Physiology should be taught as science is practiced: an inquiry-based activity to investigate the “alkaline tide”

Heidi L. Lujan and Stephen E. DiCarlo
Department of Physiology, Wayne State University School of Medicine, Detroit, Michigan

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THE AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE (AAAS) strongly recommends that “science be taught as science is practiced” (1, 2). This means that the teaching approach must be consistent with the nature of scientific inquiry (5). To add scientific inquiry to our large lecture-based physiology class of 80 students, we introduced the pioneering work of Roger S. Hubbard and replicated part of his original experiment during our discussion of gastric secretions. Specifically, Hubbard and Munford, in 1923, demonstrated that the urine of control subjects becomes more alkaline after a standard meal (3). However, in sharp contrast, the urine of patients with achlorhydria (a condition where the production of hydrochloric acid in gastric secretions of the stomach is absent) showed no increase in alkalinity after a meal. The investigators concluded that the secretion of hydrochloric acid by the stomach was the cause of the increased alkalinity of the urine after a meal. At this point, students were challenged to consider how the secretion of hydrochloric acid by the stomach caused an increased alkalinity of the urine.

To replicate part of the experiment demonstrating how the secretion of hydrochloric acid by the stomach caused an increased alkalinity of the urine, two volunteer students were selected, and, using standard pH test strips, the pH of their urine was determined in the privacy of the restrooms. Upon returning to class, one student drank a protein shake and the other student drank an equal volume of water.

Next, we began the discussion of the mechanism of H+ secretion by gastric parietal cells (Fig. 1). Students were shown that the apical membrane of the cell, which faces the lumen of the stomach, contains H+-K+-ATPase (the proton pump). Furthermore, the basolateral membrane, which faces the blood, contains Na+-K+-ATPase and a Cl-/HCO3- exchanger. Inside the parietal cell, CO2 and H2O combine to form H2CO3, which dissociates into H+ and HCO3-. H+ is secreted into the lumen of the stomach by H+-K+-ATPase, acidifying the stomach contents to help with digestion of dietary proteins. Specifically, an acidic gastric pH is required to convert inactive pepsinogen to its active form, pepsin (a proteolytic enzyme).

HCO3- is exchanged for Cl- across the basolateral membrane and thus is absorbed into gastric venous blood (the “alkaline tide”). Eventually, this HCO3- is secreted into the lumen of the small intestine (through pancreatic secretions), where it neutralizes the acidic chyme delivered from the stomach. In addition, some of this HCO3- is filtered into the urine.

We also discussed the major factors that stimulate H+ secretion by parietal cells. Specifically, we discussed the roles of the parasympathetic nervous system (vagus nerve), gastrin, and histamine. We also discussed the influence of a meal on these stimulants. Parenthetically, at this time, we also mentioned that James Black was awarded the Nobel Prize for Medicine in 1988 for work leading to the development of propranolol and cimetidine, a histamine (H2) receptor blocker, and queried if cimetidine would be useful for an individual with a gastric ulcer?

The alkaline tide, i.e., the absorption of HCO3- by gastric venous blood, can be observed by an increased alkalinity of the urine. Accordingly, at the end of the discussion (~45 min), the two students returned to the restroom and redetermined the pH of their urine; and the class predicted the results. As expected, the student who drank the protein shake had an increased alkalinity of the urine, whereas the student who drank the water had no change in urine pH. Based on the accuracy of the predictions as well as the quantity and quality of the questions, it was clear that students were engaged and learned about the digestive processes by participating in the activity. Suggestions for improving this activity include having more students participate or having students drink different substances to determine whether meal type changes outcomes. A further discussion of how blood contents end up in the urine could also be included.

It is our judgement that this inquiry-based activity, along with the historic context, worked well to inspire and motivate students because science students view physiology as a cre-
ative science where experimentation and discovery excites and drives them. Without experimentation and discovery, students become uninspired and unchallenged by physiology and transfer to other disciplines or drop out of school entirely (4). Accordingly, we recommend the adoption of inquiry-based activities during lecture classes because the activity is an exercise in thinking, in pondering the origin of ideas, concepts, and facts, an exercise in probing the relationship between ideas and data. Students get a mental workout as they think about how a topic was conceived, how data were obtained, and how conclusions were made. Finally, the activity required little additional class time and minimal preparation. This activity was also Institutional Review Board exempted, because it was not considered research and was considered an activity conducted in established or commonly accepted educational settings, involving normal educational practices.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

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