Electrolyte imbalance
(Potassium & Calcium)

Objectives:

- Understand the basic physiologic principles of potassium hemostasis.
- Know the application of physiologic and clinical principles in approaching hyperkalemia.
- Know the application of physiologic and clinical principles in approaching hypokalemia.
- Understand the basic principles of Calcium hemostasis.
- Know the application of physiologic and clinical principles in approaching hypercalcemia.

[Color index: Important | Notes | Extra]

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Resources:

Stepup to medicine,435 slides

(dr.Riyadh: said his slides are more than enough& management is not required)

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Understand the basic physiologic principles of potassium hemostasis

Basic Review

This is clinically relevant to our practice in nephrology, one of the most imp counseling is k restriction counseling
This is what we educate our pt to avoid "banana, potato, citric fruit,dates"

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

Where does K live in the body ?

- Potassium is a cation found majorly inside the cell (intracellular).
- Total body potassium is approximately 50 mmol/kg body weight.
- **Intracellular**: 100- 150 mmol/L (98 % of total body **K**).
- **Extracellular**: 3.4 – 5.5 mmol/L (2% of total body **K**) what only we can measure is extracellular K, Serum K is not a good representation of total K content in the body.But this 2% is very vital for cell function especially myocyte (skeletal_cardiac).

Where does K come from?

- The main source of K is our diet.
- **Can be found in:** Fruits, potatoes, beans, and grains. u r eating a lots of K if u r MacDonald's or محاشيfan.
- High-fat diets usually contain low amounts of potassium.
- Average daily intake approximately 50 to 100 mmol.

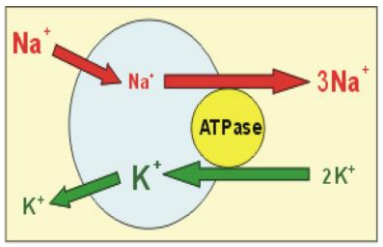
Why is K important ?

- 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 when we eat K? (Normal physiology of Potassium):

- Oral K intake →Absorbed in the intestine →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 .

What keeps the intracellular K high?



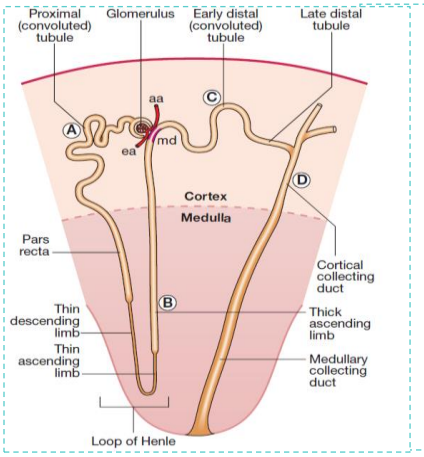
* **Insulin + Beta agonists**(catecholamine): Enhance pump function.
* **Beta blocker**: Inhibit pump function.
  - K\Na pump is very imp & vital: it keeps the balance between intracellular K & Na
  - This pump is critical to establish the resting membrane potential by creating charge difference
  - Exercise enhances pump function bc catecholamine elevates during exercise.
  - If u understand this u will understand a lot of K complications

What keeps Extracellular K low?

- The Na/K ATPase pump البومب فقط تظف لك المكان الين تشتغل الكلية وتتخلص من البوتاسيوم , زي لما يجونك ضيوف فجأة والمكان محيوس تقوم تاخذ حوستك وتخبيها بالادراج ,صح ؟)
- Renal clearance : requires normal GFR and normal aldosterone axis (Adrenal deficiency , Aldosterone resistance) الكلية جدا فعالة لكن مشكلتها كسولة وتاخذ وقت لين ماتشتغل وتحتاج الالدستيرون يرتفع عشان يحفزها
- Intestinal excretion.not very efficient & take long time

In order to Keep serum K in normal range, we need: very important to understand this

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



- Kidney can **Re**absorb(Na, uric acid, bicarbonate, Glucose)BUT it never never reabsorb K ,what it does is:
  - lowers K excretion when K level is low
  - Increases K excretion ,when K level is high
- **Where does aldosterone act?** In distal ct.
- In order to this far away segment "distal tubule' to function it needs: adequate tubular flow & normal GFR
- The most common cause of hyperkalemia in normal ppl is: tubular dehydration

لما نكون مشغولين ننسى نشرب موية , ونقعد ناكل اكل غني بالبوتاسيوم (ماكدونلز, شيبس ووو)على اخر اليوم بتلقى البول مره مركز

Potassium Excretion:

- **Renal excretion**: 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(when GFR goes down"i.e: in renal failure" ,the capacity of intestine to excrete K will go up)

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 ↓)

كم تتوقعون يحتاج ياكل الشخص الطبيعي من موزة عشان تصير عنده هايبركاليميا؟
حوالي ٢٢٠ موزه بتنفجر معدته قبل يصير عنده هايبركاليميا:٠
بينما الاشخاص الي عندهم فشل بالكلى فهم ممنوعين حتى من موزة وحده!!

What happens if K level is abnormal?

- Skeletal muscle dysfunction: weakness and paralysis
- Cardiac cell irritability: arrhythmia

What is the effect of hyperkalemia on AP?
Hyperkalemia reduces the negativity of the resting membrane potential. For example, it changes it from -80 mV to -70 mV. When the resting membrane potential drops like this, it becomes very close to the threshold potential which increases the cell excitability. When hyperkalemia is not corrected rapidly, resting membrane potential drops even more which results in reduction of the magnitude of the Vmax(maximum upstroke velocity of the action potential), causing slow conductivity.

- Once the V max declines then the serious manifestations will appear

KNOW THE APPLICATION OF PHYSIOLOGIC AND CLINICAL PRINCIPLES IN APPROACHING HYPERK\HYPOKALEMIA

POTASSIUM DISORDERS

Hyperkalemia (>5.5 mEq/L)	Hypokalemia (<3.4 mEq/L)
CAUSES	

NA/K ATPase dysfunction:
- B blockers
- Digoxin
- ↓Insulin

Massive Cell breakdown:
- Rhabdomyolysis(muscle breakdown)
- Tumor lysis syndrome(those with malignant hematological tumors who are treated with chemo→it causes lysis of the malignant cells→a huge amount of intracellular K will be released in the circulation.)
- Hemolysis
- burns.

Impaired renal function

Aldosterone axis dysfunction:
- Adrenal deffiency (Addison disease)
- Aldosterone resistance some pt with advance DM will have aldosterone resistance

Redistribution: translocation of potassium from intracellular to extracellular space:
- Acidosis (not organic acidosis)
- 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.

GI losses:
- Diarrhea.if severe
- Laxatives and enemas.when pt abuse laxative.
- Intestinal fistulas.
- Decreased potassium absorption in intestinal disorders.
- Vomiting and nasogastric drainage (volume depletion and metabolic alkalosis also result).

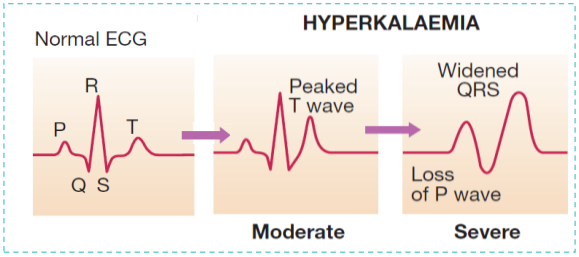
Renal losses:
- Diuretics.if significant
- Primary and secondary hyperaldosteroni

Insufficient dietary intake:if oral intake significantly decrease
- Malnutrition
- Eating disorders

Rapid transcellular shift:
- Insulin therapy which cause over stimulation of Na K pump
- Periodic paralysis (occasional episodes of muscle weakness)
- Insulin administration
- Epinephrine (β2-agonists) which cause over stimulation of Na K pump

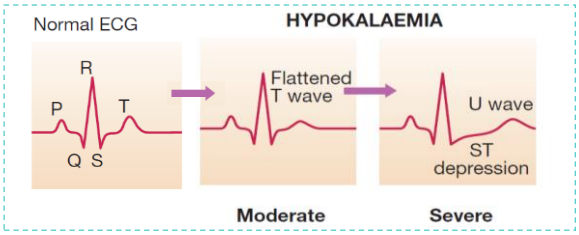
Clinical features

- Arrhythmias—The **most important** effect of hyperkalemia is on the heart. Check an ECG immediately in a hyperkalemic patient. With increasing potassium, ECG changes progress through tall, peaked T waves, QRS widening, PR interval prolongation, loss of P waves, and finally a sine-wave pattern. (bc hyperkalemia will drop the cardiac threshold, so any action potential can stimulate it)



- Muscle weakness and (rarely) flaccid paralysis.
- Decreased deep tendon reflexes.
- Respiratory failure.
- Nausea/vomiting, intestinal colic, diarrhea.

- Arrhythmias—prolongs normal cardiac conduction.
- Flattening of T waves on EKG. U waves appear if severe.



- Muscular weakness, fatigue, paralysis, and muscle cramps.
- Decreased deep tendon reflexes.
- Paralytic ileus.
- Polyuria and polydipsia.
- Nausea/vomiting.
- Exacerbates digitalis toxicity.

Treatment not imp at ur level

How to lower K level ?

1) Reduce Cardiac muscle irritability with IV Ca gluconate "membrane stabilizer"(only if EKG changes). Before giving insulin u have to stabilize the heart.

2) Push K into cells: ننظف المكان ونكب كل العفش داخل الخلايا
   - Insulin
   - Sodium bicarbonate(if pt has acidosis)
   - Beta agonists(Salbutamol 'require high dose').

   *Note: we rely more on insulin & sodium bicarbonate

3) Remove the K load:
   - Through the kidney:
     - loop diuretics(furosemide)commonly used , the loop diuretics is the most efficient , while thiazide is not efficient.
     - dialysis(pt with very advance kidney dis)
   - Through the gut : Laxatives, K chelation(Ca resonium)

How to raise K level?

1) Stop the loss (look for the cause & stop it)

2) Replace lost K with K (PO or IV* if rapid correction is urgently needed)
   *u can't give a lot of k through peripheral line bc it very irritant to the vein can cause thrombophlebitis

Understand the basic principles of Calcium hemostasis

Basic Review

Where does Ca come from?

- Total body Ca = **1000 g**.
- Diet : 1000 – 1500 mg /day in average.
- The normal serum calcium (Ca2+) range is 8.5 to 10.5 mg/dL.

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:
  - **Ionic complexes (9%)* **(Non Ionized)** (calcium phosphate, calcium carbonate, and calcium oxalate)
  - **Protein-bound complexes (40%)* **(Non Ionized)**
  - **Free ions (51%)* **(Ionized)**

    (Ionized form is the active form and the one we actually measure in the serum)what we measure in the serum represent very little amount of total ca, therefore ca range is very narrow (2.1-2.5mmol/L)

Why Ca is important(Calcium functions)?

Bone calcium:	Non bone calcium:
**Skeletal strength.* **Dynamic store*(when body needs calcium, bone will donate, to your circulation. when body has excess Ca, the bone will store it)	**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

Affect of Albumin and pH in calcium:

Albumin

Calcium in plasma exists as:

*__Protein-bound form:__ most calcium ions are bound to albumin, so the total calcium concentration fluctuates with the protein (albumin) concentration.

*__complex bound to ion.__

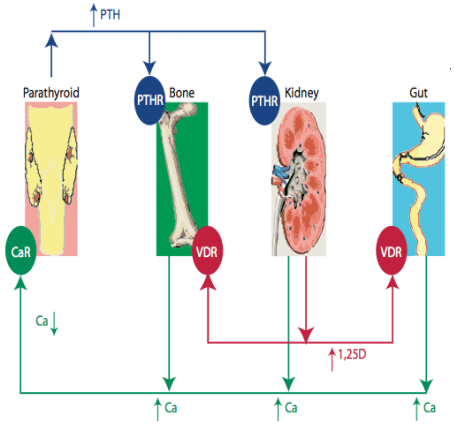
*__Free ionized form:__ physiologically **active** fraction; under **tight hormonal control (PTH)**, independent of albumin levels.

In **hypoalbuminemia** the total calcium is low, but ionized calcium is normal, and can be estimated by the following formula: total calcium—(serum albumin× 0.8).

Changes in 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.

Hormonal control of calcium:

PTH:		Vitamin D:
↑ plasma Ca + and ↓ plasma PO4 by acting on: a. **Bone:** ↑ bone resorption.(that's why whom have hyperparathyroidism for long time can develop osteomalecia) b. **Kidney:** ↑ Ca + PTH helps in last step activation of vit D in the kidney(imp)	 *R=receptor	↑ plasma Ca + and ↑ plasma PO4 by acting on: a. **Bone:** ↑ bone resorption b. **Kidney:** ↑ Ca2+ reabsorption, ↓PO4 reabsorption. c. **Gut:** ↑ Ca absorption, ↑ PO4 reabsorption.
Hormonal mechanisms maintain narrow physiologic range of 10%.		

What can go wrong ?

Oral intake	Intestinal absorption	Renal reabsorption	Renal excretion
Intestinal excretion (e.g: genetic disease and malabsorption)	Bone turnover (e.g:paget disease and malignancy)	PTH	Active Vitamin D

Know the application of physiologic and clinical principles in approaching hyper\hypocalcemia.

Calcium Disorders

Hypercalcemia	Hypocalcemia
Causes	
Increased Intestinal absorption: ○ Increased Ca intake(milk alkali syndrome) /Vitamin D intake(due to false marketing of vit D) **Increased renal reabsorption:** ○ Secondary to Hyperparathyroidism, ○ Thiazide diuretics.(bc it enhances ca reabsorption in proximal tubule) ,very important & commonly asked in the exam(thiazide cause hypercalcemia) **Increased bone resorption:** ○ Osteoclastic bone metastasis ○ Immobilization(seen in chronic bedridden pt) **High PTH:** ○ Primary hyperparathyroidism ○ Multiple Endocrine Neoplasia(malignancy in general) **High Vit D:** ○ Vit D Intoxication Causes not related to ca intake: ▪ Granuloma(which produces Ca) ▪ sarcoidosis	**Low intestinal absorption:** ▪ Decreased intake, malabsorption ▪ small bowel resection ▪ vitamin D deficiency. **Low renal absorption:** ▪ Hypoparathyroidism ▪ loop diuretics(bc it decreases ca reabsorption)very important & commonly asked in the exam ▪ tubular defects. ▪ Renal failure. **Bone remodeling:** ▪ Hungry bone syndrome(in state of sever hyperparathyroidism ,after total parathyroidectomy :the bone is hungry for ca "it was starving for years" & the stimulus of ca resorption from bone (PTH) is gone→thus the bone will cause sudden & sharp uptake of ca resulting in severe hypocalcemia) **Low PTH:** ▪ hypoparathyroidism **Low Vit D:** ▪ Renal failure
Clinical features	
Cardiovascular: ▪ *on ECG shows* ***shortened QT interval.*** من بين كل الكارديك كومبليكشن هذي الي ابيكم تتذكرونها وتجي كثير بالاختبارات	**Cardiovascular:** ▪ ***Prolonged QT interval,*** which can lead to malignant ventricular arrhythmia ,hypocalcemia should always be in the differential diagnosis for a prolonged QT interval ,Commonly asked in exam ▪ Heart failure ▪ Hypotension

Neuromuscular:

- Muscle weakness,Fatigue, Anorexia, Lethargy.
- impaired memory
- Corneal calcification

STONES:

- Nephrolithiasis
- Nephrocalcinosis(Ca deposits in the interstitium of the Kidney).
- Nephrogenic diabetes insipidus(Hypercalcemia cause a state of ADH resistance→polyurea→sever state of volume depletion)
- **Dehydration**

BONES:

- Bone pain

GIT:

- Abdominal pain
- Peptic ulcer
- **Pancreatitis** life threatening
- Constipation,
- nausea,vomiting

Increased neuromuscular irritability:

- Paresthesia (Numbness peripheral or perioral)
- Spasm (Tetany):
  - Hyperactive deep tendon reflexes.
  - *Chvostek sign*: tapping a facial nerve leads to contraction (twitching) of facial muscles.

  - *Trousseau sign*: Inflate BP cuff to a pressure higher than the patient's systolic BP for 3 minutes (occludes blood flow in forearm). This elicits carpal spasms.

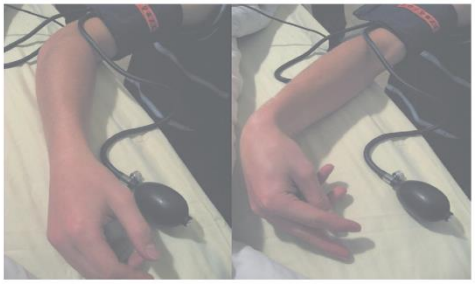


Figure 47.1 Trousseau's sign. Inflation of the sphygmomanometer cuff causes carpal muscle spasm in an individual with hypocalcaemia.

Neuropsychiatric:

- Seizure
- Dementia
- Extrapyramidal
- Papillidema
- Cataract

Autonomic:not imp

- Biliary colic
- Bronchospasm
- Diaphoresis

Rickets and osteomalacia.

HOW TO TREAT:

- **Hypocalcemia:** depends on the severity, u have 2 ways of replacing Ca either orally or IV ,symptomatic pt give initially IV ca to correct the ca level temporary then ALWAYS treat the underlying cause.

- **Hypercalcemia:** first thing give fluid for hydration then look for the cause:
  - PTH dependent 'PTH is high'
    or
  - non PTH dependent 'PTH is suppressed or normal '

TEST YOURSELF

QUESTIONS

1) **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
    e. Serum potassium

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
    e. High-potassium diet

3) **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
    e. Osteoporosis caused by hypogonadism

Answers

1) **B**. This patient has symptoms of hypercalcaemia, the major causes of which can be divided into primary, secondary and tertiary disorders. Primary usually includes malignancies such as adenomas producing PTH, secondary conditions are due to a compensatory increase in parathyroid hormone due to low serum calcium, such as in vitamin D deficiency. Secondary conditions can eventually become tertiary disorders with autonomous PTH production, such as in renal failure. The symptoms of hypercalcaemia can vary depending on severity, patients may be asymptomatic or suffer a number of features affecting different organ symptoms. General symptoms include malaise, abdominal pain and depression. Renal tubule impairment can lead to polyuria, polydipsia and nocturia. Bone pain occurs due to the effect of PTH upon bone metabolism, renal stones can also form due to increased serum calcium and dehydration. Serum calcium (**b**) must be measured first as this will be able to confirm an abnormal level of calcium in the body. Measuring PTH (**c**) may or may not provide useful diagnostic information, for example in a tumour producing excess calcium the PTH would be low. Serum phosphate (**a**) is useful to measure in patients with anorexia, weight loss and osteoporosis as this suggests deficiency, although this is very rare due to an abundance in natural foods. Plasma glucose (**d**) would be useful in a patient with suspected diabetes, however flank pain and constipation are not typical presentations and urine dipstick would reveal the presence of glucose and ketones. Derangement of serum potassium (**e**) does not produce the symptoms described in this patient. Hyperkalaemia predisposes to cardiac arrhythmias (loss of p-waves, widened QRS complex and tented T-waves) and muscle weakness, while in severe hypokalaemia there is muscle weakness, atrial and ventricular ectopics.

2) **D**. The syndrome of hyporeninemic hyperaldosteronism occurs in older diabetic patients, particularly males with congestive heart failure. The syndrome often presents when aggravating drugs are added. Beta-blockers impair renin secretion; ACE inhibitors decrease aldosterone levels; and spironolactone competes for the aldosterone receptor. Combined with diabetes and mild renal insufficiency, the result may be life-threatening hyperkalemia. Moderate renal insufficiency per se is unlikely to cause such severe hyperkalemia. Hypertonicity caused by hyperglycemia could aggravate hyperkalemia, but a blood glucose of 250 mg/dL should not cause severe hyperkalemia. Statin drugs may cause muscle injury and rhabdomyolysis, but a CK of 400 IU/L is a modest elevation (probably caused by the renal insufficiency) and would not cause severe hyperkalemia. A high-potassium diet may contribute modestly to hyperkalemia but is rarely a major factor by itself.

3) **D**. One of the commonest causes of hypocalcemia is impaired parathormone (PTH) production. Hypomagnesemia causes decreased production of PTH as well as decreased end-organ response to the hormone. Alcohol causes increased urinary losses of magnesium which then leads to the mentioned effects on PTH and ultimately to hypocalcemia. While pancreatitis can cause hypocalcemia, this patient's presentation does not suggest the condition. Osteoporosis and poor dietary intake do not lead to hypocalcemia unless the patient has vitamin D deficiency. Routine calcium levels are not accurate in the setting of a low albumin. To estimate the true calcium level, one may add 0.8 mg/dL to the observed calcium level for every 1 g reduction in the albumin level (from 4 used as normal). In this case, the albumin is not far from 4 and hence the calculation would change the low calcium level very little. An ionized calcium level is consistent and accurate regardless of the albumin level of a patient