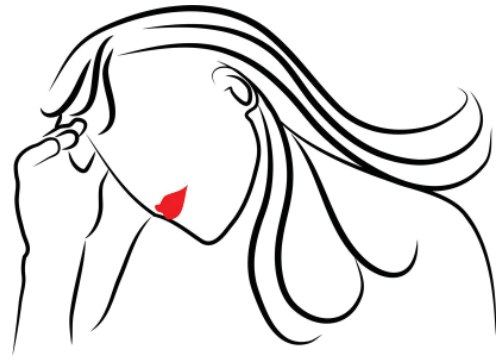


One Headache After Another: Physiology Edition

by

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Part I – Blood Work

“Chris. Michelle. You go on... I’ll catch up in a minute.”

Mary hid her fear as she struggled to catch her breath. She had been so excited to go hiking with her children. Chris and Michelle were both home on fall break, and Mary had been looking forward to the family time. But she felt like she was hyperventilating, and now her chest was starting to hurt.

“What, we’ve finally outlasted you on the trails?” Chris joked as he looked over his shoulder. “Mom, are you ok? You look awful.”

“Don’t panic, but I think I need to go to the hospital.”

“Michelle! Go get the car!” Chris yelled ahead.

“Please don’t panic—I just want to get it checked out.”

“Michelle!”

After what seemed like an eternity, they arrived at the hospital. As Chris and Michelle helped their mother into the waiting room, the ER attendant noticed them and ushered the family into a small room. Dr. Rosen promptly took Mary’s medical history and ordered an EKG, chest x-ray, blood tests, and urinalysis.

The tests were completed in short order, and about an hour later, Dr. Rosen appeared in the exam room. “I have some good news, and a little bad news. The good news is...”

“Dr. Rosen to the ER, Code Blue. Stat!” said the voice on the PA.

“Sorry, that’s my cue. But don’t worry, you’ll be fine...once we get you off of the Topamax®. This might take a while, so I’m leaving your chart. I hope I’ll be back to review the test results with you, but it might be someone else,” said the doctor as the door swung shut.

“Mom, isn’t Topamax your migraine medicine?” asked Michelle.

“Yes. It was originally designed as an epilepsy treatment, but I take it to prevent those migraines that used to put me in bed all day. How could it be causing this?” Mary wondered out loud.

Chris broke the tension, saying, “These are your records, right? Let’s see what we can figure out.” He flipped open her chart. On the top of the pile were Mary’s blood test results:

	Normal range	Mary's results*
Hemoglobin (g/dL)	12.0–15.0	12.8
Hematocrit (%)	36–44	37.5
Creatine kinase cardiac isozyme	0–3.9%	1
Creatine kinase MM isozyme	96–100%	99
Creatinine	0.5–1.4	0.9
pH	7.35–7.45	7.31
pCO ₂ (mmHg)	38–52	18.1
pCO ₂ (mM)	20–27	9.5
pO ₂ (mmHg)	70–100	121.0
HCO ₃ ⁻ (mM)	19–25	8.9
Glucose (mg/dL)	90–140	112
*Based upon data from J.E. Burmeister, R.R. Pereira, E.M. Hartke, and M. Kreuz. 2005. <i>Neuro-Psiquiatr</i> 63(2-B): 532–534.		

Question

1. What appears to be Mary's problem(s), from the results of her blood work? What sort of change has occurred in her acid-base balance? If there is more than one problem in her blood work results, is there a relationship among those factors?

Part II – Buffers

Dr. Rosen reappeared in the cubicle. “Sorry for the interruption, and for leaving you in suspense. The good news is that you did not have a heart attack. But I do think you’re having an unusual reaction to Topamax. It appears to be inhibiting your renal carbonic anhydrase, leading to metabolic acidosis. We’ll be giving you an IV, and you should taper off your Topamax under your family physician’s supervision.”

Dr. Rosen checked his pager and said, “Sorry, it’s one of those days. Again, you’ll be all right, and the nurse will be with you shortly to start the IV.” He turned on his heel and left just as quickly as he had appeared.

“Mom, don’t worry,” said Chris. “I’m going to call one of my friends at college. He should be able to help us figure this out.”

Chris dials his cell phone; yours rings. After you complete the following questions, write a one- or two-paragraph explanation to help Chris understand what’s going on with his mom.

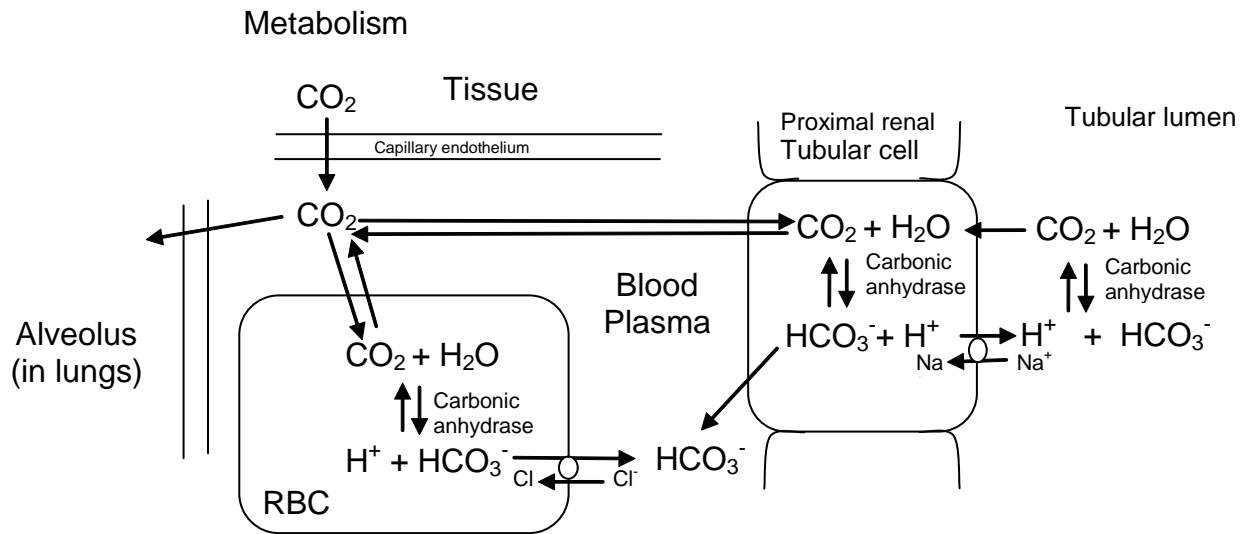
Questions

- 2a. Bicarbonate is one of the main buffers in the blood. Provide a definition of a buffer.
- 2b. Give an equation that allows one to calculate the pH of a buffer solution.
- 2c. Provide the specific form of this equation, including each chemical species, that will allow you to calculate the pH of a bicarbonate buffered solution.

Part III – Regulation

Questions

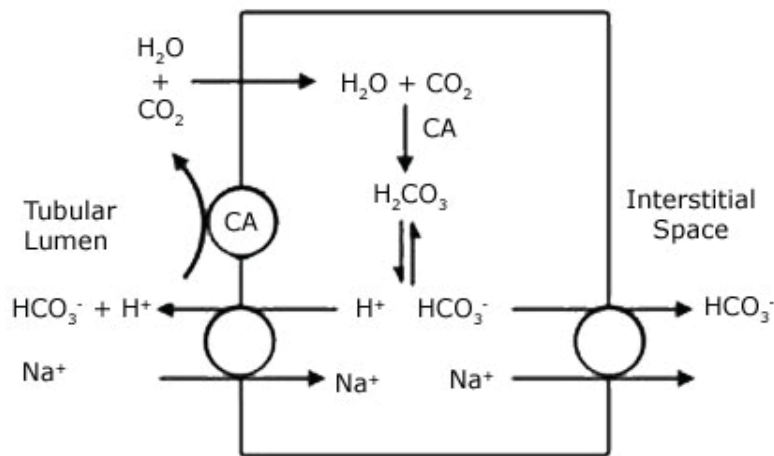
3. Blood pH is normally regulated by the respiratory system to control the level of CO_2 (g) and by the urinary system to control the levels of HCO_3^- and non-volatile acids in the blood.



Given the overall reaction, CO_2 (g) + H_2O (l) \rightleftharpoons H_2CO_3 (aq) \rightleftharpoons HCO_3^- (aq) + H^+ (aq), what effect would each of the following have on blood pH? Explain.

- Hyperventilating
 - Holding your breath for an extended period of time
 - Chronic diarrhea
 - Excessive ingestion of baking soda
4. One of the effects of Topamax is to inhibit carbonic anhydrase. Predict the effect of Topamax on the function of each of the following cells:
- Osteoclasts (bone)
 - Parietal cells (stomach)
 - Red blood cells (blood)
 - Epithelial cells of the proximal tubules (kidney)
5. The carbonic anhydrase in proximal tubule epithelial cells are particularly sensitive to inhibition by Topamax. Use the diagram of transport in the epithelial cells of the proximal tubule provided on the next page* and your understanding of the function of the kidney to provide a step-by-step explanation of how the inhibitory action of Topamax caused the disturbances in Mary's blood chemistry.

*Figure on next page based on S. Drage, D. Wilkinson. "Acid Base Balance," Update in *Anaesthesia*, 13 (2001): Article 12. http://www.nda.ox.ac.uk/wfsa/html/u13/u1312_02.htm, accessed 5/12/09.



6. Predict the effect of Topamax on the pH of her urine. (Choose one below.)
- Caused no change in pH
 - Led to a decrease in pH
 - Led to an increase in pH

Explain your answer in terms of the mechanisms of acid-base handling by the kidney.

7. Mary has an acid-base disturbance that is being compensated for with another body system. Identify the specific type of disturbance and trace out the physiological pathway responsible for the compensating action.
8. The same type of acid-base disturbance occurs in all of the following circumstances. Which one is most analogous (most closely matches) Mary's condition? Explain.
- Uncontrolled diabetes mellitus
 - Excess administration or ingestion of an acidifying agent or drug
 - Chronic diarrhea
9. Which of the following treatments would you recommend to correct Mary's problem? Explain what effect each treatment would have upon her blood pH.
- Breathing in a paper bag
 - An IV containing pure HCO_3^- in an isotonic solution
 - Holding her breath for as long as she can
 - An IV containing pure ammonia in an isotonic solution
10. Propose a reason why Mary developed the symptoms of her acid-base disturbance while hiking which hadn't been apparent in her normal daily routine.



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