A Perfect Storm in the Operating Room: Anesthesia and Skeletal Muscle Contractions

by
Kelley W. Grorud
Biological Sciences Department
Edgewood College, Madison WI

Part I – A Very Bad Day

"Doctor, come quickly. We're losing the patient!"

"Losing the patient? How can we be losing the patient? I'm still scrubbing!"

Dr. Lopez walked into the operating room. "John, what's going on?"

"Glad you're here, Adriana. We could use a hand. This patient is not happy with the anesthetic." John Wilson, the anesthesiologist, was hovering over the patient's head and giving orders to nurses nearby.

Adriana Lopez, an orthopedic surgeon, surveyed the scene. This patient was here for minor surgery. He had been complaining of knee pain. As a seasoned athlete herself, Dr. Lopez had agreed to "clean up" some loose connective tissue in the patient's knee – the result of an old injury.

Dr. Lopez couldn't believe what she was seeing. The patient was rigid and his skin looked patchy; in some places it was almost blue. "How are his vitals?"

"Breathing is rapid, heart rate at 120, pressure is 60/56 and his temperature is 106."

Adriana quickly made her way to the head of the table. "How can I help?" The doctors consulted and a flurry of activity filled the room.

In the corner of the room, a small 18-year-old girl stood staring at the scene. She was pale as a ghost. Softly, two questions drifted from her corner to the doctors. "What's wrong with that man? Is he going to die?"

Assignment 1

1. Fill in the chart below. Use "+" if the patient's vital sign is higher than normal, "–" if the sign is lower than normal, or "x" if the sign is normal. If you need to, use your text or another resource to determine normal values.

Vital Sign	Increase/Decrease/Normal
Respiration Rate	
Heart Rate	
Blood Pressure	
Body Temperature	

2. If you were the doctors on the scene, what diagnosis would you give this patient? (You may use the internet to help diagnose the patient.)
3. Jot down some notes about your diagnosis, and bring these to class with you for discussion.

Part II – A Veritable Metabolic Storm

Both doctors turned to the corner to see Emily, Dr. Wilson's niece. She was visiting the hospital as an assignment for her high school biology class. She was supposed to be shadowing a doctor for the day, and would need to report back to her class with what she saw and did.

"Emily, why don't you come over here and I will explain what is going on."

Emily gave her uncle a tentative look and crossed the room. She stood several feet away from the table, not wanting to look at the patient. After several minutes, which seemed to last for hours, the activity in the room slowed down and the doctors gave the nurses a few simple instructions. The man would survive.

John, Emily's uncle, spoke first. "This patient just had a bad reaction to the anesthetic. His temperature rose very rapidly, which can be dangerous to your organs. The same sort of thing can happen when you have a bad fever. We just removed the anesthetic and are bringing his temperature back down. This condition is called malignant hyperthermia, and, yes, people can and have died from it. Fortunately, today we caught the problem in time and I think we moved quickly enough to prevent any permanent problems. We won't be doing this surgery today."

Emily looked at her uncle in disbelief. Malignant hyperthermia? This man could have died? She never thought shadowing an anesthesiologist would be so…exciting? terrifying? She wasn't sure what exactly, but she was sure her class would love the story.

She looked at the doctors. "What causes malignant hyperthermia?"

The doctors looked at each other. "John, I think this question is for you. If you don't need me, I think I will go question the family for a bit more of their medical history and to warn them that genetics are a factor here—they may want to report this to their general practitioners in the future." With a wink and a wave to Emily, Dr. Lopez left the operating room. Behind her, the nurses began wheeling the patient out of the operating room and into the recovery room.

Emily looked at her uncle, "Well?'

"Malignant hyperthermia is a genetic condition," he began, "which causes the patient's temperature to rise to a dangerously high level when they are exposed to certain anesthetics. Patients with MH also get muscle rigidity, which is why that poor gentleman looked so stiff after I started administering anesthetic. They also have changes in breathing, heart rate, and blood pressure. All of these can be dangerous, but the changes that are seen in muscle are at the heart of the problem. As the muscles get tense, they also become damaged, which releases chemicals into a person's blood stream. As my professor in med. school put it, 'MH causes a veritable metabolic storm.'"

"A veritable storm?" began Emily. "I'm not sure I get it. Do you have anything I can read that explains the disease in English?" She smiled at her uncle, hoping he got the joke.

"You know what," her uncle smiled back. "I think I might have some information that will help."

Clearly, he wasn't offended.

Assignment 2

1. In groups, review your notes on MH from Assignment 1.
2. Read the following sections of *Making Anesthesia Safer: Unraveling the Malignant Hyperthermia Puzzle* (available at http://sciencecases.lib.buffalo.edu/cs/admin/Supplemental/UploadFolder/Making_anesthesia_safer.pdf):
   - Anesthesia triggers multiple-familial deaths
   - The first signs
   - Serendipitous discovery of an experimental model
3. In the above article, what is the "veritable metabolic storm" that the author refers to? What molecular changes are reported in pig muscles during a MH state?

4. Review muscle contraction. Send one person in your group to collect the "Steps of Muscle Contraction" cards from your instructor. In your group, arrange these cards in correct order to represent what happens during muscle contraction.
5. When you have placed all the cards in correct order, prepare a list (below) of the steps that require ATP or Ca^{2+}.
   - Steps that require ATP:
   - Steps that require Ca^{2+}:

Part III – Am I Susceptible?

After a long shift in the operating room, John was catching a few winks on a bed in the hospital. He was just drifting off when his cell phone rang loudly in his pocket.

"Hi Uncle John," Emily said cheerily. "Do you have a second?'

"For you, anything," John replied, sitting up.

Emily began, "I was telling a friend about my time at the hospital and she asked me a question I didn't know the answer to. I read the information you gave me and the answer wasn't there either. We were wondering, how do you know if you have malignant hyperthermia? You don't find out the first time you have surgery, do you?"

John smiled. His niece surely was inquisitive and her questions were spot on—he'd swear someday she would be a doctor.

"Well," he started, "you know the reading I gave you also had information about pigs. In pigs, you can simply give them a little anesthetic and see if their muscles go rigid. Most of the time, when you remove the anesthetic the pig will go on to live a normal life. In humans, though, that technique would be too risky—and that kind of testing in humans is unethical. Instead scientists have come up with a way to test muscle biopsies. Do you know what a biopsy is?"

"That's when a doctor takes a small sample from your body," Emily said. "Right?"

"Yep," her uncle replied through a yawn, "Well, there are centers across the U.S. where people who think they may be susceptible can meet with scientists and run some tests. The scientists take some muscle biopsies, and then put them in a bath with chemicals that are similar to blood. They then expose the biopsies to anesthetics and test which muscles contract the most forcibly. From what you know about MH, can you guess which contracts with the most force, healthy muscle or muscle susceptible to MH? You know what, I will mail you some more information on this topic."

Assignment 3

1. Predict if healthy muscle or muscle with MH will contract with the most force.
2. To check you answer to the first question, read the following sections of *Making Anesthesia Safer: Unraveling the Malignant Hyperthermia Puzzle* (available at http://sciencecases.lib.buffalo.edu/cs/admin/Supplemental/UploadFolder/Making_anesthesia_safer.pdf):
   - Working together to discover the triggers
   - Predicting susceptibility in humans
   - Developing a grading scale
3. Even though screening tests exist, most people aren't checked for the disease. Why not? What types of people (or what populations) would be most likely to be screened before they had their first surgery?

Part IV – Show and Tell

A couple days later, as Emily was preparing for her class presentation, a package arrived in the mail for her. She tore the package open to find more information from her uncle, and a short note:

> I know your presentation is coming up soon. I thought this would help. Let me know if you have more questions. It was a treat to have you visit me at work. You are welcome to come back and watch anytime. I get the feeling after this visit that we might soon have another doctor in the family.
>
> Love, Uncle John

"Just in time!" Emily cried.

After reading the information, she sat at her desk trying to develop an outline for the presentation. After a few minutes, she realized that what had driven her learning about the disease were the questions she had asked. She decided that questions could guide her presentation, and she settled on an outline for her presentation that focused around the questions listed below.

Outline

- How do muscles contract?
- What is malignant hyperthermia?
- What triggers malignant hyperthermia?
- What is the "metabolic storm" that develops during malignant hyperthermia?
- How does malignant hyperthermia disrupt muscle physiology?
- Why does body temperature rise during malignant hyperthermia?
- How can you tell if you have malignant hyperthermia?
- What drug is used to treat malignant hyperthermia and what are the mechanisms of action of how this drug works?
- Why doesn't the antidote to malignant hyperthermia impact smooth or cardiac muscle?

Assignment 4

1. Read the following sections of *Making Anesthesia Safer: Unraveling the Malignant Hyperthermia Puzzle* (available at http://sciencecases.lib.buffalo.edu/cs/admin/Supplemental/UploadFolder/Making_anesthesia_safer.pdf):
   - Preventing death after onset
   - Disseminating what we know
   - Why patients are still dying
   - Understanding the biology of MH
   - What's next?
2. Prepare short answers for each question in Emily's outline.
3. As a group, develop a pamphlet, brochure, poster, or some other material that could be used to educate others about malignant hyperthermia. Your project should be designed to educate the general public—not science savvy students or instructors. You should include information about the molecular basis of the disease, muscle physiology, how MH is detected, and how MH is treated. You may include other information as well. Your grade will depend on the quality of the information presented and the creativity you use in presenting this information.