If you’re preparing for the United States Medical Licensing Examination® (USMLE®) Step 2 exam, you might want to know which questions are most often missed by test-prep takers. Check out this example from Kaplan Medical, and read an expert explanation of the answer. Also check out all posts in this series.

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This month’s stumper

A 32-year-old man comes to his physician with one year of worsening nausea, abdominal pain, constipation, diffuse bone pain, and intermittent headaches. The patient has a 10 pack-year history of smoking and denies use of alcohol or recreational drugs. His blood pressure is 130/80 mm Hg, pulse 90 per minute, respirations 18 per minute, temperature 37°C (98.6°F). The exam shows dry mucous membranes and mild left lower quadrant abdominal pain on deep palpation. CBC/Serum lab studies show:

- WBC: 7,000 mm$^3$
- Hemoglobin: 14 g/dL
- Hematocrit: 50%
- Platelets: 250,000 mm$^3$
- Na$^+$: 145 mEq/L
K⁺: 5.0 mEq/L
Cl⁻: 100 mEq/L
HCO₃⁻: 24 mEq/L
BUN: 30 mg/dL
Creatinine: 1.0 mg/dL
Glucose: 100 mg/dL
Albumin: 4 g/dL
Phosphate: 3.0 mg/dL
PTH: 60 pg/dL (N= 11 - 54 pg/dL)

The chest X-ray is normal. What is the most appropriate next step in the management of this patient's current condition?

A. MRI of the thyroid/parathyroid gland.
B. PTH-related protein measurement.
C. Sestamibi scan of the neck.
D. Urinary calcium level.
E. Vitamin D level.
The correct answer is D.

Kaplan Medical explains why

This patient has the classic symptoms of hypercalcemia: abdominal pain, bone pain, constipation, and headaches. Hypercalcemia may be due to hyperparathyroidism, benign familial hypocalciuric hypercalcemia (FHH), malignancy (due to PTH-related protein), or elevated Vitamin D levels due to ingestion or granulomatous diseases.

The first step in workup is a parathyroid hormone level, elevated in this case. The most common cause of hypercalcemia in the general population is primary hyperparathyroidism. The two most common causes of PTH-dependent hypercalcemia are primary hyperparathyroidism and FHH. FHH is the genetic lack of the calcium-sensing receptor on the parathyroid gland and in the kidney, leading to elevated PTH (and consequent hypercalcemia) with low renal calcium excretion.

In contrast, in primary hyperparathyroidism the renal calcium excretion is elevated, as it is in most hypercalcemic patients. Therefore, a way to differentiate the two conditions is to obtain a urinary calcium level; a low urinary calcium level and a positive family history will point toward the diagnosis of FHH, while an elevated urine calcium suggests primary hyperparathyroidism.

Why the other answers are wrong

Choice A: CT and MRI of the thyroid/parathyroid are options for presurgical evaluation of the parathyroids, but should not be done before the urine calcium, in order to avoid unnecessary testing.

Choice B: PTH-related protein measurement should be drawn when malignancy is considered to be the cause of the hypercalcemia. Besides his 10 pack-year smoking history, this patient is young, has a normal chest X ray, and malignancy is not evident in this case. Squamous cell carcinomas are most associated with this paraneoplastic syndrome.

Choice C: Nuclear Sestamibi scan of the neck is used to preoperatively localize a parathyroid adenoma in primary hyperparathyroidism. It would be appropriate in a patient whose urinary calcium
is elevated, but not before doing the urine calcium to exclude FHH.

**Choice E:** Vitamin D is a fat-soluble vitamin that, in excess, is associated with hypercalcemia. This may be due to dietary ingestion or to some malignant and granulomatous diseases that produce Vitamin D. Hypercalcemia secondary to elevated vitamin D toxicity would cause a non-PTH dependent hypercalcemia; on labs, this would show a low PTH and a high serum phosphorous level. This patient has an elevated PTH level; therefore, the patient’s condition must result from one of the PTH-dependent causes.

**Tips to remember**

Symptoms of hypercalcemia include bone pain, recurrent kidney stones, and headaches.

The most common cause of hypercalcemia is primary hyperparathyroidism.

The first diagnostic test for hypercalcemia is a serum PTH level; if elevated, a urine calcium level should be done to exclude familial hypocalciuric hyperparathyroidism.