UGS

Physiology

Doctor 2021

Sheet (2)

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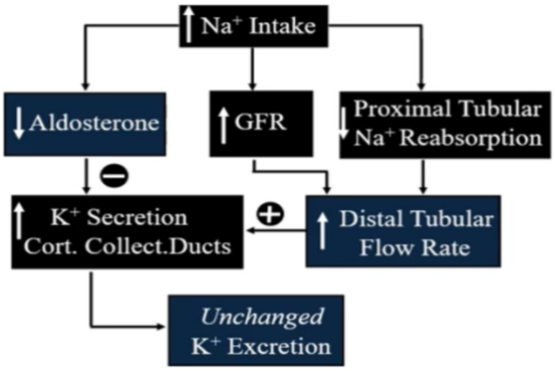
The effect of changing Na^+ intake on K+ excretion: unchanged

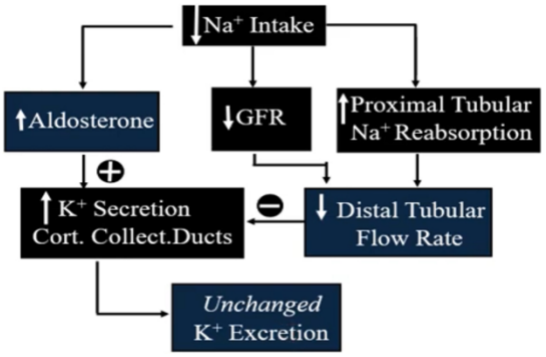
- **Increasing Na^+ intake:**
  1. **Increases GFR** and **decreases proximal tubular Na^+ reabsorption** and both of these effects will **increase distal tubular flow rate** (volume tubular expansion in the distal tubule) which will **increase K^+ secretion** (because of increasing the gradient that favours the secretion).



  2. **Inhibits aldosterone** which **reduces K^+ secretion.**

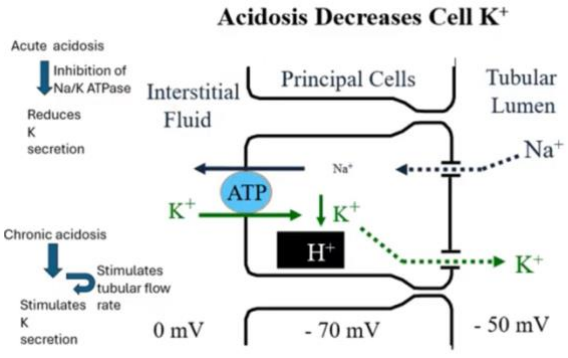
  So, increasing Na^+ intake will cause two opposing effects on K^+ secretion which will counterbalance each other leading to **unchanged K^+ excretion.** Having different outcomes from increasing Na^+ intake is very important to keep K^+ excretion normal and unchanged.

The opposite is true in low Na^+ intake, leading to unchanged K^+ excretion, because of the counterbalancing effects on K^+ secretion between the increased aldosterone and the reduced distal tubular flow rate by the reduced GFR and increased proximal proximal tubular Na^+ reabsorption.

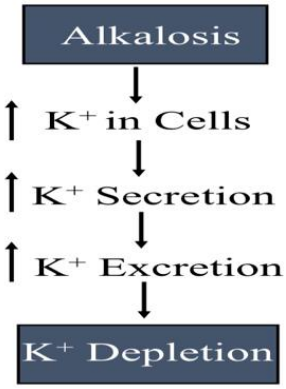


The effect of acidosis on k^+ excretion:

- **Acute acidosis:** inhibits Na^+ / K^+ATPase (on the interstitial side) **decreasing K^+ secretion**, also it decreases the permeability of K^+ (on the luminal side).
- **Chronic acidosis:** inhibits the proximal tubular Na+ reabsorption which increases the tubular flow rate **increasing K^+ secretion**.



The effect of alkalosis on k^+ excretion:



Opposite to acute acidosis, alkalosis increases the intracellular K^+, increasing K^+ secretion and excretion leading to more K^+ depletion.

Causes of Hyperkalemia:

- **Renal failure.**
- **Decreased distal nephron flow** (decreased tubular flow rate) **(heart failure, severe volume depletion, NSAID** decrease GFR**, etc).**
- **Decreased aldosterone or decreased effect of aldosterone**
  - **adrenal insufficiency.**
  - **K^+ sparing diuretics (spironolactone, eplerenone).**
- **Metabolic acidosis (hyperkalemia is mild).**
- **Diabetes which predispose to kidney disease, acidosis, ↓insulin** (insulin insufficiency).

Causes of Hypokalemia:

- **Very low intake of K^+.**
- **Metabolic alkalosis** which increase the secretion of K^+.
- **Excess insulin.**
- **GI loss of K^+**
  - **diarrhea.**
- **Increased distal tubular flow** (increasing k+ secretion) **which results from:**
  - **salt wasting nephropathies**
  - **osmotic diuretcs**
  - **loop diuretics**
- **Excess aldosterone or other mineralocorticoids** increasing k+ secretion.

Question:

• Which of the following would cause the most serious hypokalemia?

A) A decrease in potassium intake from 150 mEq/day to 60 mEq/day.

B) An increase in sodium intake from 100 to 200 mEq/day.

C) Excessive aldosterone secretion plus high sodium intake.

D) Excessive aldosterone secretion plus low sodium intake.

E) A patient with Addison's disease.

F) Treatment with a beta-adrenergic blocker.

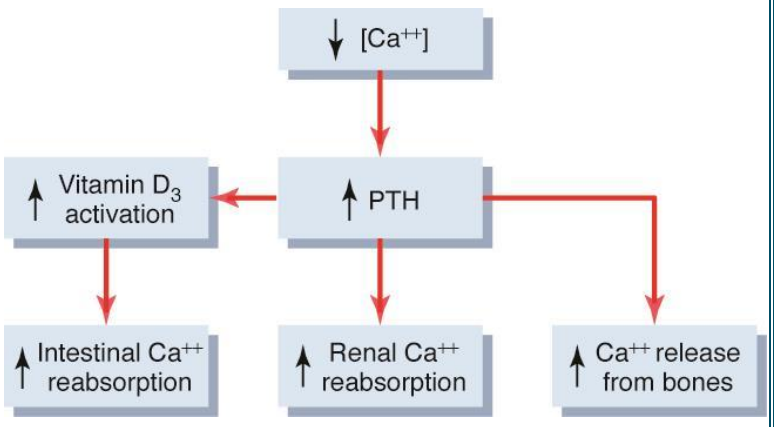
G) Treatment with spironolactone.

Answer: C

Compensatory responses to decreased plasma ionized calcium

ECF Ca2+ conc. is normally controlled tightly to the level of 2.4mlEq/L. About 15% of the total calcium in the plasma is ionized and the rest is either bound to proteins or complexed with either phosphate or citrate.

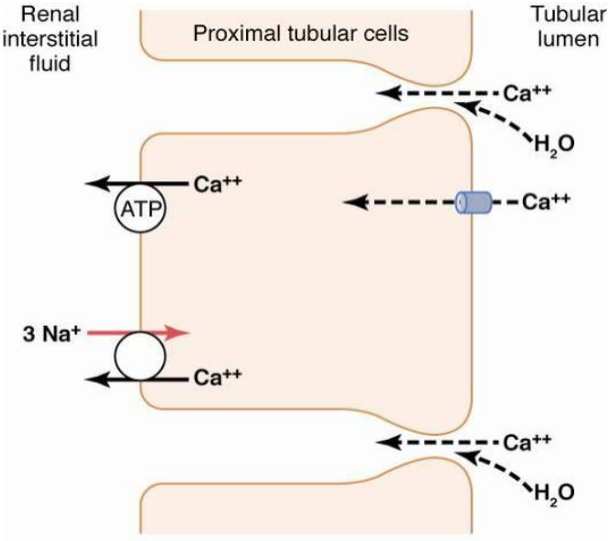
The major regulator of calcium in plasma is **PTH** which acts (in low Ca2+) mainly on the **kidney** to increase reabsorption of calcium as well as on **bones** to increase calcium release by increasing osteoclastic activity. PTH also affects activates **vitamin D_3** (to Calcitriol) which increases the **intestinal** calcium reabsorption.



Proximal tubular calcium reabsorption

Calcium reabsorption in the proximal convoluted tubular occurs **mainly by the paracellular pathway dissolved with water** and only **20% through the**

transcellular route (down its electrochemical gradient) from the tubular lumen into the cells, and then leaves the cells to the interstitium by **Ca^{2+} ATPase** channel and by **Na^{+}/Ca^{2+} counter transporter** ($3Na^{+}$ in and Ca^{2+} out to the interstitium).



Ca^{2+} reabsorption happens also at the thick ascending loop of henle (by the paracellular route) and distal tubule.

PTH also increases Ca^{2+} reabsorption as we said before.

Integration of Renal Mechanisms for Regulation of Body Fluids

Excretion = Filtration - Reabsorption + Secretion

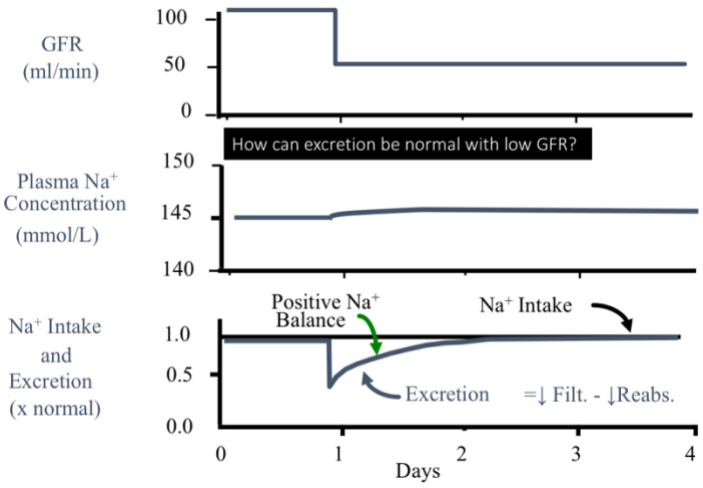
If there is a steady - state:

- **Fluid Excretion = Fluid Intake**
- **Electrolyte Excretion = Electrolyte intake**

Effect of Decreased GFR on Sodium

Reduction of GFR to a half will:

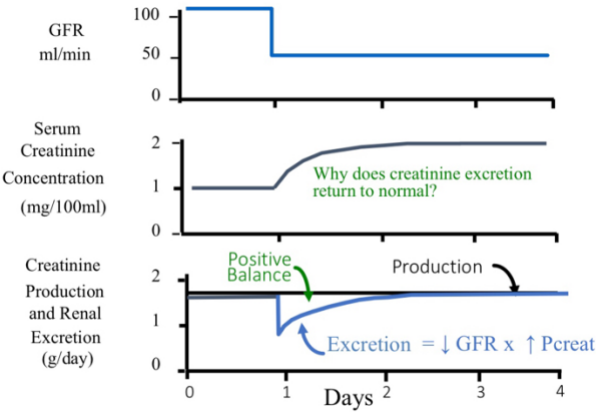
- **Increase the plasma [Na^{+}]** (only a little).
- Cause a sudden drop of Na^{+} excretion, which will then gradually be balanced by increased Na+ intake after a couple of days. **Excretion returns to normal.**



The reason why the excretion is reduced and then returned back to normal even though GFR is still reduced is because the **Na^{+} reabsorption is reduced** and readjusted to the new filtration (GFR), so it decreased and as we know

Excretion = Filtration – Reabsorption, so because of the reduction of reabsorption the excretion returned to normal.

Effect of Decreased GFR on Creatinine

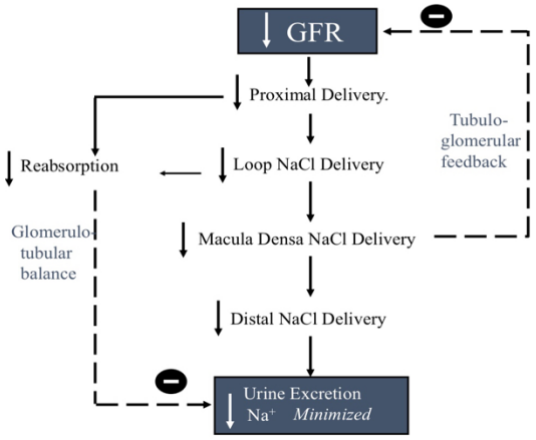


Reduction of GFR to a half will:

- **Increase the plasma creatinine level.**
- Cause a sudden drop in creatinine excretion which will then gradually be increased to equal production. **Excretion returns to normal.**

The reason why excretion is increased is because creatinine is poorly reabsorbed and is also secreted, so a **reduction in GFR** will actually increase the plasma level of creatinine because this will decrease its excretion and clearance which equals GFR (as we said in the mid material ☺) and it will remain in the plasma.

Increased creatinine level in plasma with the decreased GFR will counterbalance each other giving us a normal creatinine excretion. Excretion = GFR x plasma creatinine.



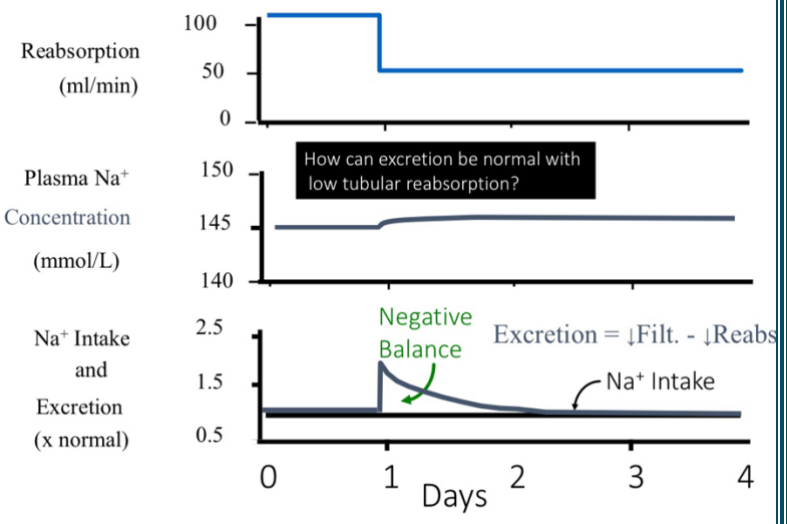
Reduction in GFR will decrease NaCl delivery in proximal tubule, loop henle, macula densa and distal tubule. And for that we have two corrective mechanisms which minimise the reduction in urine excretion of Na^+ (Na^+ excretion remains unchanged):

1. **Tubulo-glomerular feedback** (decreased NaCl in macula densa increases GFR).
2. **Glomerulo-tubular balance** (decreased NaCl in proximal tubule decreases reabsorption to match the reduced GFR).

Effect of Decreased Reabsorption on Sodium Balance

Decreased reabsorption in the proximal tubule to a half will:

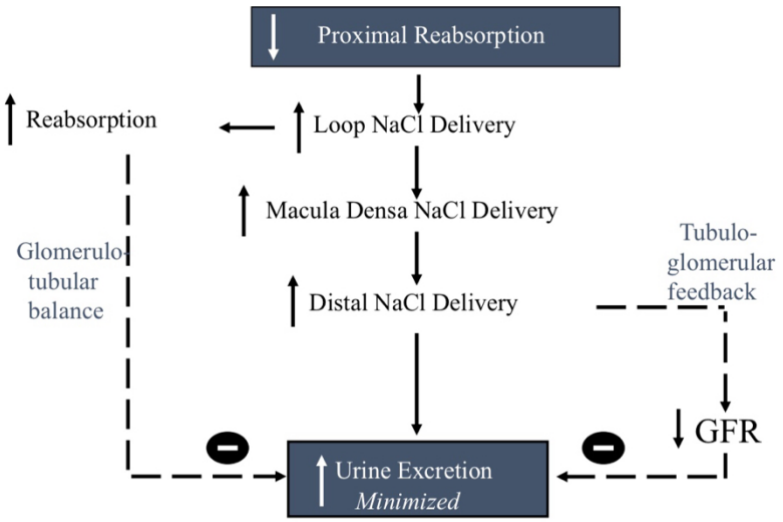
- At first the Na+ excretion will increase and gradually decrease to balance the Na+ intake.



The reason why excretion decreased and returned to normal is because Excretion = Filtration – Reabsorption. So, when reabsorption is decreased there will be an autoregulation of filtration and it will be decreased (by the tubulo-glomerular feedback mechanism to maintain normal excretion) to maintain normal excretion.

Maintenance of Sodium Balance After Decreased Proximal Reabsorption

Reduction of proximal reabsorption leads to more NaCl in loop of henle, macula densa and distal tubule which by tubulo-glomerular feedback decreases GFR and reduce Na^+ excretion. At the same time the increased NaCl in loop of henle will increase reabsorption to match the increased NaCl levels by glomerulo-tubular balance reducing Na^+ excretion even more and returning it to normal.



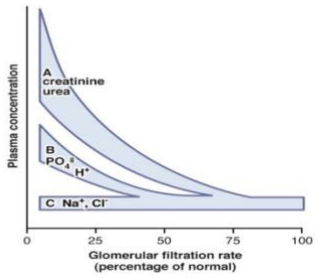
*The following slides weren't mentioned by the doctor:

Hierarchy of Responses to Disturbances of Body Fluid Regulation:

In steady-state, Intake = Output

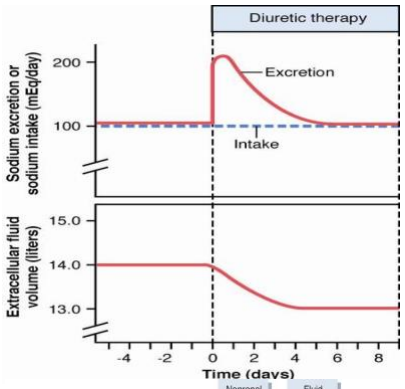
1. Local renal mechanisms:
    - changes in GFR.
    - changes in tubular reabsorption.
    - changes in tubular secretion.
2. Systemic mechanisms (which can affect the whole body):
    - changes in hormones.
    - changes in sympathetic activity.
    - changes in blood pressure.
    - changes in blood composition.

Plasma concentrations of solutes in chronic renal failure

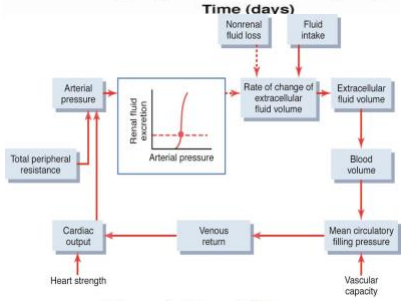


Sodium excretion and extracellular fluid volume during diuretic administration. Compensations that Permit Na+ balance:

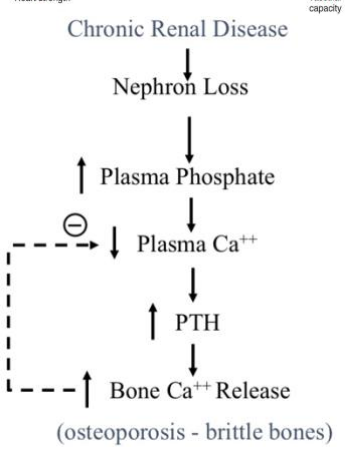
- ↓ blood pressure
- ↑ renin, angiotensin II
- ↑ aldosterone



Renal-Body Fluid Feedback- Increased Fluid (Na+) Intake.



Hormonal Response to Chronic Renal Disease – PTH.



Integrated Responses to High Na+ Intake.

Excretion Na+ = Filtration Na+ - Reabsorption Na+

1. Small increase in GFR.
2. Decreased Na+ Reabsorption is caused by:
    - small increase in blood pressure
    - increased peritubular capillary pressure
    - decreased angiotensin II
    - decreased aldosterone
    - Increased natriuretic hormones (e.g. ANP)

Net effect = increased Na+ excretion.

تذكر أن الدنيا فانية فاستغلها في طاعة الله
