Running Off Track:
A Case Study in Renal Physiology

by
Maria-Elena Conin, Lea C. George, Joshua D. Kumin, and Philip J. Stephens
Department of Biology
Villanova University, Villanova, PA

Part I — Rough Run

Cara was a high school student on the track team and training for her upcoming cross-country meet. She woke up bright and early to complete a 10-mile run. Her workout ended up taking her a little longer than usual and she was sweating profusely.

As Cara cooled down from her run, Cara’s Mom yelled from the kitchen, “Cara, your breakfast is ready! Come eat. You look so pale!”

“Oh, really? I’m starving; maybe that’s why? What did you make?”

“Your favorite... eggs benedict with a side of toast and orange juice. So, how was your run? It seemed like it took you longer than usual.”

“I felt a little more tired than I usually do, but I stayed strong. Nothing to worry about,” Cara assured her.

“You need to stay healthy for the invitational meet on Saturday. As you well know, your performance on Saturday will determine your eligibility for states. Maybe you should reschedule your date with ... ”

“Mom! I’ll be fine. Trust me,” Cara exclaimed.

Cara finished her breakfast and, while taking a hot shower, felt a cramp developing in her left leg. Not thinking too much about it she took a naproxen tablet, rubbed the cramp and proceeded on with her day. After studying for about an hour she realized that the naproxen wasn’t working because her muscles still felt sore. Oh no...this is bad timing. I have a date with Phil tonight, Cara thought. So, she took another naproxen tablet.

Half an hour later, Cara felt dizzy and lightheaded and her skin began to feel clammy, which she believed was due to the humidity. She felt her heart race and tried to calm herself, but the leg cramps started coming back. Although Cara prided herself on a high threshold for pain, she finally told her mom that something was wrong and that she needed to go to the hospital.

Questions

1. List the problems that Cara experienced.
2. Can you see any common features in Cara’s problems?
3. Do you think Cara overreacted by saying she wanted to go to the hospital?
4. Do you have a prognosis for Cara’s problems?
Part II – Dehydration?

“Cara, honey, I think you’re overreacting. How about I take you to the urgent care?”

“Fine, Mom!”

The nurse at the urgent care took Cara’s history and physical.

<table>
<thead>
<tr>
<th>History and Physical Report</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient:</strong> Cara Pearson</td>
</tr>
<tr>
<td><strong>History</strong></td>
</tr>
<tr>
<td>Chief complaint:</td>
</tr>
<tr>
<td>Lightheadedness, fatigue,</td>
</tr>
<tr>
<td>muscle cramps</td>
</tr>
<tr>
<td>Past medical history:</td>
</tr>
<tr>
<td>Polycystic ovarian syndrome</td>
</tr>
<tr>
<td>[Treatment → 150 mg spironolactone daily]</td>
</tr>
<tr>
<td>Past surgical history:</td>
</tr>
<tr>
<td>Wisdom teeth removed (3 months ago)</td>
</tr>
<tr>
<td>Drug allergies:</td>
</tr>
<tr>
<td>Penicillin</td>
</tr>
<tr>
<td><strong>Physical</strong></td>
</tr>
<tr>
<td>Age: 17</td>
</tr>
<tr>
<td>Height: 5’6”</td>
</tr>
<tr>
<td>Weight: 130 lbs.</td>
</tr>
<tr>
<td>Temperature: 97.8°</td>
</tr>
<tr>
<td>Heart rate: 110 beats/min (normal: 60–100)</td>
</tr>
<tr>
<td>Blood pressure: 98/56 (normal: 120/80)</td>
</tr>
<tr>
<td>Pinch skin: skin bounces back slowly.</td>
</tr>
</tbody>
</table>

“Wow, Mom, my heart rate’s high; it’s usually around 60.”

“Maybe you’re just nervous, honey.”

The nurse decided that Cara was probably experiencing dehydration from her run. She recommended rest and drinking plenty of fluids like water and Gatorade.

**Questions:**

1. What new information has been revealed?
2. Which of Cara’s problems could have been caused by dehydration?
3. Which problems could have been caused by something other than dehydration?
4. Where is blood pressure monitored in your body?
5. Which part of the autonomic nervous system is activated when blood pressure is low?
6. What is the effect of this part of the autonomic nervous system on heart rate and stroke volume?
7. If Cara is correct and her resting heart rate is usually around 60, why is her blood pressure low?
8. Would you like to change or modify your prognosis?
Part III – Big Date

After driving home from urgent care, Cara began to get ready for her big date night with Phil. She had a new dress picked out and invited her friend, Marissa, over to help with her hair and makeup.

“You look great! Phil’s going to be blown away,” Marissa encouraged her friend.

“I hope so. Though, I’m still a little nervous. I think I’m going to take a couple of my prescription pills. I missed my dose this morning.”

“Are you sure?” Marissa asked.

“Yeah, it’s alright. And I think it makes me look and feel better,” Cara said reassuringly.

Phil arrived to pick up Cara for the date. Ever the gentleman, he had picked out a nice romantic Italian restaurant. Cara ordered spaghetti marinara and Phil ordered fettuccine alfredo.

They finished dinner and headed to the movies. Cara was not a fan of scary movies but agreed because Phil wanted to see it. About halfway through the movie, she started feeling a little light-headed and her heart started racing. *It’s probably the blood in the scary movie messing with me*, she thought. She tried to calm herself, not wanting to ruin their first date.

She turned to Phil, “Sorry, but I think something’s wrong! I feel sick!” Phil guided her out of the movie theater, where she then collapsed and complained that her chest felt really tight. Cara thought to herself, *Oh no, I think I’m going to be sick. How embarrassing! There isn’t going to be a second date.*

Phil called 911 and an ambulance quickly arrived.

**Questions**

1. Make a list of any new problems Cara is experiencing. Do any of Cara’s new problems correlate with your previous prognosis?
2. Why is Cara having chest tightness?
3. How does the nurse’s diagnosis of dehydration affect the blood pressure and circulation?
4. What did Cara eat for dinner? How could her food choice at dinner cause these problems?
5. List tests that the doctors should perform at the hospital.
Part IV – Aldosterone

Cara’s mother arrived at the hospital as the EMT moved Cara into the emergency room where she was placed under the care of a new resident. The resident began to check her vitals and took a report of Cara’s problems while her mother anxiously paced back and forth. He then listened to her breathing sounds, which appeared normal. Next, the resident ordered an ECG, chest x-ray, CT brain scan, and metabolic profile of Cara’s blood work. In the meantime, he asked about her previous medical history, any medication she was currently on, and what she ate recently.

“I just ate spaghetti marinara. I am on spironolactone because I have polycystic ovarian syndrome. I took two tablets right before dinner because I forgot to take it this morning. After my run earlier in the day, I had intense muscle cramps so I ended up taking two naproxen tablets. I was starting to feel better in the afternoon so I thought I would be okay to go on my date.”

The resident asked, “How much water did you drink today?”

“Not much,” Cara admitted ashamedly.

“Well, you should know spironolactone is a diuretic. Your physician should have told you to drink plenty of water when you are taking this drug. It works as an aldosterone receptor antagonist in the cells of the distal tubule in your kidney, which means that you will lose a lot of water. You need to stay hydrated,” warned the resident.

The resident then left to pick up the test results.

Questions

1. Fill in the table to predict the results of the initial tests.

<table>
<thead>
<tr>
<th>Tests</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate</td>
<td></td>
</tr>
<tr>
<td>EKG</td>
<td></td>
</tr>
<tr>
<td>Chest x-ray</td>
<td></td>
</tr>
<tr>
<td>CT scan</td>
<td></td>
</tr>
<tr>
<td>Blood K⁺</td>
<td></td>
</tr>
<tr>
<td>Blood Na⁺</td>
<td></td>
</tr>
</tbody>
</table>

2. Aldosterone is responsible for controlling blood sodium and potassium levels. What type of hormone is aldosterone and which cells secrete it?
3. Use the diagram below to indicate the following:
   i. How aldosterone enters the (Principal) cell in the distal tubule of the nephrons.
   ii. The location of the aldosterone receptor.
   iii. Where the aldosterone-receptor complex has its effect in the Principal cell.
   iv. The location of the sodium/potassium/ATPase pump.
   v. The location of the sodium channels.
   vi. The location of the potassium channels.
   vii. The effect the aldosterone-receptor complex on the channels and the pump.
   viii. The net movement of potassium and sodium ions between the filtrate and the blood when the aldosterone-receptor complex is activated.
   ix. The net movement of potassium and sodium ions between the filtrate and the blood when the aldosterone-receptor complex is activated.
   x. Place an “x” where spironolactone affects this system.
Part V – Electrolyte Imbalance

The resident returned with the tests results: the CT brain scan was normal, the EKG showed an elevated heart rate with arrhythmia, the chest x-ray was normal, and the blood work showed an electrolyte imbalance.

Here is a partial list of Cara’s blood work:

<table>
<thead>
<tr>
<th>Test</th>
<th>Cara</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose, Serum (mg/dL)</td>
<td>82</td>
<td>65–99</td>
</tr>
<tr>
<td>Uric Acid, Serum (mg/dL)</td>
<td>4.2</td>
<td>2.5–7.1</td>
</tr>
<tr>
<td>Creatinine, Serum (mg/dL)</td>
<td>1.2</td>
<td>0.57–1.00</td>
</tr>
<tr>
<td>Sodium, Serum (mEq/L)</td>
<td>133</td>
<td>134–144</td>
</tr>
<tr>
<td>Potassium, Serum (mEq/L)</td>
<td>7.0</td>
<td>3.5–5.2</td>
</tr>
<tr>
<td>Chloride, Serum (mEq/L)</td>
<td>103</td>
<td>97–108</td>
</tr>
<tr>
<td>Calcium, Serum (mg/dL)</td>
<td>9.5</td>
<td>8.7–10.2</td>
</tr>
</tbody>
</table>

Questions

1. What abnormal values are evident in Cara’s blood work?
2. What could cause an elevated heart rate?
3. What minerals do tomatoes have in high concentration?
4. Could the tomatoes have had an effect on the level of that mineral in Cara’s blood?
5. Use the Nernst equation (below) to calculate the equilibrium potential for potassium in a normal patient and in Cara; assume \([K]^+\) in is 150 mEq/L in Cara and in normal patients, and \([K]^+\) out is 4 mEq/L in normal patients.
   \[
   E_{K^+} \text{ (millivolts)} = 61 \log_{10} \left( \frac{[K]^+_{\text{out}}}{[K]^+_{\text{in}}} \right)
   \]
6. If the resting membrane potential exhibits the same change as the equilibrium potential for potassium, predict how Cara’s ion imbalance will affect a cell’s resting membrane potential; would Cara’s resting membrane potential be hyperpolarized or depolarized?
Part VI – Membrane Depolarization

The resident and attending returned and talked to Cara and her mother.

“Cara, you are suffering from hyperkalemia, which means you have more potassium in your blood than normal. Two things happened to you today to create the perfect storm. First you ate a meal high in potassium and second you took a high dose of spironolactone. The drug blocks the action of a hormone in your body called aldosterone, which works to rid your body of excess potassium, exchanging it for sodium. Decreased aldosterone activity means the level of potassium in your blood increased while the level of sodium decreased. Also, the loss of sodium in your urine causes you to also lose water.”

“So I guess that’s why it’s a diuretic,” interrupted Cara.

“Exactly. The elevated potassium levels in the fluid around your cells is responsible for your heart arrhythmia, high heart rate and muscle cramps. I recommend staying away from potassium-rich foods like bananas and tomatoes.”

“Usually I do; I only eat apples and oranges.”

“I also suggest taking acetaminophen instead of NSAIDS, like naproxen, as it is thought that there may be some drug interaction that further increases hyperkalemia. You have to be careful what you eat; your body is losing a lot of water and sodium so hydration is key when you are on spironolactone. I recommend that your diet consists of low potassium and high sodium meals as well as a lot of water or Gatorade, especially while you are training. This could have been a lot worse if you hadn't come in for treatment. Are there any concerns you would like to address?” asked the resident.

“No. Thank you so much! I'll try to be more careful in the future,” said Cara.

Questions

1. Refer to the diagram you made in Part IV and describe how spironolactone acts as a diuretic.
2. Where is the pacemaker for the heart?
3. How could membrane depolarization created by elevated blood potassium level cause an increase in Cara's heart rate?
4. How could the membrane depolarization created by the elevated blood potassium level cause arrhythmias?
5. How could the membrane depolarization created by the elevated blood potassium level cause muscle cramping?