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Electrolytic Imbalance II

(Potassium & Calcium)

★ 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.

★ Resources Used in This lecture:

Slides, Step-up to medicine, Master the boards

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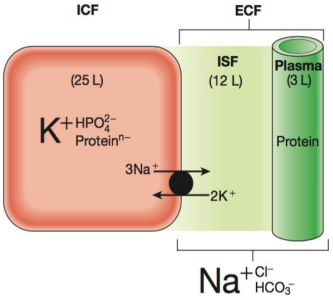
★ Potassium



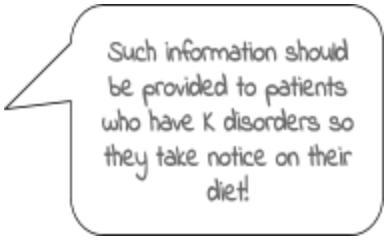
Potassium is the major intracellular cation, and the steep concentration gradient for potassium across the cell membrane of excitable cells plays an important part in generating the resting membrane potential and allowing the propagation of the action potential that is crucial to normal functioning of nerve, muscle and cardiac tissues.

Potassium levels: (3.5 to 5 mEq/L) 98% is intracellular

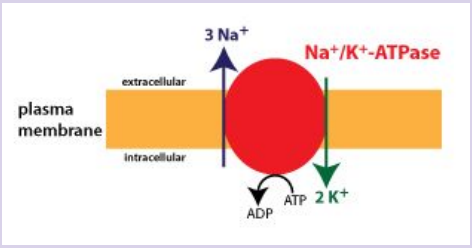
- **Sources**:
  - Fruits, potatoes, beans, and grains.
  - High-fat diets usually contain low amounts of potassium.
  - Average daily intake approximately 50 to 100 mmol.

**Potassium content of selected food*

Food and drinks	Potassium content (mmol)
A small banana (85g)	8.6
French fries (150g)	17.7
Orange juice (200ml)	7.9
Potato crisps (20g)	5.1



★ Potassium Normal Physiology

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.
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).

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) • Extracellular K concentration (3.4 – 5.5 mmol/L)
What keeps the Intracellular K *high*?	•Insulin , Beta agonists *enhance* the K/Na pump function •Beta Blockers *inhibit* the pump function
What keeps Extracellular K *low*?	•The Na/K ATPase pump •Renal clearance : requires normal GFR and normal aldosterone axis (Adrenal deficiency , Aldosterone resistance) •Intestinal excretion
How do we loose K ?	➔ **Renal clearance:** Primary mechanism, very efficient until GFR < 30 ml/min ➔ **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
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

Serum potassium is affected by pH:
alkalosis can lead to hypokalemia, whereas acidosis can lead to hyperkalemia.

WHY? 1-Due to transcellular shifting: when acidosis there's excess hydrogen ions so cells will pick up the hydrogen and release K in exchange and vice versa. In addition to hyperkalemia inhibit renal ammonia synthesis and reabsorption. Thus, net acid excretion is impaired and results in metabolic acidosis. This further exacerbate hyperkalemia due to K movement out of cells.

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

1. Normally functioning Na/K ATPase pump
2. Intact renal response

So any problem in these or what was mentioned previously can predispose to potassium disorders!

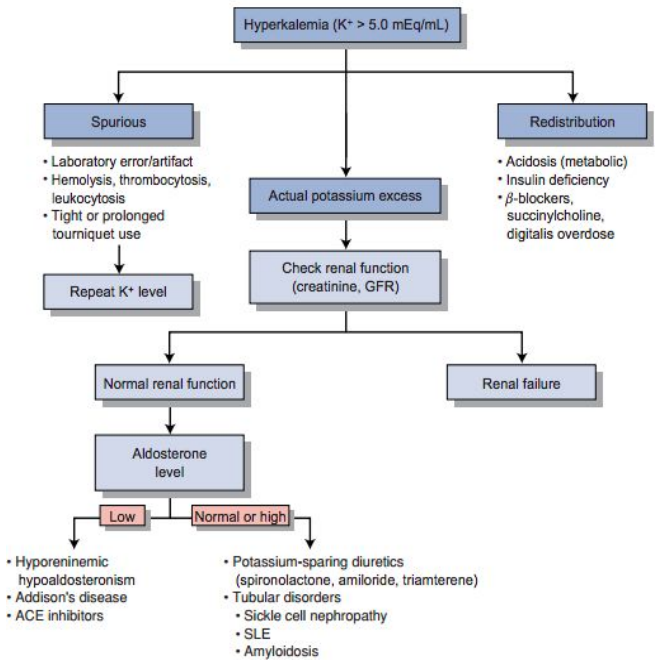
★ Potassium Disorders

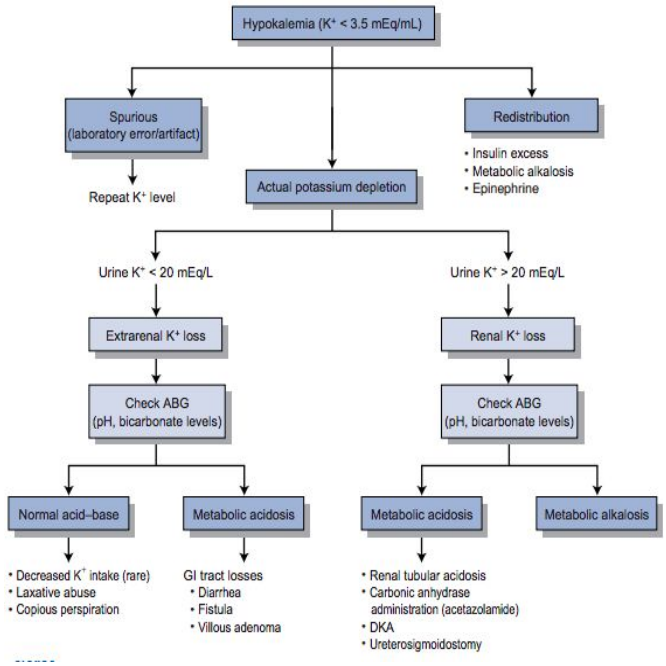
Hyperkalemia (> 5.5 mEq/L)	**Hypokalemia** (< 3.4 mEq/L)
Acidosis and anything resulting in cell lysis increase serum K (force K *out* of cells)	Alkalosis and insulin administration may cause hypokalemia because they cause a shift of K *into* the cells
Causes	
1. Increased total-body potassium - Renal failure (acute or chronic). - Addison disease. - Potassium-sparing diuretics (spironolactone). - Hyporeninemic hypoaldosteronism. - ACE inhibitors. - Iatrogenic overdose—exercise particular caution when administering potassium to patients with renal failure! - Blood transfusion. **2. Redistribution**: translocation of potassium from intracellular to extracellular space. - Acidosis (not organic acidosis) - Tissue/cell breakdown—rhabdomyolysis (muscle breakdown), hemolysis, burns. - GI bleeding. - Insulin deficiency—Insulin stimulates the Na+ -K+ -ATPase and causes K+ to shift into cells. Therefore, insulin deficiency and hypertonicity (high glucose) promote K+ shifts from ICF to ECF - Rapid administration of β -blocker.	**1. GI losses:** - Vomiting and nasogastric drainage (volume depletion and metabolic alkalosis also result). - Diarrhea. - Laxatives. - Decreased potassium absorption in intestinal disorders. **2. Renal losses**: - Diuretics - Renal tubular or parenchymal disease - Primary and secondary hyperaldosteronism. - Excessive glucocorticoids - Magnesium deficiency[1] - Bartter syndrome[2] **3. Other causes:** - Insufficient dietary intake - Insulin administration - Certain antibiotics especially Bactrim and amphotericin B. - Profuse sweating - Epinephrine (β 2-agonists)[3]  The presence or absence of HTN is useful in differentiating the causes. If the patient is hypertensive, excessive aldosterone activity is likely, if the patient is normotensive, either GI or renal loss of K is likely

[1] There are magnesium-dependent potassium channels. (When magnesium is low, they open and spill potassium into the urine.)
[2] Chronic volume depletion secondary to an autosomal-recessive defect in salt reabsorption in the thick ascending limb of the loop of Henle leads to hyperplasia of juxtaglomerular apparatus, which leads to increased renin levels and secondary aldosterone elevations
[3] Hypokalemia occurs in 50% to 60% of trauma patients, perhaps due to increased epinephrine levels.

Hyperkalemia (> 5.5 mEq/L)	Hypokalemia (< 3.4 mEq/L)
Clinical features	
1. Arrhythmias—The most important effect of hyperkalemia is on the *heart*, Check an ECG immediately in a hyperkalemic patient. With increasing potassium ">6", ECG changes progress through *tall, peaked T waves, QRS widening, PR interval prolongation, loss of P waves, and finally a sine-wave pattern.* **2. Muscle weakness** and (rarely) flaccid paralysis. **3. Decreased deep tendon reflexes.** **4. Respiratory failure.** **5. Nausea/vomiting, intestinal colic, diarrhea.**	**1. Arrhythmias**—prolongs normal cardiac conduction, flattening of T waves on ECG. U waves appear if severe **2. Muscular weakness, fatigue, paralysis, and muscle cramps** **3. Decreased deep tendon reflexes** **4. Paralytic ileus** **5. Polyuria and polydipsia** **6. Nausea/vomiting** **7. Exacerbates digitalis toxicity**

Always monitor K+ levels in patients taking digoxin. It is common for these patients to be taking diuretics as well (for CHF), which can cause hypokalemia. Hypokalemia predisposes the patient to digoxin toxicity.



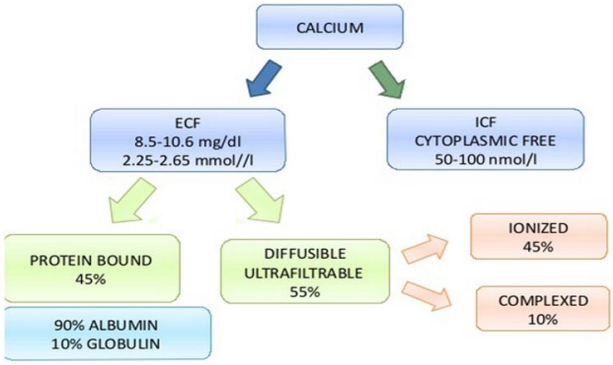


Hyperkalemia (> 5.5 mEq/L)	**Hypokalemia** (< 3.4 mEq/L)
Treatment	
***If the hyperkalemia is *severe*, or if *ECG changes* are present, first give IV calcium.** ✓ *Calcium* stabilizes the resting membrane potential of the myocardial membrane— that is, it decreases membrane excitability. ✓ Use caution in giving calcium to patients on digoxin. (Hypercalcemia predisposes the patient to digoxin toxicity.) ***Shift potassium into the intracellular compartment.** ✓ *Glucose and insulin* (Glucose alone will stimulate insulin from β-cells, but exogenous insulin is more rapid) Give both to prevent hypoglycemia. ✓ Inhaled beta agonist. ✓ *Sodium bicarbonate*. - Increases pH level, shifts K+ into cells. - An emergency measure in severe hyperkalemia. ***Remove potassium from the body.** ✓ Kayexalate—GI potassium exchange resin (Na+ /K+ exchange in GI tract) absorbs K+ in the colon, preventing reabsorption (passed in stool). ✓ Hemodialysis. - Most rapid and effective way of lowering plasma K+. - Reserved for intractable hyperkalemia and for those with renal failure. ✓ Diuretics (furosemide).	***Identify and treat the underlying cause.** ***Discontinue any medications that can aggravate hypokalemia.** ***Oral KCl is the preferred (safest) method of replacement and is appropriate in most instances.** ***IV KCl can be given if hypokalemia is severe (less than 2.5)or if the patient has arrhythmias secondary to hypokalemia.** ○ Give slowly to avoid hyperkalemia. ○ Monitor K+ concentration and monitor cardiac rhythm when giving IV potassium. ○ Infusion pearls. • Maximum infusion rate of 10 mEq/hr in peripheral IV line. • Maximum infusion rate of 20 mEq/hr in central line. • May add 1% lidocaine to bag to decrease pain (potassium burns!) ***As with calcium, it is difficult to correct the potassium level if any hypomagnesemia is not corrected first.**

Calcium the most abundant mineral in the body, is found in some foods, added to others, available as a dietary supplement,..etc. Calcium is required for skeletal strength and dynamic store vascular contraction and vasodilation, muscle function, nerve transmission, intracellular signaling and hormonal secretion, though less than *1% of total body calcium* is needed to support most of the critical metabolic functions!

★ Calcium Normal Physiology

- Daily intake, from diet is 1-1.5 gram/day
- Total body Calcium is 1 kilo (1000 grams):
- **99%** is present in the skeleton
- **1% n**<u>on-bone calcium</u>:
  - ✓ Free ions (51%)
  - ✓ Protein-bound complexes (40%)
  - ✓ Ionic complex (9%) (Calcium phosphate, calcium bicarbonate and calcium oxalate) the one we measure.



Calcium balance is regulated by **hormonal control**, but the levels are also affected by **albumin** and **pH**.

✓ Hormonal Control:

Hormone	Effect	Mechaism
Parathyroid Hormone	↑ plasma Ca ↓ plasma PO4	**1. Bone:** ↑ bone resorption. **2. Kidney:** ↑ Ca reabsorption, ↓ PO4 reabsorption. **3. Gut:** activation of vitamin D.
Calcitonin	↓ plasma Ca ↓ plasma PO4	**1. Bone:** ↓ bone resorption **2. Kidney:** ↓ Ca reabsorption, ↑ PO4 reabsorption **3. Gut:** ↓ postprandial[4] Ca2+ absorption
Vitamin D	↑ plasma Ca ↑ plasma PO4	**1. Bone:** ↑ bone resorption **2. Kidney:** ↑ Ca reabsorption, ↓ PO4 reabsorption **3. Gut:** ↑ Ca absorption, ↑ PO4 reabsorption

PTH (hypercalcemic hormone), active vitamin D and serum ionized Ca level what keeps the Ca balanced in the body.

[4] during or relating to the period after a meal

✓ Albumin

The protein-bound and ionized form is affected by the Albumin. If Albumin is bound to calcium it'll lower the ionized form (active form) As that being said, in hypoalbuminemia the total calcium is low, but ionized calcium is normal.

✓ pH

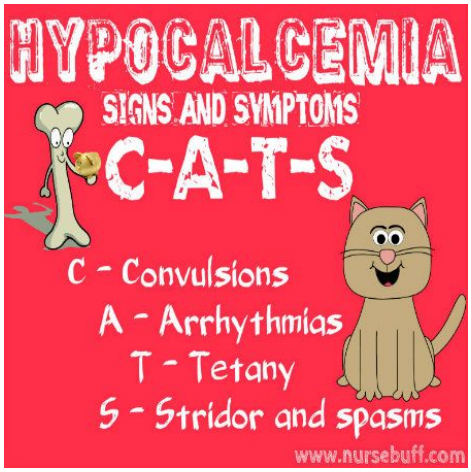
pH alter the ratio of calcium binding. An increase in pH increases the binding of calcium to albumin. Therefore, in alkalemic states (especially acute respiratory alkalosis), total calcium is normal, but ionized calcium is low and the patient frequently manifests the signs and symptoms of hypocalcemia.

★ Calcium Disorders:

Hypercalcemia (> 10.5 mEq/L)	**Hypocalcemia** (< 8.5 mEq/L)
Increased Intestinal absorption ● Increased Ca/Vitamin D intake. **Increased renal reabsorption** ● Hyperparathyroidism, Thiazide diuretics **Increased bone resorption** ● Osteoclastic bone metastasis, Immobilization	**Low intestinal absorption** ● Decreased intake, malabsorption, small bowel resection and vitamin D deficiency. **Low renal absorption** ● Hypoparathyroidism, loop diuretics and tubular defects. ● Renal failure (Low vitamin D) **Bone remodeling** ● Hungry bone syndrome[5].
Causes	
Endocrinopathies: 1- Hyperparathyroidism 2-Renal failure **Malignancies:** 1-Metastatic; bone 2-Lung cancer, release PTH like hormone **Pharmacologic:** 1-Vitamin D intoxication, increase GI absorption of c 2- Milk-alkali syndrome	1-**Hypoparathyroidism** (Most common causes) usually due to surgery of the thyroid 2-**Acute pancreatitis**, deposition of calcium lowers serum Ca. 3-**Renal insufficiency**, decreased production of 1,25 Dihydroxyvitamin D 4-**Vitamin D deficiency** 5-**Malabsorption** 6-**Osteoblastic metastases**

[5] hungry bone syndrome following parathyroidectomy is not well understood; When the stimulus for breaking down the bone is removed, calcitonin is acutely released and bone, "hungry" for calcium, increases its uptake from serum resulting in severe hypocalcemia.

Hypercalcemia (> 10.5 mEq/L)	**Hypocalcemia** (< 8.5 mEq/L)
Clinical Features	
"STONES" Nephrolithiasis, Nephrocalcinosis. **"BONES"** Bone aches and pains, Osteitis fibrosa cystica ("brown tumors") predispose to pathologic fractures. **"GRUNTS AND GROANS"** Muscle pain and weakness, Pancreatitis, Peptic ulcer, Gout, Constipation. **"PSYCHIATRIC OVERTONES"** Depression, Fatigue, Anorexia, Lethargy. **Other findings:** Polydipsia, Polyuria, Hypertension, *on ECG shows shortened QT interval.*	**Neuropsychiatric**: Seizure, Dementia, Extrapyramidal papilledema, Cataract. **Cardiovascular**: Prolonged QT interval, Heart failure, Hypotension. **Neuromuscular**: Paresthesia spasm, Chvostek's and Trousseau's signs. **Autonomic**: Biliary colic, Bronchospasm, Diaphoresis. **Rickets and osteomalacia**
Treatment	
Increase urinary excretion: 1- IV fluids (NS) 2- Diuretics **Inhibit Bone resorption** 1-Bisphosphonate 2-Calcitonin	**Symptomatic**: IV calcium **Long term**: oral calcium



★ MCQs

1- A patient is admitted with vomiting and diarrhea from gastroenteritis. His volume status is corrected with intravenous uids and the diarrhea resolves. His pH is 7.40 and his serum bicarbonate has normalized. Despite vigorous oral and intravenous replacement, his potassium level fails to rise. What should you do?

A. Consult nephrology

B. Magnesium level

C. Parathyroid hormone level

D. Intracellular pH level

E. 24-hour urine potassium level

Answer: B. Hypomagnesemia can lead to increased urinary loss of potassium. If mag- nesium is replaced, it will close up the magnesium-dependent potassium channels and stop urinary loss. Although magnesium is necessary for parathyroid hormone release, this would have nothing to do with potassium levels. Try not to consult on Step 2. You are supposed to handle anything that is based on knowledge. Consultations are gener- ally indicated only for procedures such as catheterization or endoscopy. Although there will be increased potassium on a 24-hour urine with hypomagnesemia, there is no point in performing this test because you still have to detect and treat hypomagnesemia.

2- A woman with ESRD and glucose 6-phosphate dehydrogenase de ciency skips dialysis for a few weeks and then is crushed in a motor vehicle accident. She is taking dapsone and has recently eaten fava beans. What is the most urgent step?

A. Initiate dialysis

B. EKG

C. Bicarbonate administration d. Insulin administration

D. Kayexalate

Answer: B. All of these interventions may be helpful in a person with life-threatening hyperkalemia. The most important step is to determine if there are EKG changes from hyperkalemia. If the EKG is abnormal, she needs calcium chloride or gluconate in order to protect her heart while the other interventions are performed. Kayexalate and dialy- sis take hours to remove potassium from the body. Bicarbonate and insulin work in 15 to 20 minutes, but they are not as instantaneous in effect as giving calcium.