

Earthquakes Damage Cells, Too: A Case Study in the Cellular Physiology of Cholera

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Introduction

Thirty-two-year-old Bedeline was brought, almost comatose, into a clinic in Port-au-Prince, Haiti, in December 2010. The previous January an earthquake had devastated the country, destroying buildings and the scant public infrastructure that had existed before the earthquake. As a result, large numbers of Haitians were living in incredibly crowded encampments without a clean water supply or sanitation facilities. In recent months, a surge of patients with severe dehydration and diarrhea like Bedeline had begun arriving at medical clinics throughout the region.

Kathryn, a physician working with Doctors Without Borders, had started to examine Bedeline. As she worked, the thought kept running through her mind that the earthquake wasn't over—it was just wreaking havoc in cells instead of buildings now.

Bedeline had severe diarrhea and was producing watery stools at a rate of nearly 1L/hour. Her skin appeared shriveled, and when a fold of skin was pinched, it remained so for several minutes. Microscopic examination of her stool by darkfield microscopy revealed the presence of a large number of *Vibrio cholerae* bacteria. Bedeline couldn't drink, so intravenous isotonic NaCl was administered. When she was fully conscious, she was given a rehydration solution to drink. This oral rehydration solution contained glucose, NaCl, KCl, and NaHCO_3 .

After about five days Bedeline had recovered sufficiently to leave the clinic. Kathryn thoroughly explained to Bedline the recommendations being circulated by the Haitian Ministry of Public Health and Population (MSPP):

- Drink and use safe water.
- Wash your hands often, using soap and water.
- Use latrines or bury feces and do not defecate in any body of water.
- Cook food well, keep it covered, eat it hot, and peel fruits and vegetables.
- Clean up safely in the kitchen and in places where the family bathes and washes clothes.

Questions

1. Explain the rationale for the MSPP recommendations in terms of the transmission mechanism(s) for cholera.
2. Cholera toxin preferentially targets intestinal epithelial cells (as opposed to esophageal cells or stomach cells). Hypothesize a reason for this specificity.

Part I – Transmission and Cellular Signaling

In preparation for her time in Haiti, Kathryn had referred to a textbook to refresh her memory on the underlying physiology of the disorder. In doing so, she came across the following passage from *Molecular Biology of the Cell, 4th ed.*:

The ganglioside G_{M1} ...acts as a cell-surface receptor for the bacterial toxin that causes the debilitating diarrhea of cholera. Cholera toxin binds to and enters only those cells that have G_{M1} on their surface, including intestinal epithelial cells. Its entry into the cell leads to a prolonged increase in the concentration of intracellular cyclic AMP, which in turn causes a large efflux of... water into the intestine.

The G_{M1} ganglioside is a specific membrane glycolipid molecule and is shown in the figure below.

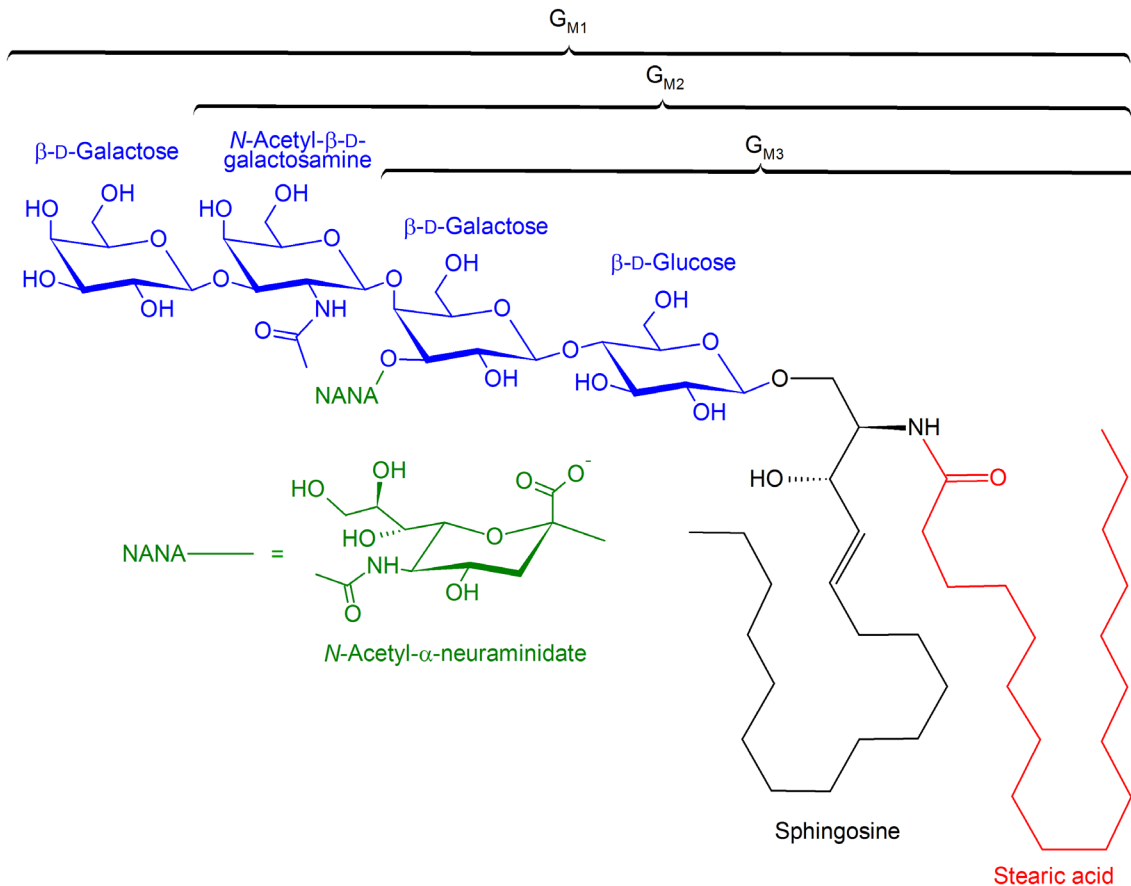


Figure 1. Structure of G_{M1} , G_{M2} , G_{M3} . Sphingosine is a fatty chain and the stearic acid is a fatty acid tail.

Referenced from *Principles of Biochemistry, 3rd ed.*, by Donald Voet, Judith Voet and Charlotte Pratt, p.253, drawn by Wikipedia User LHcheM, used in accordance with the Creative Commons Attribution-Share Alike 3.0 Unported license, http://en.wikipedia.org/wiki/File:Structure_of_GM1,_GM2,_GM3.png.

Questions

- Predict and diagram the cell-signaling pathway that is likely to be targeted by the toxin.
- Would cholera toxin cause activation or inhibition of this signaling pathway?

Reference

Alberts, et al. *Molecular Biology of the Cell, 4th Edition*. New York, NY: Garland Science.

Part II – Pathophysiology of Cholera

Question

5. What is the pathologic mechanism of Bedeline's diarrhea? Why is she dehydrated?

During her time in Haiti, Kathryn was bothered by the nearly week-long recovery time for patients who survived the cholera infection and frequently wished for a faster-acting pharmaceutical to improve patient outcomes.

Question

6. If a row of intestinal epithelial tissue were cultured in a laboratory and were exposed to cholera toxin, the cells would presumably secrete Cl^- from the luminal membrane. A researcher wants to treat the cells with a chemical that will stop the secretion. Propose a chemical mechanism that the researcher should try and justify your proposal.

Part III – Fluid Shifts and Oral Rehydration Therapy

Consider Bedeline's condition and answer the following questions.

Questions

7. Describe, at the cellular and molecular levels using appropriate vocabulary, why Beldine has shriveled skin.
8. How do intravenous fluids improve Bedeline's condition?
9. What is the rationale for administering the oral rehydration solution to Bedeline as opposed to plain water?
10. How are the effects of the oral rehydration solution different than the predicted effects of an orally administered electrolyte solution? Your answer should span the molecular through organismal levels of organization.
11. Why can the NaCl solution without glucose be administered by IV but not orally? Your answer should span the molecular through organismal levels of organization.

Part IV – Scientific Thinking

Questions

12. Why were antibiotics not the first line of treatment for Bedeline? And, why does Bedeline recover in five days with no antibiotics?
13. What further treatments beyond IV fluids and oral rehydration solutions might researchers work to develop for the treatment of cholera? Explain your rationale.



Image credit: The photo in the title block of this case shows one of the many impromptu tent cities that Haitians set up across the capital after an earthquake measuring 7 plus on the Richter scale rocked Port au Prince Haiti just before 5 pm, January 12, 2010. UN Photo/Logan Abassi United Nations Development Programme. Used in accordance with the Creative Commons Attribution 2.0 Generic license. http://commons.wikimedia.org/wiki/File:Haiti_earthquake_aftermath_tent_city.jpg.

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