Medicine
TEAM 437

MED437
KING SAUD UNIVERSITY

Body Cations: K and Ca

Objectives :

1. Understand the basic physiologic principles of potassium hemostasis
2. Know the application of physiologic and clinical principles in approaching hyperkalemia
3. Know the application of physiologic and clinical principles in approaching hypokalemia
4. Understand the basic principles of Calcium hemostasis
5. Know the application of physiologic and clinical principles in approaching hypercalcemia

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Resources :

Dr. Riyadh Al Sehli Slides & notes

Potassium:

- Where does **K** come from?
- How much **K** do we eat every day?
- How do we lose the **K**?
- Where does **K** in the body live?
- How does **K** move?
- Is **K** important?
- What keeps **K** in normal range?
- What happens if **K** level is abnormal?
- What causes high **K**?
- What causes low **K**?

Where does K come from?

- Depending on diet, the normal daily intake can vary.
- Fruits, potatoes, beans, and grains. Orange, banana, dates, and tomatoes.
- High-fat diets usually contain low amounts of potassium.
- Average daily intake is approximately 50 to 100 mmol.

For your own information.

Table 1 Potassium content of selected foods

Foods and drinks	Potassium content (mmol)
1 small banana (85 g)	8.6
Blueberries (100 g)	1.9
White mushrooms (75 g)	8.1
Broccoli, cooked (75 g)	5.8
Green beans, cooked (75 g)	3.9
Onions, cooked (75 g)	1.5
French fries (150 g)	17.7
Parboiled rice (150 g)	2.2
Spaghetti, without egg (150 g)	2.3
Orange juice (200 ml)	7.9
Milk, full fat (200 ml)	7.7
Coca Cola (200 ml)	0.1
Potato crisps (20 g)	5.1
Milk chocolate bar (20 g)	2.4
White chocolate (20 g)	1.8
Wine gums (20 g)	1.8

How do we loose K?

★ **Renal clearance:** Main exit
Primary mechanism, very efficient until GFR < 30 ml/min. lose its efficiency

★ **Intestinal excretion:**
Only handles 10 % of the daily K load.
Efficiency can be **enhanced in renal failure** but it is variable from one person to another.

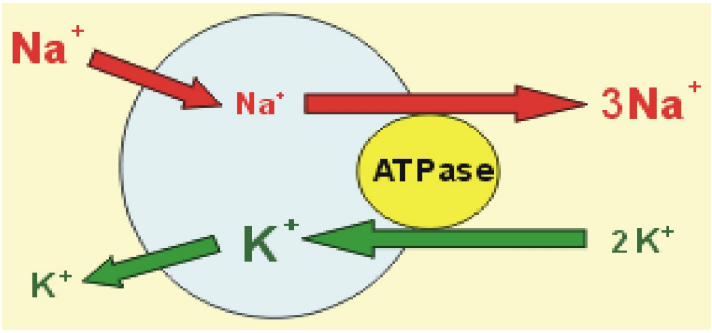
Where does K live in the body?

- Total body K is approximately 50 mmol/kg body weight.
- K is the most abundant intracellular cation (100- 150 mmol/L) → 98% of total body K.
- Extracellular K concentration (3.4 – 5.5 mmol/L) → **2%** of total body K.

very narrow range

The amount that we actually measure, very critical for the Action Potential

What keeps the IC K high ?



- Enhance ATPase => Hypokalemia
- Inhibit ATPase => Hyperkalemia

- Insulin, Beta agonists (Salbutamol) **enhance** the pump function. treatment for hyperkalemia.
- Beta Blockers **inhibit** the pump function. treatment for hypokalemia.

What keeps EC K low?

★ 1. The Na/K ATPase pump.

★ 2. Renal clearance requires
- Normal **GFR** blood flow &
- Normal **aldosterone axis** very critical! .

3. Intestinal excretion.

What happens when we eat K?

Oral [K] intake is initially absorbed in the intestine and enters portal circulation.

Increased ECF [K] stimulates insulin release

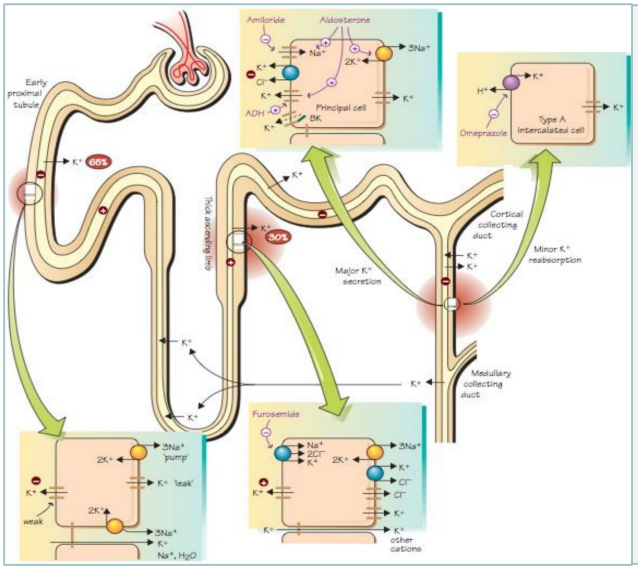
Insulin facilitates [K] entry into intracellular compartment by stimulating cell membrane Na/K ATPase pump

The transient rise in serum [K] stimulates renal and intestinal clearance of extra K

Mild transient hyperkalemia:
1. Insulin release (fast)=> Push k+ inside the cells 2-3 hs
2. Aldosterone release (slow) => distally in the collecting duct => get rid of extra k+ 8-12 hs, sometimes aldosterone doesn't work because it needs enough GFR to work.

In order to Keep serum K in normal range, We need:

1. Normally functioning Na/K ATPase pump.
2. Intact renal response Normal GFR and Aldosterone (secretion and action).



- Kidney can't regulate K^+ because Kidney NEVER reabsorb K^+
- It either increase secretion of K^+ or do nothing
- 60% of Na reabsorbed in proximal tubules
- 30% of Na reabsorbed in loop of henle
- 5% of Na reabsorbed in distal convoluted tubules
- 5% of Na reabsorbed in collecting duct:
  - Aldosterones works here
  - secretion of K^+ happen here in exchange with Na
- So if there is a problem with Na reabsorption it will affect K^+ secretion

- Drugs that can cause **Hyper**kalemia:
  - Spironolactone => blocks aldosterone.
  - Amiloride => blocks Na reabsorption in distal tubules and collecting duct.
- Drugs that can cause **Hypo**kalemia:
  - Thiazide and Loop diuretics => blocks Na reabsorption in proximal parts & loop of henle => a lot of reabsorption occurs in distal tubules which will cause increase K^+ secretion and hypokalemia.

- Patients with dehydration or decrease GFR
  - => no Na will be reabsorbed in distal tubules and collecting duct => no K^+ secretion => hyperkalemia

Why is K important?

- Maintains electrical gradient across cell membranes,
  i.e. resting membrane potential essential for generation of **action potential.**
- Essential for intracellular metabolism e.g protein synthesis.

What happens of K level is abnormal?

- Skeletal muscle dysfunction: weakness and paralysis (advanced).
- Cardiac cell irritability: arrhythmia. very imp hypokalemia or hyperkalemia (both)

Hyperkalemia
[K] >5.5

NA/K ATPase Dysfunction
B blockers
Digoxin
↓ Insulin

Massive Cell Breakdown
Rhabdomyolysis
Tumor lysis syndrome

Impaired Renal Function
Low GFR

Aldosterone axis Dysfunction
Adrenal deficiency
Aldosterone resistance

Can you eat too much K?

- If GFR is normal, renal clearance of K has a huge adaptive capacity.
- K intake is restricted only if:
  - GFR is reduced.
  - Existing aldosterone axis dysfunction.
  - Na/K ATPase is not efficient (blocked by drugs, ↓ Insulin).

Normal aldosterone and GFR will never develop hyperkalemia because of diet

Hypokalemia
[K] <3.4

↓ Oral intake

Malnutrition
Eating disorders vomiting

Rapid transcellular shift

Insulin therapy
Periodic paralysis

↑ Renal loss

Diuretics thiazide and loop(furosemide) diuretics
Too much aldosterone happen in dehydration

↑ Intestinal loss

Diarrhea
Laxative abuse

How to raise K level?

- Stop the loss. Treat the underlying cause
- Replace lost K with K (PO or IV if rapid correction is urgently needed).

General rule: we advice pts with renal impairment to restrict K intake but if they developed hypokalemia then we advice them to increase their diet intake, even those with CKD

How to lower K level?

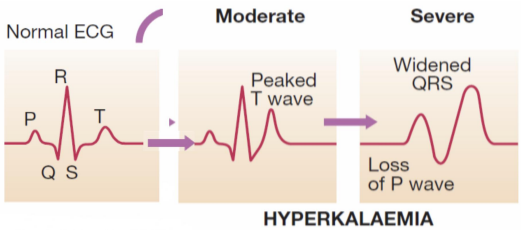
Remember that patients on **dialysis** nothing will work with them except dialysis!

- Reduce Cardiac muscle irritability with IV Ca gluconate (only if EKG changes).
- Push K into cells: Insulin preferable , Beta agonists we don't use it usually because of side effects.
- Remove the K load:
  - Through the kidney: diuretics, dialysis.
  - Through the gut: Laxatives, K chelation (Ca resonium). More stable pts in mild cases.

K>7 mmol/L or **hyperkalemia** with **EKG changes** :

1. Peak T wave
2. Prolongation of all waves

- We use Ca gluconate. Ca can raise the RMB to its baseline (not lower K) so stabilizes the cardiac muscle.



Extra

Hyperkalemia changes in ECG:

➢ Formation of "Sine Wave" :

As K^+ levels rise further, the situation is becoming critical. The combination of broadening QRS complexes and tall T waves produces a sine wave pattern on the ECG. Cardiovascular collapse and death are imminent.

➢ Ventricular fibrillation:

Untreated hyperkalemia leads to chaotic depolarization of ventricular myocardium: ventricular fibrillation. No cardiac output is present.

Hypokalemia changes on ECG?

- Flattening of T waves.
- U waves appear if severe with ST depression.

Calcium:

- Where does **Ca** come from?
- How much **Ca** do we eat every day?
- How do we lose the **Ca**?
- Where does **Ca** in the body live?
- How does **Ca** move?
- Why is **Ca** important?
- What keeps **Ca** in normal range?
- What happens if **Ca** level is abnormal?
- What causes high **Ca**?
- What causes low **Ca**?

Where does Ca come from?

- Diet: 1000–1500 mg /day in average.
- Total body Ca = 1000 g.

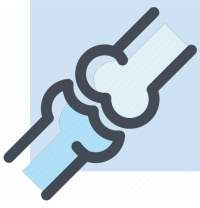
Where does Ca live ?

- The vast majority of total body calcium **99%** is present in the skeleton.
- Non-bone calcium represents **1%** of total body calcium.
  - Free ions (51%).
  - Protein-bound complexes (40%).
  - Ionic complexes (9%) [calcium phosphate, calcium carbonate, and calcium oxalate] ionized form. We always use the ionized Ca because it's functionally active , normal range of Ca (2.1-2.5 mmol/L)

Why Ca is important?

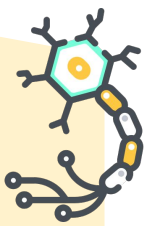
Bone Ca

- ❑ Skeletal strength.
- ❑ Dynamic store.



Non-Bone Ca

cellular function



- ❑ Extra- and intracellular signaling.
- ❑ Nerve impulse transmission.
- ❑ Muscle contraction.

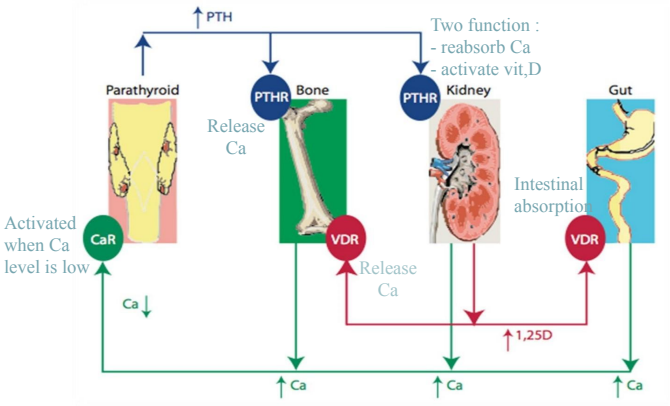
What keeps Ca in balance ?

- Total intake
- Rate of intestinal absorption
- Intestinal excretion
- Renal reabsorption
- Renal excretion
- Bone turnover. All these parameters are controlled by:
    1. PTH.
    2. Active Vitamin D.
    3. Serum Ionized Ca level stimulate hormones .

PTH is a hypercalcemic hormone:

- ↑ Release of Ca form bones (bone resorption).
- ↑ Renal absorption of Ca. In the proximal part of nephron
- Activates Vitamin D in the kidney.

Active Vitamin D is also hypercalcemic:



- ↑ Intestinal absorption of Ca.
- ↑ Bone resorption.
- Hormonal mechanisms maintain narrow physiologic range of 10%.
    - of normal range.

In Chronic kidney disease vit.D won't be activated => vit.D deficiency => secondary hypocalcemia => activate PTH=> secondary parathyroidism => increase fracture

What can go wrong?

- Oral intake
- Intestinal absorption
- Renal reabsorption
- Renal excretion
- Intestinal excretion
- Bone turnover

Mediated by

- PTH
- Active Vitamin D

Very Important, focus on highlights

Clinical Manifestations of Hypercalcemia

Renal "stones"
- Nephrolithiasis
- Nephrogenic diabetes insipidus
- Dehydration
- Nephrocalcinosis

Skeleton "bones"
- Bone pain
- Arthritis
- Osteoporosis
- Osteitis fibrosa cystica in hyperparathyroidism (subperiosteal resorption, bone cysts)

Gastrointestinal "abdominal moans"
- Nausea, vomiting
- Anorexia, weight loss
- Constipation can be an early sign
- Abdominal pain
- Pancreatitis
- Peptic ulcer disease

Neuromuscular "psychic groans"
- Impaired concentration and memory
- Confusion, stupor, coma — specially seen in elderly
- Lethargy and fatigue
- Muscle weakness
- Corneal calcification (band keratopathy)

Cardiovascular
- Hypertension
- Shortened QT interval on electrocardiogram
- Cardiac arrhythmias
- Vascular calcification

Other
- Itching
- Keratitis, conjunctivitis

Hypercalcemia

↑ Intestinal Absorption

Increased intake
Increased Vit D

↑ Renal reabsorption

Hyperparathyroidism
Thiazide diuretics

↑ Bone resorption

Osteoclastic bone metastasis the worst
Immobilization mild effect

↑ PTH

Primary hyperparathyroidism the worst
Multiple Endocrine Neoplasia

↑ Vit D

Intoxication

Hypocalcemia

↓ Intestinal absorption

Decreased intake
Malabsorption
Small bowel resection
Vit D deficiency

↓ Renal reabsorption

Hypoparathyroidism
Loop diuretics
Tubular defects

Bone remodeling

Hungry bone syndrome
Patients with advanced chronic kidney disease or dialysis

↓ PTH

Hypoparathyroidism

↓ Vit D

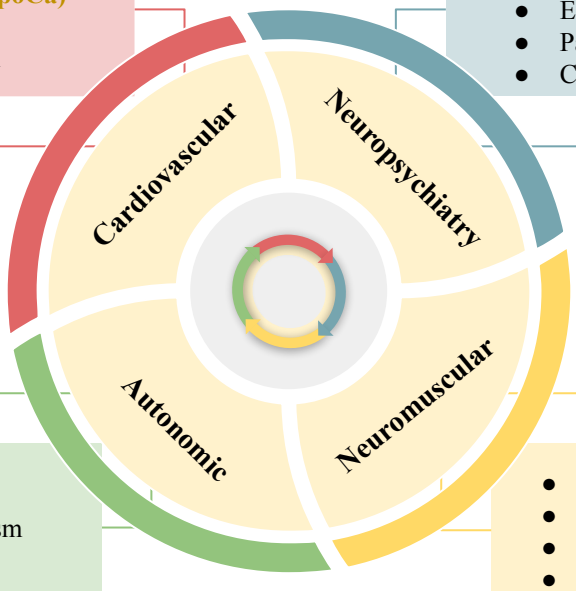
Renal failure

Patients with hyperparathyroidism when treated, their bone will suck all calcium in blood leading to severe hypocalcemia and some cases can be life-threatening; this is Hungry bone syndrome >> bone are lacking Ca

Loop diuretics => hypocalcemia
Thiazide => hypercalcemia
Both cause hypokalemia

Clinical features

1st line of treatment is treating the underlying cause



- **Prolonged QT interval (hypoCa)**
- Heart failure
- Hypotension

- Seizure
- Dementia
- Extrapyramidal
- Papilledema
- Cataract

Hypercalcemia :
Polyurea
Polydipsia
Diabetes insipidus

- Biliary colic
- Bronchospasm
- Diaphoresis

- Paresthesia => Perioral numbness usually
- **Spasm**
- Chvostek's sign
- Trousseau's sign

This is hypocalcemia symptoms

Summary

Potassium imbalance	
Basic information	Total body K is 50 mmol/kg body weight and it comes from our diet. Majorly intracellular (98% of total body K) and 2% is extracellular . Main importance: Maintains electrical gradient across cell membranes i.e.: resting membrane potential. In order to keep serum K in normal range, we need: 1. Functional Na/K ATPase pump. 2. Intact renal clearance = normal GFR and normal aldosterone axis (normal secretion and action). K intake restricted if: 1. GFR is reduced. 2. Existing aldosterone axis dysfunction. 3. Na/K ATPase is not efficient (blocked by drugs or Insulin ↓)
Hyperkalemia	**Causes:** 1. NA/K ATPase dysfunction. 2. Massive cell breakdown. 3. Impaired renal function. 4. Aldosterone axis dysfunction. **Clinical feature:** Arrhythmias, on ECG: tall, peaked T waves, QRS widening, PR interval prolongation, loss of P waves, and finally a sine-wave pattern. (because hyperkalemia will drop the cardiac threshold, so any action potential can stimulate it) **Treatment (goal: reduce K level)** Reduce cardiac muscle irritability with IV Ca gluconate ”membrane stabilizer” (only if EKG changes) Push K into cells through: ● Insulin ● Sodium bicarbonate (if pt has acidosis) ● Beta agonists (Salbutamol ‘requires high dose‘) Remove K load: ● Through kidney loop diuretics (furosemide) ● Through gut: Laxatives, K chelation (Ca resonium)
Hypokalemia	**Causes:** 1. GI losses: diarrhea – laxatives 2. Renal losses: diuretics – hyperaldosteronism 3. Insufficient dietary intake: malnutrition – eating disorders 4. Rapid transcellular shift: insulin - epinephrine **Clinical feature:** Arrhythmias, on ECG: prolonged normal cardiac conduction and flattening of T waves. U waves appear if severe.

Summary

Calcium imbalance	
Basic information	99%of Ca in skeleton (skeletal strength – dynamic store) and 1% is non- bone Ca (cell signaling – nerve impulse transmission - muscle contraction) Ca balance is kept by: total intake - rate of intestinal absorption and excretion - renal reabsorption and excretion - bone turnover All parameters above are controlled by: PTH (bone – kidney) – Active VitD (bone – kidney – gut) – Serum Ionized Ca level. Hormonal mechanisms (PTH – VitD both increase Ca) maintain narrow physiologic range of 10%
Hypercalcemia	**Causes:** 1. Increased Intestinal absorption: increased Ca/VitD intake 2. Increased renal reabsorption: Hyperparathyroidism - Thiazide diuretics 3. Increased bone resorption: osteoclastic bone metastasis - immobilization 4. High PTH: primary hyperparathyroidism - Multiple Endocrine Neoplasia 5. High VitD: VitD intoxication **Clinical features:** Cardiovascular: vascular calcification, hypertension. Neuromuscular: muscle weakness – fatigue – lethargy – impaired memory. Renal Stones: Nephrocalcinosis - Nephrogenic diabetes insipidus - Dehydration. Bones: pain - arthritis. GIT: abdominal pain - peptic ulcer – pancreatitis - constipation – nausea –vomiting.
Hypocalcemia	**Causes:** 1. Low intestinal absorption: decreased intake - malabsorption - small bowel resection - VitD deficiency 2. Low renal absorption: hypoparathyroidism - loop diuretics - tubular defects - renal failure 3. Bone remodeling: hungry bone syndrome. 4. Low PTH: hypoparathyroidism. 5.Low VitD: renal failure **Clinical features:** Cardiovascular: Prolonged QT interval – HF – HTN Increased neuromuscular irritability: paresthesia - spasm (tetany): (Chvostek sign - Trousseau sign) Neuropsychiatric: seizure - dementia - extrapyramidal - papilledema – cataract.

Questions

1. **What is the mechanism behind using insulin in treatment of hyperkalemia?**
   a. Increase renal loss of K
   b. Trans shift of K
   c. Cell lysis
   d. Help cardiac membrane from damage

2. **A 65-year-old diabetic man with a creatinine of 1.6 was started on an angiotensin-converting enzyme inhibitor for hypertension and presents to the emergency room with weakness. His other medications include atorvastatin for hypercholesterolemia, metoprolol and spironolactone for congestive heart failure, insulin for diabetes, and aspirin. Laboratory studies include: K: 7.2 mEq/L Creatinine: 1.8 mg/dL Glucose: 250 mg/dL CK: 400 IU/L Which of the following is the most likely cause of hyperkalemia in this patient?**
   a. Worsening renal function
   b. Uncontrolled diabetes
   c. Statin-induced rhabdomyolysis
   d. Drug-induced effect on the renin-angiotensin-aldosterone system

3. **A 21-year-old woman complains of urinary frequency, nocturia, constipation and polydipsia. Her symptoms started 2 weeks ago and prior to this she would urinate twice a day and never at night. She has also noticed general malaise and some pain in her left flank. A urine dipstick is normal. The most appropriate investigation is:**
   a. Serum phosphate
   b. Serum calcium
   c. Parathyroid hormone (PTH)
   d. Plasma glucose

4. **Which of the following is an indication for treatment with IV Ca gluconate for a patient with hyperkalemia?**
   a. Respiratory failure
   b. Nausea/vomiting
   c. Peaked T wave
   d. Muscle weakness

5. **Which of the following ECG changes can be found in a patient with hypercalcemia?**
   a. Peaked T wave
   b. ST elevation
   c. U wave
   d. Prolonged Q-T interval

6. **Which patient is at risk for hyperkalemia?**
   a. A patient with parathyroid cancer
   b. Patient with Cushing‘s Syndrome
   c. Patient with Addison‘s Disease
   d. Patient with breast cancer

7. **Which of the following is not a known cause of hypercalcemia?**
   a. Sarcoidosis
   b. Use of thiazide diuretics
   c. Loop diuretics
   d. High intake of Vit D.

8. **A 27-year-old alcoholic man presents with decreased appetite, mild generalized weakness, intermittent mild abdominal pain, perioral numbness, and some cramping of his hands and feet. His physical examination is initially normal. His laboratory returns with a sodium level of 140 mEq/L, potassium 4.0 mEq/L, calcium 6.9 mg/dL, albumin 3.5 g/dL, magnesium 0.7 mg/dL, and phosphorus 2.0 mg/dL. You go back to the patient and find that he has both a positive Trousseau and a positive Chvostek sign. Which of the following is the most likely cause of the hypocalcemia?**
   a. Poor dietary intake
   b. Hypoalbuminemia
   c. Pancreatitis
   d. Decreased end-organ response to parathyroid hormone because of hypomagnesemia

Explanation

Answers:
1. B 2. D 3. B 4. C 5. D 6. C 7. C 8. D