

A Stressful Semester: The Regulation of Cortisol Release

by

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Part I – Home for the Holidays

After a stressful week of final exams, Claire was finally back at home for winter break. Although she was weary after a long plane flight, she was happy to see her family again.

“Don’t worry, I’ve got it!” she said as she dragged her suitcase up the steps, waving her dad away. She had brought the suitcase across the country with her; she could certainly get it up her own front steps!

“Are you sure you don’t want help, Claire? You look exhausted.” Her dad sounded worried. Claire could see concern in everyone’s faces. Just as she was about to assure them again that she could handle it, she stumbled as she tried to lift the suitcase up the next step. The suitcase hit her in the leg and Claire was surprised to see that her skin had torn, and she was bleeding. It was just a small carry-on suitcase with some clothes and a couple of books in it. Surely bumping into it shouldn’t have caused her anything more than a small bruise! Claire’s family helped her up, brought the suitcase inside the house, and Claire sat down on the couch, happy to see her younger sister Mia.

“Claire! I’ve missed you so much, I’m so glad you’re home!” exclaimed Mia.

“I’m really glad to be home too,” said Claire. “I can’t believe my first semester is done. College is no joke! I’ve learned a lot of biology, but it’s also been a really stressful few months.”

“I know you got off to a rough start with your roommates. Did things improve at all? Are you getting along better now that you have had time to get to know each other?” asked Mia.

“They’re nice people,” said Claire, “but I still end up doing most of the cleaning all the time, and I almost always need to remind at least one of them to get their rent check in on time. I’ve had so little time to meet any other people.”

“I see why that’s stressful for you,” said Mia. “How did your finals go?”

“It’s been so hard to juggle my classes and my Macy’s job,” said Claire. “I had almost no time to study. I’m worried about some of my grades this semester, for the first time in my life! I think the stress is really getting to me. I’ve been breaking out a lot on my face and even though I’m doing my best to eat healthily, and I exercise when I can, a lot of my clothes aren’t fitting anymore. I don’t know why I’m gaining so much weight.”

“Well, a lot of people gain weight when they’re stressed,” said Mia. “I am worried about you though, Claire. You always seemed tired when we talked on the phone, and your hair even seems thinner than it used to be. You have a couple of bruises on your arms and legs too.”

“I’ve told you how stressed I’ve been this semester,” said Claire. “I don’t know what else it could be. If I go to the doctor, they’ll probably just say that stress is taking a toll on me and it’s making me tired and clumsy.”

Part II – Dr. Hernandez’s Office

“You’re right, Claire. Most of your symptoms could certainly be related to the stress of moving away from home and the pressures of your first semester as a biology major,” Dr. Hernandez said. “Weight gain, acne, and fatigue are all very common.”

“My family thinks something else might be going on,” said Claire, “and I did find it weird when I started bleeding after my suitcase hit my leg. It seems like I end up with a bruise every time another student bumps into me in the hallway.”

“That is unusual,” admitted Dr. Hernandez. “Your blood pressure is a little high. I’m also noticing that you have a little bit of hair growing on your face. Has that always been there?”

“I don’t think so. I’m not sure,” Claire admitted. “I’ve been so stressed lately that I haven’t been paying much attention to my appearance. I only noticed I was gaining weight when my clothes stopped fitting. It’s really embarrassing, but I think I put on weight so quickly I have a couple of ugly purple stretch marks on my stomach.”

Dr. Hernandez looked at her notes. “Has your menstrual cycle been irregular lately?”

“Uh...let me check my app,” said Claire. She opened her phone and noticed that she was long overdue for her period this month, and that the previous month she had only recorded two days of spotting. “Yeah, I guess it has. I haven’t given it much thought. Doesn’t stress affect when you get your period sometimes?”

“Stress can certainly cause menstrual irregularities,” said Dr. Hernandez, “but I think we should refer you to an endocrinologist who can run tests when you are home for spring break.”

Questions

3. The general term used to describe the stimulus for cortisol release is stress. What is physiological stress?
4. List the functional zones of the adrenal cortex.
5. Which zone of the adrenal gland primarily secretes the glucocorticoid cortisol?
6. Diagram negative feedback control of plasma concentrations of cortisol by the hypothalamus and pituitary.
7. To which chemical class of hormones does cortisol belong?
8. How are cortisol and other adrenal steroids transported in the blood?
9. Where would you expect to find receptors for cortisol?
10. What additional symptoms does the visit to Dr. Hernandez reveal?

Part III – Clinical Testing

Under the care of Dr. Scott, an endocrinologist, Claire underwent several tests at a local hospital. Her results follow:

Test 1. Plasma Concentrations of Cortisol, Glucose and Electrolytes.

<i>Date</i>	<i>Serum Concentrations</i>	<i>Claire's Data</i>	<i>Normal Range</i>	<i>Units</i>
3/18	Sodium	139	134–144	mmol/L
3/18	Potassium	4.9	3.5–5.2	mmol/L
3/18	Chloride	100	96–106	mmol/L
3/18	Calcium	9.9	8.7–10.2	mg/dL
3/18	Phosphorus	3.4	2.5–4.5	mg/dL
3/18	Glucose	130	70–100	mg/dL
3/18	Morning Serum Cortisol (9 am)	780	170–700	nmol/L
3/18	Morning ACTH (9 am)	110	10–50	pg/mL
3/18	Evening Cortisol (11 pm)	380	< 50	nmol/L
3/18	Evening ACTH (11 pm)	63	5–10	pg/mL
3/19	Morning Cortisol (9 am)	1800	170–700	nmol/L
3/19	Morning ACTH (9 am)	113	10–50	pg/mL
3/19	Evening Cortisol (11 pm)	517	< 50	nmol/L
3/19	Evening ACTH (11 pm)	94	5–10	pg/mL

Test 2. Twenty-Four Hour Urinary Free Cortisol.

<i>Date</i>	<i>Variable</i>	<i>Claire's Data</i>	<i>Normal Range</i>	<i>Units</i>
3/23	24-h Urinary Free Cortisol	17	< 10	mg/24-h

Test 3. Low Dose Dexamethasone Suppression Test.

Claire received a single oral dose of 1mg dexamethasone between 11:00 p.m. and midnight. The next morning, her plasma concentration of cortisol was measured at 8:00 before she ate breakfast.

<i>Date</i>	<i>Variable</i>	<i>Claire's Data</i>	<i>Normal Range</i>	<i>Units</i>
3/26	Serum Cortisol	780	<50	nmol/L

Test 4. Pituitary Contrast-Enhanced Magnetic Resonance Imaging (MRI).

Test results pending.

Questions

11. Use the table below to summarize the data from Claire's tests. In the "Normal?" column, answer "Yes" or "No." If the results of a test are not normal, then place an "X" in the appropriate column (either "High" or "Low").

<i>Date</i>	<i>Test</i>	<i>Normal?</i>	<i>High</i>	<i>Low</i>
3/18	Serum electrolytes			
3/18	Serum glucose			
3/18	Morning Serum Cortisol (9 am)			
3/18	Morning ACTH (9 am)			
3/18	Evening Cortisol (11 pm)			
3/18	Evening ACTH (11 pm)			
3/19	Morning Serum Cortisol (9 am)			
3/19	Morning ACTH (9 am)			
3/19	Evening Cortisol (11 pm)			
3/19	Evening ACTH (11 pm)			
3/23	24-h Urinary Free Cortisol			
3/26	Serum Cortisol (Suppression Test)			

12. What is the difference between Cushing's disease and Cushing's syndrome?
13. Does Claire have the disease or the syndrome? (*Tip*: refer to the negative feedback diagram in Question 6.)
14. The results for the magnetic resonance imaging (MRI) scan of Claire's pituitary are still being analyzed. What, if anything, would you expect the MRI scan of Claire's pituitary (Test 4) to show that would confirm your answer to Question 13?
15. Describe Claire's condition as primary or secondary, and as hyposecretion or hypersecretion.
16. Why were Claire's urinary and serum cortisol levels tested at various timepoints, as opposed to "once and done"?
17. Why does Claire have high blood glucose?
18. Cortisol is a glucocorticoid. Explain the origin of the term "glucocorticoid."

Part IV – Dr. Scott’s Office

“All of the tests we ran indicated that your cortisol levels are extremely high,” said Dr. Scott. “Additional tests indicated that you have a very rare condition called Cushing’s disease.”

“Cushing’s disease?” repeated Claire, feeling shocked. “I’ve never heard of that before.”

“That’s not surprising,” said Dr. Scott. “It’s incredibly rare. I’ve only had one other patient with this condition in the 20 years I’ve been practicing endocrinology!”

“So...what causes it?” Claire wondered.

“Well, cortisol is produced in the adrenal glands, which are located above your kidneys,” Dr. Scott began.

Claire frowned. “So, why did I have to get an MRI scan of my brain?”

“Cortisol release is controlled by the release of another hormone called ACTH, which is secreted from the pituitary gland, which is located behind your nose, in a pocket called the sella turcica of the sphenoid bone at the base of the brain.”

“OK,” said Claire, trying to follow along. “So...if I have too much ACTH, would I also have too much cortisol?”

“Exactly,” said Dr. Scott, “and based on the results of your ACTH levels, that’s exactly what’s happening. Some patients have high cortisol with normal ACTH, which suggests a problem with the adrenal glands. You have high cortisol and high ACTH, which suggests the problem is at the pituitary level.”

“Why is my pituitary gland making so much ACTH?” asked Claire.

“Well, the MRI scan shows that you have a small, benign tumor, known as an adenoma, on your pituitary gland. The tumor is secreting ACTH, which is resulting in constant signaling to your adrenal glands to produce more cortisol. It explains all of your symptoms.”

“What’s the treatment for it?”

“We’ll work out a treatment plan for you and you’ll eventually be back to your old self,” said Dr. Scott.

Claire felt relieved. “It wasn’t just stress getting to me after all!”

Question

21. Do some research and suggest two or three possible treatment plans for Claire. Describe any advantages or disadvantages to your treatments.