

Lee Family Problems: The Yin and Yang of Membrane Physiology

by

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Part I – Welcome Back

“Home never looked so good,” thought Elaina Lee as the car pulled up the long driveway of her rural home.

Elaina had just spent a semester in the Democratic Republic of Congo in central Africa. She had a renewed appreciation for smooth roads and comfortable cars, and looked forward to electricity and plumbing that worked.

After two 8-hour flights and a 2-hour car ride, Elaina could not wait to shower and enjoy a home-cooked meal. The front door opened and her mother stood waiting with her arms out stretched. Elaina hugged her mother and went upstairs to shower and change into her most comfortable sweats.

Mrs. Lee yelled up the steps, “Elaina, are you coming down? Food will be ready in two minutes.”

“I’m coming,” Elaina replied, “but I don’t think I want to eat anything. It’s been a long day. I think I might just go to bed.”

“But I made your favorite. You made a special request remember? Besides, I was hoping to see some of those pictures you’ve been raving about.”

“I know. I was looking forward to it too, more than you know. But I’m suddenly not feeling well. I’m kind of nauseous and dizzy. Is the air conditioning on high? It feels so cold in here.”

“No it’s not. Are you feeling okay?” Mrs. Lee placed her hand on Elaina’s forehead, “You feel very warm.”

Elaina brushed her mom’s hand away and stood up abruptly. “I feel like I’m going to throw up!”

Elaina ran into the bathroom with seconds to spare.

As she held back her daughter’s hair, Elaina’s mother could see her daughter’s thin frame trembling with chills. Just when she started to feel a sense of relief having her daughter back, she couldn’t help but think that maybe it wasn’t such a good idea for her to have gone to Africa.

Mrs. Lee picked up her cell phone and called her son, “Nick! Where are you?!”

“I’m walking in now Mom. I know Elaina just got home from her trip. That’s why I cut my workout at the gym.”

As Elaina’s brother Nick walked in, Mrs. Lee yelled down the stairs, “Elaina looks really sick. You’re the EMT. Come check her out!”

Her brother casually walked up the steps and into the bathroom where his sister was hugging the toilet. He put down his water bottle and started examining Elaina.

Questions

1. List Elaina's signs and symptoms.
2. If you were in Nick's position, what questions would you ask Elaina? Try to predict Elaina's response to your questions.
3. As an EMT (Emergency Medical Technician), what tests would you perform to help find out what is wrong with Elaina?
4. Do you think Elaina should go to the Emergency Room at this point?

Part II – Family Trip to the Emergency Room

“Hi, Sis. So tell me what happened.”

“She’s burning up!” exclaimed Mrs. Lee.

“Relax, Mom. I’m just feeling a little nauseous; eight-hour flights can do that to people,” mumbled Elaina.

“Hey Mom, can you get me some ice?” Nick said as his mom rushed downstairs.

“I’m so glad you came home to see me. What’s the ice for?” said Elaina.

“To get rid of Mom,” Nick responded. “Any idea what might have caused the nausea? What did you eat today?” Nick took her wrist and looked at his watch.

“I don’t really know what is causing the nausea. All I’ve eaten is a salad at the layover in Madrid, and I ate the inflight meal on the flight home.”

“You mentioned the other day that you ran out of drugs for your heart problem.”

“Yes, I started having those atrial fibrillation problems again so I went to a local doctor. He said that he had an herbal remedy and gave me some drops to take when I felt my heart problem coming on.”

“When did you last take the medicine?”

“You know how much I hate flying. I took a dose as I was leaving Africa, another when we were about to take off from Madrid, and then a third when we hit a lot of turbulence as we were landing in the U.S. I was feeling really anxious.”

Nick frowned. “Can I see the bottle?”

Nick placed the unlabeled bottle in his pocket and put his hand on Elaina’s forehead. “Mom said that you were burning up, but you don’t feel that warm to me. Then again my hands are always warm.”

Elaina started shaking uncontrollably. Nick quickly moved nearby objects in the bathroom out of the way so Elaina wouldn’t hurt herself. Their mother returned with ice in hand and she and Nick could only stand back helplessly and watch. When the episode stopped, Nick said, “I think we need to get you to the hospital, Sis. You might have given yourself an overdose and we don’t even know what the medication is. Mom can you bring the car out front?”

Nick helped Elaina downstairs. “Mom, my legs are tired from the gym. Can you take Elaina’s other arm?” Mother and brother helped Elaina into the car.

They arrived in the ER and Elaina was quickly admitted.

“Hi Doc.”

“Hey Nick, where’s your uniform?” asked one of the ER doctors.

“I’m here with my kid sister Elaina. She just got back from the Congo. I think she may have had a reaction to an herbal medicine she was given in Africa because she had a mild seizure about 30 minutes ago.”

The doctor examined Elaina, asked some questions, and then a nurse came in to take blood.

Mrs. Lee told Nick, “You haven’t eaten any dinner yet. Take this money and go to the cafeteria and get some food.”

Nick soon returned with two burgers, a large order of fries, and two containers of juice as the doctor re-entered Elaina’s room.

“I’ve got your chart right here,” said the doctor.

Table 1 – A Partial List of Elaina’s Vital Signs

<i>Vitals</i>	<i>Elaina</i>	<i>Normal</i>
<i>Blood Pressure</i>	126/84 (Hypertension)	90–120/60–80
<i>Pulse Rate</i>	105 bpm (Tachycardia)	60–100 bpm
<i>Temperature</i>	98.8 °F	98.6 °F

Table 2 – A Partial List of Results from Elaina’s Blood Work

<i>Measurement</i>	<i>Elaina</i>	<i>Normal</i>
<i>White Blood Cell Count</i>	7,800 cells/mm ³	4500–10,500 cells/mm ³
<i>Sodium (mM)</i>	142	135–145
<i>Potassium (mM)</i>	6.2	3.5–5.2
<i>Triiodothyronine (T₃) (ng/dL)</i>	11.2	59–174
<i>Tetraiodothyronine or thyroxine (T₄) (ng/dL)</i>	7.3	4.5–12
<i>Thyroid Stimulation Hormone (TSH) (ng/dL)</i>	1.8	0.3–3.0

Questions

1. What new signs and symptoms is Elaina experiencing?
2. Use the Nernst equation (below) to calculate the equilibrium potential for potassium in a normal patient and in Elaina. Assume that the ion level in the interstitial fluid is the same as that in the blood plasma, and also assume that the intracellular concentration of potassium is 150 mM in Elaina and in normal patients.

$$E_{K^+} \text{ (millivolts)} = 61 \log_{10} \left(\frac{[K^+]_{\text{out}}}{[K^+]_{\text{in}}} \right)$$

3. If the resting membrane potential exhibits the same change as the equilibrium potential for potassium, predict how Elaina’s ion imbalance will affect a cell’s resting membrane potential; would Elaina’s resting membrane potential be hyperpolarized or depolarized?
4. Draw a graph (resting membrane potential in millivolts vs. time) and place a “0” label towards the top of the vertical axis.
 - a. Draw a horizontal line to represent the resting membrane potential of a normal patient (about -70 millivolts); label this line E_{rest} .
 - b. Draw a second horizontal line about 15 millivolts more depolarized with respect to E_{rest} to represent the threshold membrane potential for action potential production; label this line E_t .
 - c. Now draw a third horizontal line in a different color to show Elaina’s resting membrane potential (question #3); label this line E_{Elaina} . The placement of this line is an approximation but should show whether Elaina’s membrane potential is hyperpolarized or depolarized with respect to the normal resting potential.
5. E_t represents the threshold membrane potential for action potential production and is about 15 millivolts more depolarized than E_{rest} . If the value for E_t in Elaina is numerically identical to that of a normal patient, what would be the effect of Elaina’s change in resting membrane potential on the amount of depolarization required to produce an action potential?
6. Can this change (the difference between the resting membrane potential and threshold) explain any of Elaina’s symptoms? If so, state which ones and explain why.

Part III – More Trouble

“We are having the herbal medicine tested in the lab but I think it may be a drug called Digoxin, which is an extract from plants like the foxglove,” the doctor explained. “It is cheaper and more readily available than many of the drugs we use in this country. However, I think that you may have taken more than the desired dosage.”

“I hate flying and I was feeling stressed yesterday, so I took it as I was leaving Africa, when we were about to take off from Madrid, and then when we hit a lot of turbulence as we were landing in the US. The doctor said it was natural, so I didn’t think a little more would make a big difference,” said Elaina.

“Don’t worry. We’re just glad that everything seems okay now,” said the doctor.

“So what happened?” asked Elaina.

“I think you had an overdose of Digoxin. You’re in luck because I wrote a paper on this for my undergraduate pharmacology course,” the doctor said with a smile. “Na/K-ATPase pumps are located in your cell membranes and help control the concentration of sodium and potassium ions inside and outside of your cells. These ion levels must remain reasonably constant because they are instrumental in producing the negative potential inside your cells. Now, some cells produce action potentials, which involve the membrane potential changing very quickly from negative to positive and back to negative. These action potentials allow certain cells, like nerves and muscles, to signal one another so that you can make muscles contract and produce movement. Excess Digoxin inhibits Na/K-ATPase pumps so that the membrane potentials become less negative and too many action potentials are produced. Your blood ions levels are consistent with this notion, and I believe that this change in membrane potential was responsible for your seizure.”

“Will I have any more seizures?” asked Elaina.

“Digoxin has a very long half-life, about 36 hours, and takes about 7 days to completely clear your body. However, there is an antidote so if the lab finds that the herbal remedy is in fact Digoxin, we’ll administer the antidote. This treatment blocks the action of Digoxin and your kidneys will gradually eliminate the drug from your body. You should stay the night and we’ll repeat the blood work again tomorrow.”

The nurse transferred Elaina to a room in the hospital.

“Hey mom, I know you have an interview tomorrow morning. Go home and relax. The worst is over; I’ll stay the night here with Elaina,” Nick told his mother.

After some convincing, Mrs. Lee ultimately said her goodbyes and went home.

Nick waited for Elaina to go to sleep and then fell asleep in a chair nearby.

The next morning Nick woke up to a noise outside. He glanced over at Elaina to make sure she was still asleep, and then yawned. He stretched out his arms and his legs, but his legs didn’t move.

Nick screamed, “Nurse, help! I can’t move my legs!”

Questions

1. List Nick’s current signs and symptoms.
2. Has Nick shown any previous signs and symptoms?
3. What tests would you perform on Nick? For each test, outline the results you would expect.

Part IV – What Is Nick’s Problem?

Nick was admitted and the doctor ordered blood work.

“Okay Nick, have there been any major changes in your diet or life style recently?”

“No, I really haven’t had any changes at all. I eat the same food and go to the gym regularly. I’ve noticed I’ve felt unusually tired after the gym and have been sleeping longer than normally.”

The doctor nodded, “Have you felt any muscle weakness or drowsiness while you were at the gym?”

“Yes. I feel tired when I’ve finished exercising,” replied Nick. “But then who doesn’t leave the gym feeling tired? I’m trying to strength train, but I haven’t gotten anywhere. I’ve lost a few pounds so I assume that I am doing something right.”

“Okay. I want to run some tests to try to identify what caused your paralysis.”

Table 3 – A Partial List of Nick’s Vital Signs

<i>Vitals</i>	<i>Nick</i>	<i>Normal</i>
<i>Blood Pressure</i>	88/58 (Hypotension)	90–120/60–80
<i>Pulse Rate</i>	52 bpm (Bradycardia)	60–100 bpm
<i>Temperature</i>	99.2 °F	98.6 °F

Table 4 – A Partial List of Results from Nick’s Blood Work

<i>Measurement</i>	<i>Nick</i>	<i>Normal</i>
<i>White Blood Cell Count</i>	7,800 cells/mm ³	4500–10,500 cells/mm ³
<i>Sodium (mM)</i>	148	135–145
<i>Potassium (mM)</i>	2.2	3.5–5.2
<i>Triiodothyronine (T₃) (ng/dL)</i>	300	59–174
<i>Tetraiodothyronine or thyroxine (T₄) (ng/dL)</i>	36	4.5–12
<i>Thyroid Stimulation Hormone (TSH) (ng/dL)</i>	0.01	0.3–3.0

Questions

1. What is abnormal about Nick’s blood work?
2. How do you interpret the observation that the levels of T₃ and T₄ in Nick’s blood are higher than normal but the level of TSH is lower?
3. What is the effect of Nick’s T₃ and T₄ levels on the number and the activity of Na/K-ATPase pumps?
4. Predict how this rate of Na/K-ATPase pump activity would affect the extracellular concentrations of sodium and potassium.
5. Is your prediction consistent with the observed levels of sodium and potassium in Nick’s blood?
6. In Elaina’s case, a high level of extracellular potassium caused her cell membranes to depolarize. However, Nick’s blood work showed that he has a low level of extracellular potassium. When compared with a normal patient, predict the effect of Nick’s potassium imbalance on the resting membrane potential of his cells.
7. Return to your graph of resting membrane potential (in millivolts) vs. time. Draw a horizontal line to show Nick’s resting membrane potential; label this line E_{Nick}. The placement of this line is an approximation, but should show whether Nick’s membrane potential is hyperpolarized or depolarized with respect to the normal resting potential.

8. If the value for Nick's threshold potential (E_t) is the same as a normal patient, what is the effect of the above change in Nick's resting membrane potential on the amount of depolarization required to bring his membrane potential to threshold and produce an action potential?
9. Can this change (the difference between the resting membrane potential and threshold) explain any of Nick's symptoms? If so, state which ones and explain why.

Part V – Thyrotoxic Periodic Paralysis

“You are suffering from low blood potassium levels, a condition called hypokalemia, which we will treat with oral potassium supplements,” Nick’s doctor explained to him.

“I can see how this treatment will fix my short-term problem, but is there a long-term problem I should be concerned about?” asked Nick.

“I think that you have Thyrotoxic Periodic Paralysis, or TPP. This is a genetic disorder typically found in individuals of Hispanic or Asian descent, and it can be up to 75 times more likely to occur in males than in females in some Asian communities.”

“So I guess TPP is not my sister’s problem, but she has something else instead,” said Nick.

“I think you are correct. Her problem was hyperkalemia or high blood potassium levels, which is the exact opposite to yours, and was solely due to an overdose of Digoxin. She should be fine when her body clears the drug and she gets back on her old medication,” said the doctor.

“Awesome. So what does this TPP do?” asked Nick.

“Your genetic predisposition causes your thyroid to be over active. The two thyroid hormones, T3 and T4, increase the number and the activity of the Na/K-ATPase pumps in your cell membranes. This results in too much potassium being taken up into your cells and leaves you with a low level of potassium in your blood. This produces a resting membrane potential that is more negative than normal.”

The doctor continued: “Hypokalemia can be made even worse by a strenuous workout because exercise stimulates your adrenal gland to secrete adrenaline, which increases Na/K-ATPase pump activity. That’s okay during exercise because the action potentials that make your muscles contract cause potassium to leave your muscles. However, when you stop exercising, the pumps continue working at their high rate. This can produce very low blood potassium levels, which may cause temporary paralysis. Some patients tell me that mild exercise, like walking, after a workout can decrease the likelihood of paralysis.”

“I get it. After I exercise, the hypokalemia gets even worse so my cells are even more hyperpolarized. So this morning my muscle fibers couldn’t depolarize enough to produce action potentials and my legs wouldn’t move. So can you cure me?” asked Nick.

“I’m afraid it’s a genetic disorder and there is no cure; however, it can be managed as long as you follow your treatment. Your body excretes potassium but has no way of storing it, so try to eat a balanced, low salt diet and eat foods high in potassium. I will give you a prescription for oral potassium supplements; make sure you take them as directed. Do not make your workouts too strenuous and don’t forget to warm down. Finally, take it easy on the carbohydrates because insulin stimulates Na/K-ATPase pump activity, so a high sugar intake could make your situation worse.”

Questions

1. How will Nick’s problems be alleviated by potassium supplements?
2. How will Nick’s problems be alleviated by a low sodium diet?
3. Why should Nick not work out too strenuously?
4. How would a low carbohydrate diet alleviate Nick’s problems?
5. What would be the long-term treatment if Nick’s symptoms became worse?



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