

Bones, Stones, Groans and Moans: A Calcium Story

by

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Part I – A Morning Walk

“You know Louise, my primary care provider sometimes does the most preposterous things,” commented Amelia. The two friends were out together in the park on a lovely spring day.

“Tell me about it,” said Louise.

“Well, just yesterday I was in for my annual physical and Dr. Liu told me I was in excellent condition for my age; no problems with blood pressure nor any risk of diabetes. You know, I take good care of myself...”

“You sure do,” Louise said with a smile, “This is so lovely. I should go for walks in the park as often as you do. I’m sure the doctor was impressed you do this, every day!”

“That he was,” said Amelia proudly. “He said to keep up the good work and sent me home. Yet, a few hours later, I received a call from one of the nurses. She explained my calcium levels were too high. High! Hasn’t the doctor always told us that we need to be getting more calcium?”

“Yes of course!” exclaimed Louise. “I remember all the old slogans... calcium for strong bones and teeth! Support your bones today; they will support you tomorrow! You can’t stand without calcium!”

“Well, then the nurse started asking me all these questions, like whether I use the bathroom more often than I used to. I do of course... but that’s only natural, I’m nearly 75 after all! She wanted to know whether I have any abdominal pain or constipation, which I do not, thank heavens, and then, get this, Louise, she asked me if my blood pressure was high! The doctor just told me the day before that my blood pressure was quite healthy for a woman of my age.”

“Goodness. Was she even reading your file?” asked Louise.

“Apparently not,” Amelia agreed. “Anyways, next she asked me if I’ve been forgetful and tired recently. What a ridiculous question; doesn’t that happen to us all at this age?”

“I forget my keys all the time!” said Louise.

“Exactly. I don’t know what she was going on about. Too much calcium. How absurd!”

Questions

1. What is calcium homeostasis?

2. Why is calcium homeostasis tightly regulated?

3. What are the concentrations of total calcium in the intracellular fluid, interstitial fluid and plasma?

4. What different forms of calcium circulate in plasma? What is the significance of the ionized or free fraction of calcium?

5. Complete Table 1. List the three main hormones that regulate calcium homeostasis. Describe their actions on the target organs they affect.

Table 1. Hormones that regulate calcium homeostasis.

<i>Hormone</i>	<i>Target Organ(s)</i>	<i>Actions</i>

6. What might be making Amelia's calcium levels high?

Part II – At the Doctor’s Office

“Let me explain this for you,” Dr. Liu told Amelia. “I know it’s confusing to hear that high calcium levels are not actually a good thing.”

“It sure is!” exclaimed Amelia. “All my life I’ve been told how important calcium is for your bones and your teeth!”

“That’s correct,” said Dr. Liu. “However, an excess of any nutrient can cause problems in the body. In the case of excess calcium, we are concerned about ‘bones, stones, groans and moans.’ Some patients experience bone pain (bones) and get kidney stones (stones). Too much calcium can decrease intestinal functioning, which causes constipation (groans). Appropriate levels of calcium are also crucial to a healthy brain, and too much can lead to memory loss, depression, and fatigue (psychic moans). Constriction of the blood vessels by too much calcium can also lead to high blood pressure.”

“So that’s why the nurse was asking me all those questions,” said Amelia. “I thought she had no idea what she was talking about on the phone! Thankfully I haven’t been experiencing anything you’re talking about, and you told me just last week my blood pressure was normal.”

“I did,” said Dr. Liu. “You appear to be in excellent health for your age, Amelia. Most of the time, patients with a high calcium reading don’t present any symptoms at all, however, that doesn’t mean that we shouldn’t find out what is causing this excess calcium.”

“But if this isn’t causing me any problems, why do I need to worry about it?” asked Amelia.

“You’re feeling all right now,” said Dr. Liu, “but if this persists, it may cause you problems over time. The biggest concern is that the calcium we detected in your bloodstream is actually coming out of your bones.”

“Coming out of my bones?” Amelia had never heard that this could happen.

“This can severely weaken your bones over time,” said Dr. Liu. “We need to run a few more tests. I’m going to need some more blood tests from you, and I want to check that your kidneys are working normally. I’m also going to order a DEXA scan, which is a test that will determine your bone density. After we have these results, we should have a clearer picture of what’s going on.”

Questions

7. Using the information in Table 1, draw two feedback loops that illustrate the physiological responses that act to restore calcium homeostasis when (i) the plasma concentration of calcium rises above the set-point, and when (ii) the plasma concentration of calcium falls below the set-point. Include a figure legend (summary) for each feedback loop.
8. How does the body detect calcium levels?
9. Explain how parathyroid hormone secretion is regulated.
10. How does the body get vitamin D? Describe the pathway that produces 1,25-dihydroxyvitamin D and its relevance to calcium homeostasis.

11. Look at the data in Tables 2 and 3. Which tests are not normal?

Table 2. Amelia's blood pressure, bone density and kidney function test results.

<i>Test</i>	<i>Amelia's Data</i>	<i>Normal Range</i>	<i>Units</i>
Systolic blood pressure	116	<120	mmHg
Diastolic blood pressure	75	<80	mmHg
Bone density score	-1	-1 and above = normal -1.1 to -2.4 = below normal -2.5 and below = osteoporosis	
Glomerular filtration rate	96	90–120	ml/min/1.73m ²

Table 3. Amelia's blood test results.

<i>Plasma Concentrations</i>	<i>Amelia's Data</i>	<i>Normal Range</i>	<i>Units</i>
Sodium	141	134–144	mmol/L
Potassium	4.0	3.5–5.2	mmol/L
Chloride	106	96–106	mmol/L
Total Calcium	2.8	2.2–2.6	mmol/L
Free Calcium	1.4	1.1–1.3	mmol/L
Phosphate	0.6	0.8–1.4	mmol/L
Albumin	4.7	3.5–5.5	g/dL
Thyroid stimulating hormone (TSH)	1.47	0.45–4.50	uIU/mL
Thyroxine (T ₄)	9.3	4.5–12.0	ug/dL
1,25-dihydroxyvitamin D	55	30–100	ng/mL
Parathyroid hormone	80	10–65	pg/mL

12. What might lead to high levels of calcium and low levels of phosphate? (*Tip*: Refer to the information in Table 1.)

Part III – Follow-up with Dr. Liu

“As we’ve seen already, you aren’t presenting many symptoms of hypercalcemia,” said Dr. Liu. “Your blood pressure and kidney function are normal, and right now your bone density is also within the normal range.”

“Excellent,” said Amelia. “Is there anything else?”

“Your blood test results still show excess calcium, as well as levels of phosphate that are low. While your bone density is currently normal, it is on the low end of the normal range, and it’s for the best if it doesn’t drop any lower.”

“OK, but what does this all mean?” asked Amelia, still confused. “If all my tests are coming back saying I’m healthy, then what is the problem? How do I even have high calcium in the first place?”

“Your hormone test results provide the answers here,” continued Dr. Liu. “Everything came back normal, except for your results for parathyroid hormone. This hormone is secreted by your parathyroid glands, which are found in your neck. This hormone is essential for maintenance of calcium levels in the body.”

“So, I have high calcium because I have too much parathyroid hormone?” asked Amelia.

“Yes,” said Dr. Liu. “Based on your results, you have what is called primary hyperparathyroidism, leading to bone resorption and hypercalcemia.”

“But I don’t understand why you are worried about my bone density. I thought my bone density was normal” said Amelia.

“For now it is,” said Dr. Liu, “but, if your parathyroid glands continue to secrete too much parathyroid hormone your bones will weaken as a result.”

“But why are my glands doing this?” Amelia was worried now. Until coming to the doctor, she hadn’t thought she had any problem at all! “Is there a way to fix it?”

Questions

13. Distinguish between primary and secondary hyperparathyroidism. Explain why Amelia has primary hyperthyroidism.

14. Amelia understands that she has high calcium levels because she has too much parathyroid hormone, but she does not appear to understand where the calcium is coming from. Refer to your feedback loop and explain to Amelia:
 - a. the meaning of bone resorption and how excess parathyroid hormone affects bone resorption.

 - b. how the effects of excess parathyroid hormone on the kidneys and intestine contribute to high levels of calcium in the blood.

15. What is the most common cause of primary hyperparathyroidism?

16. List the symptoms of hypercalcemia mentioned in the case study. Explain why the symptoms of hypercalcemia are often described as “bones, stones, groans and psychic moans.”

Part IV – Another Morning Walk

“I’m glad to catch up with you again, Amelia,” said Louise. “I’ve been worried about you. I heard that you had surgery three weeks ago! What happened? Last time we chatted, I thought your doctor was being preposterous!”

“Yes, well, that’s what I thought too,” said Amelia. “He insisted on running some more tests and of course most of them came back normal... I’m perfectly healthy really, but anyway, this calcium problem turned out to be a problem with one of my parathyroid glands.”

“Parathyroid glands? I’ve never heard of them!”

“Well, I hadn’t either,” said Amelia, “but according to the doctor it’s very important for keeping calcium at a healthy level, and mine—get this, Louise—mine was telling my body to take calcium out of my bones and into my bloodstream!”

“My goodness!” Louise still looked perplexed. “But you haven’t had any bone problems. You don’t have osteoporosis, do you?”

“Not yet I don’t,” said Amelia, “but I would have if they hadn’t found what causes it. I was still very skeptical because, as you know, I felt fine and I look after myself, but the doctor insisted on doing a SPECT scan. Something using gamma rays, I think he said. The things they can do in medicine nowadays! Anyway, the scan showed that I had a tumor on one of my parathyroid glands.”

“A tumor!” Louise looked aghast. “Will you need chemotherapy?”

“No, no, it wasn’t cancerous, thank goodness. It was an adenoma. That means it was a benign tumor that was producing large amounts of hormones in an uncontrolled manner.”

“So, you had surgery to remove it?” asked Louise.

“Yes, I had one of the parathyroid glands removed. The adenoma was caught early enough that there is no irreversible damage to my bones or my kidneys. Can you believe that?”

“My goodness!” exclaimed Louise. “I guess your doctor wasn’t crazy after all!”

Questions

17. What is a SPECT scan? What useful information does it provide?
18. Amelia had surgery. How would removal of one of the parathyroid glands (the adenoma) affect parathyroid hormone secretion and calcium levels?
19. Amelia wanted to avoid developing osteoporosis. What is osteoporosis? What is the mechanism that causes it?
20. Osteoporosis is more common in elderly women than in elderly men. Why is that?

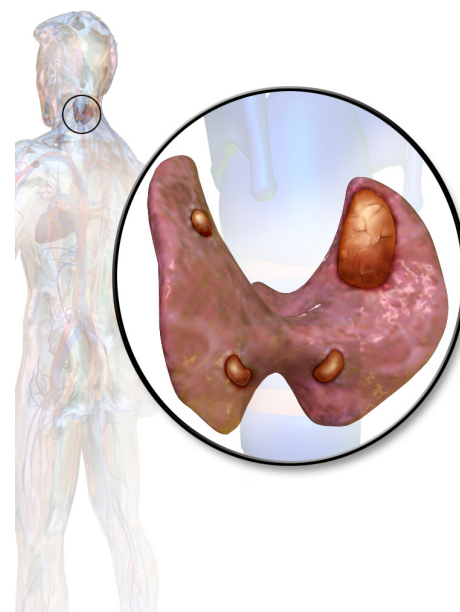


Figure 1. Parathyroid adenoma.

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