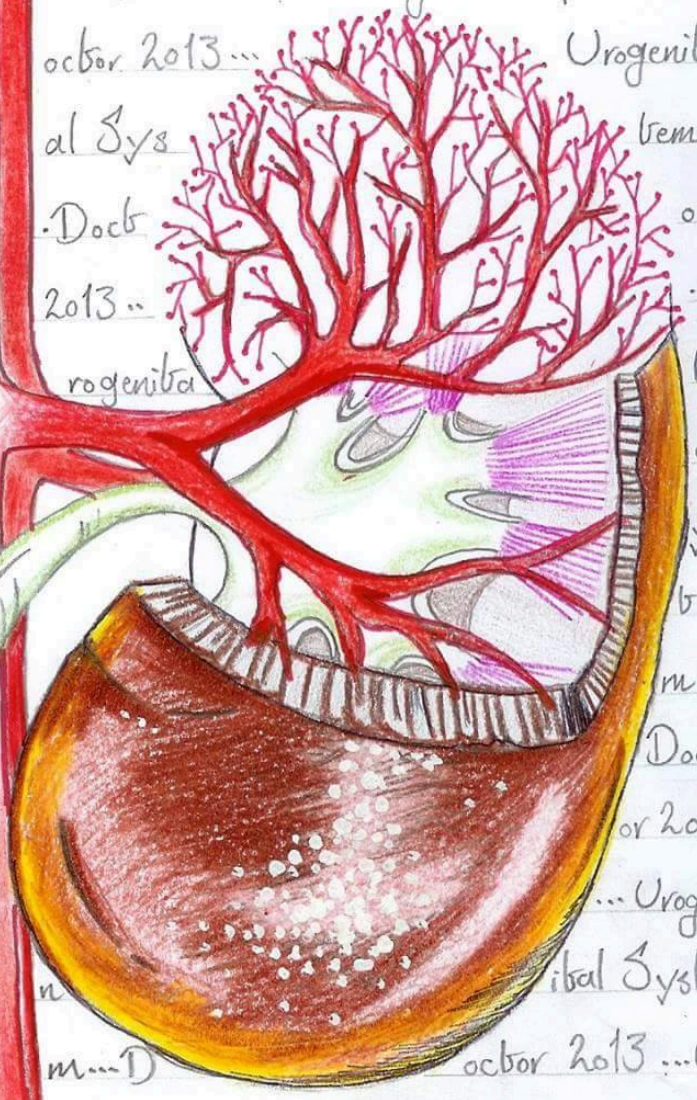

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Nernst equation

Resting membrane potential is negative, the more the potassium ions inside the less the negativity.

K+ in urine comes from 2 sources; one source is the filtered not reabsorbed, the other is from secreted K+ (and this is in case of too much potassium ingestion, most of K+ in urine is secreted at the distal part of the tubules.)

***Principle cells at the distal part of the tubules are responsible for K+ secretion. They reabsorb Na+ and secrete K+**.

They have an apical and basolateral sides.

To induce more potassium secretion, you have to keep in mind 3 things:

1) increase K+ concentration inside the cells i.e. increase the gradient between the cell and urine, this is achieved by activating Na+/K+ pump. So any drug that would inhibit this disrupts the gradient for K+ secretion

2) have potassium channels on the apical side of the cells.

3) remove potassium ions from the lumen to attain the gradient in favor of secretion.

* Anything that increases the flow of tubular fluid will result in more K+ secretion and hypokalemia. That's how diuretics induce hypokalemia; using diuretics keeps the fluid in tubules and thus increase flow at the distal part of tubules, thus remove potassium from lumen (more K+ secretion>> hypokalemia).

Some facts about secretion:

- Tubular secretion is the transfer of materials from peritubular capillaries to the renal tubular lumen.
- Tubular secretion is primarily the result of active transport.
- Usually only a few substances are secreted.

Aldosterone: a steroid that enters cells by simple diffusion and bind to its receptors, changing the machinery of the cell, transcription and translation of proteins.

It activates enzymes needed to make ATP, inserts K+ channels at the apical side.

It reabsorbs Na+ thus its concentration inside cells increases>> activation of Na+/K+ pump (to expel 3 Na+ and lets 2K+ inside). All this is to increase secretion of potassium.

In Addison disease: deficiency in adrenal cortical hormones like Aldosterone and Cortisone. (No aldosterone>> Hyperkalemia)

In Conns disease: too much aldosterone>> too much sodium reabsorption, too much water reabsorption, hypervolemia, hypertension (As you know hypertension is 90% primary, 10%

secondary and conns disease is one of the causes of the secondary hypertension)

>>Hypokalemia

How much total potassium in the ECF?

14 liter *4 mEq/liter=56 or about 60 mEq of potassium available in the ECF

{60% is TBW (42 liters water of a 70 KG man, 28 liters ICF, and 14 liters ECF, 14 L are divided into 11liters water (further divided into 10L (in the gel form) and 1liter which is the free portion of water available all time in the extracellular space , 3L plasma)}

A large meal (lunch) contains about 50 mEq of K+ distributed in 14 liters of ECF (50/14 is about 3.5 mEq) so a person who has [K+] = 4mEq for example before the meal, he will have a total of 7.5 mEq after it, and this is extremely dangerous affecting the excitability of heart.

So what happens to regulate K+ concentration in blood?

Once you start eating, insulin is secreted. It's true that Insulin main function is to drive glucose in but it also has an important function in driving K+ inside cells and keeps it as a bank. K+ inside is 150 mEq if it is 152 this is a big deal, a huge amount! So what happens that in about 6 hours or so, K+ gradually goes out from cells and the kidney would secrete it, but the point is that it shouldn't increase suddenly in the plasma from 4 to 7!

Acidosis: when H+ concentration is increased in blood.

pH in cells is low and can take more H+ exchanged with K+, so in acidosis we have hyperkalemia (Normal PH is 7.35-7.45 below this level is acidosis, above this level is alkalosis). *For every .1 decrease in PH, there is .2 - 1.7 mEq increase in K+ extracellularily.

*A patient with diabetic ketoacidosis; too much: insulin, K+ (hyperkalemia), and H+ in blood. We start giving him insulin to correct hyperglycemia, and eventually it will drive K+ inside cells, ending up with hypokalemia. **Both hypo and hyperkalemia are dangerous, so you should give him K+ along with insulin to maintain normal K+ levels in the plasma.**

Chronic Acidosis inhibit Na+/K+ pump**; it increases Na+ inside cells and decrease K+ inside cells and decrease K+ secretion (another effect on the level of the kidney).**

In summary about K+:

Potassium intake should equal potassium output= 100.

Most of K+ is excreted from our bodies through the kidney by 2 roots; filtration not reabsorbed and secretion.

If you ingest too much potassium, most of it is secreted.

Beta blockers: like propranolol inhibit potassium uptake by cells, beta receptors help in K+ entering cells so if you have **B-blockers you have hyperkalemia**. Exercise increases K+ in plasma significantly through alpha receptors.

Now we'll talk about osmolarity:

Plasma osmolarity is 285 mOsmol per liter which equals interstitial osmolarity.

If we have hyperosmolar interstitium; water leaves the cells to the interstitium, cells shrink, K+ increases in cells, increasing the gradient for K+ and thus K+ increases in the extracellular space. Osmolarity increases

How kidney deals with Calcium:

99% of calcium in body is inside bones, small fraction is in the extracellular space, intracellular calcium is very low.

Concentration of Calcium is 10^-3 molar

Calcium in blood is in 2 forms: 50% is bound to proteins, 50% is free. We care about the free fraction because the bound fraction is not gonna affect the cell's excitability. . **In alkalosis, the bound fraction is more so we have hypocalcaemia. In acidosis the free is more, so we have hypercalcaemia**

65% of the filtered Calcium is reabsorbed in the proximal tubules.

25% in the thick ascending

8% in the distal

Almost only 1% is left for excretion

Hypercalcuria is effective in stone formation, collect 24 hour urine and see how much calcium is excreted per day

What increases Calcium reabsorption? Parathhormone PTH

What decreases Calcium reabsorption? Loop diuretics, Lasix

Thiazide increase Calcium reabsorption in the distal tubules, so in case of hypercalcuria we give thiazide. But in children it may cause renal damage.

So we ask parents to control his salt intake (the child shouldn't eat chips for example) because a lot of salt intake would increase calcium secretion. He also should drink a lot of water until the color of urine is the same as water.

If he's responding and hypercalcuria is only a little bit this is good, but if he's not then we may consider giving him Thiazide forever! And this is a problem for a 5-year-old child.

The question is WHY DO WE DRINK WATER?

Water Homeostasis. It is important to release metabolites.

How much should we drink? Minimum water intake is

Why other species of animals don't need to drink water (what are the mechanisms they have?) We as humans have many waste products we should remove like urea, Creatinine, sodium, K+, acids, phosphates.

If we are to assume that a bed ridden person doing no kind of physical activities must remove 700 m osmole per day.

His kidney makes a maximum concentration of urine up to 1400 mosmole/liter

Then half of liter= 500 mL (700 m osmole) of urine must be formed a day **(Minimum Obligatory urine output)**

Below this, we call it oligouria (Oligo means little).

*Sometimes they say less than 450mL, and in newborns oligouria is less than 1mL/Kg/hour

So the doctor says this number works for all (children and adults): Any urine output less than 300 mL/meter squared* body surface area (can be calculated using height and weight, it's usually 1.7) is OLIGOURIA and it's a sign of acute renal failure.

But other species living in desserts can make concentrated urine up to **10,000 so little solvent is needed to carry waste products.** (It is as if they urinate salts only).

*Cholera patients for example die from dehydration not the bacteria is the cause.

In the collecting duct: we have the last modification of tubular fluid (last chance to reabsorb)

At the end of medullary collecting tubules, we call it URINE.

How does the kidney make diluted urine (i.e. of an osmolarity less than 300 mosmole)?

We just need to reabsorb sodium and chloride without water, by removing sodium chloride and leaving water we make diluted urine.

How does kidney make concentrated urine of 1400 m osmole (of more than 300 m osmole)?

We know that the interstitial osmolarity is 300 m osmole. We don't have active water reabsorption (to remove water and keep salts, there is no such concept; water moves passively), and this stayed a mystery to scientists until they figured out that the interstitium osmolarity in medulla is actually more than 300! It is 1400 m osmole. This would simply explain it that water will get out (open channels) of tubules to have equal osmolarities of 1400 so we have concentrated urine of 1400 m osmole.

Then the question was how can the kidney maintain a hyperosmolar interstitium?

1) They studied the kidney using micro- technique and found that in the thick ascending portion there is Single effect, we know that whenever salt moves, water will follow except in this segment (they are nor permeable to water) making a hyperosmolar interstitium.

2) Urea is reabsorbed (it is unusual to reabsorb a waste product!)

But these 2 mechanisms are the reason behind the medulla having a hyperosmolar interstitium. (Nacl and urea, and we need water channels at the medullary collecting ducts to be open and this requires the presence of ADH)

About 700 due to NaCl. 500 due to urea a total of 1200 m osmole in the interstitium.

THE END