NATIONAL CENTER FOR CASE STUDY TEACHING IN SCIENCE

Cholera and Conflict in Yemen

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Introduction

Cholera, an ancient disease that was mostly eradicated due to the rise in personal hygiene and public health along with structural improvements in water filtration, has been seen on the rise again in rural areas across the globe. The *Vibrio cholerae* bacterium, has been sweeping through the war-torn areas of Yemen in the Middle East as well as small rural areas of Southeast Asia. Cholera is a bacterial infection caused by drinking water that has been contaminated with the bacterium through animal fecal droppings or by consuming undercooked meat of an infected animal. This disease presents about 3–5 million cases a year with almost 100,000–120,000 deaths, mostly resulting from a lack of access to proper treatment [1].

The cholera bacterium has a very short incubation period of about 12 hours to 5 days and usually severely impacts young children, the elderly, and those with a weakened immune system such as pregnant women. Typical symptoms include profuse watery diarrhea, vomiting, and muscle cramps. When left untreated, severe dehydration can rapidly lead to shock and even death within a couple of hours. The bacterium *Vibrio cholerae*, which contains the cholera toxin (CTX), is transmissible by the fecal-oral route because the bacteria is still present in a person's feces when they defecate.

The toxin in the bacterium is composed of a multitude of genes that encode the CTX protein. Interestingly, the CTX genes are actually carried by a bacteriophage called the CTXϕ bacteriophage. The phage binds to *V. cholerae* by attaching to the bacterium's toxin-coregulated pilus (TCP). The binding between the protein coat of the virus and the TCP mediates membrane fusion and then the virus integrates its CTX genes into the bacterium, creating a pathogenic strain of *V. cholerae* that can transcribe the CTX gene. This strain of *V. cholerae* first binds to the intestine through its filamentous pili, and then creates and secretes the CTX toxin into the epithelial cells of the intestine; these steps result in a bacteria sample that is pathogenic for cholera [2].

The CTX protein is endocytosed into the epithelial cells of the small intestine and broken up into two subunits, CTA1 and CTA2. CTA1 activates ADP-ribosylation and causes suppression of GTP hydrolysis. The prevention of GTP hydrolysis is problematic, since it leads to an increase in the concentration of cAMP. The high levels of cAMP in the cell activate the CFTR channel, which consequently leads to an efflux of chloride ions into the intestinal lumen. This elevated chloride ion concentration in the intestinal lumen attracts sodium ions through tight junctions in the epithelial cells. The high concentration of ions in the intestinal lumen prevents water from entering the epithelial cells by disrupting the normal osmotic gradient. As a consequence, an infected person is not able to absorb water from his or her intestinal tract, thus causing diarrhea and dehydration [3].

The best preventative measure against cholera infection is to receive an oral vaccine. The vaccine consists of two doses, which both need to be taken in order to get full protection for about five years [4]. This is not perfect, however, as cholera outbreaks typically occur in rural or poor areas with poor access to healthcare. For those who cannot receive the vaccine, the mainstay treatment of cholera is rehydration therapy. Due to the large loss in fluids, the patient must be kept hydrated and their salt balance must be maintained. This can be as simple as preparing an oral solution with salt and sugar to help replenish the fluids and electrolytes lost due to the diarrhea, or in more severe cases of dehydration, intravenous injections consisting of electrolytes may be needed. Proper hydration is needed until the body has cleared the bacteria. In conjunction with rehydration through IV, a patient may also receive antibiotics to combat the bacterial infection, however they are only used moderately and for more severe cases [5, 11, 12]. While antibiotics have been used along with rehydration therapy, cholera has adapted over the years and many strains are now antibiotic resistant and do not respond to many of the provided treatments. *V. cholerae* is a gram-negative bacterium, which means the cell has an extra layer of protection by creating an outer membrane lined with lipopolysaccharides. This extra protection makes it almost impossible for antibiotic medications to penetrate the cytoplasmic membrane and disrupt the bacteria's function.

Medical treatments aside, the simplest yet most effective way to avoid contracting cholera is through proper personal hygiene and implementation of strong water filtration systems. Proper hygiene preventive measures include washing hands thoroughly, avoiding defecation near water sources, and ensuring that water is filtered before consumption or personal contact [6]. There are methods, physical and chemical, that can be used to purify water. Physical methods include boiling, filtration, UV radiation and solar water disinfection while chemical methods include chlorination and iodine treatment. Boiling is a simple method that can destroy *V. cholera* bacteria, however a disadvantage is that boiling may not be accessible to everyone as some developing countries have limited access to fuel. Biosand filters help purify water by breaking down organic material and pathogens such as *V. cholerae* using sand and a biological layer [7]. Thought to be the most effective method, UV radiation damages microorganisms' DNA thereby preventing them from reproducing and infecting others. Solar water disinfection relies on the combination of two methods that already destroy pathogenic microorganisms, specifically UV radiation and high temperatures, to further ensure that the bacteria gets destroyed. Solar water disinfection is performed by placing water in plastic water bottles and leaving them exposed to sunlight for six hours [8]. Chlorination of water is a low-cost method for killing microbial waterborne pathogens such as *V. cholera* through the use of chlorine tablets (commonly known as pot chlorination) and it could be used in community wells where they are the main source of water for the people [9]. However, the use of pot chlorination has come under question after a study on its effectiveness in fighting cholera in Guinea community wells demonstrated little effect in 2008 [10]. With all these methods, it comes down to a country's ability, budget, and spread of awareness to implement these methods.

Questions

1. Is cholera a bacterial or viral infection?
2. What part(s) of the body does the cholera toxin mostly impact?
3. How is CTX introduced to a patient? Does it have to be taken into the body through eating/drinking or is it airborne like the flu?
4. In which areas of the world is cholera most likely to be found and who is it most likely to effect? Provide multiple examples.
5. What are preventative measures that somebody can take to minimize their risk of contracting the disease?
6. If there were a cholera outbreak in a rural area, what would be the best way to contain it? How could you prevent it from spreading to a more densely populated area of the region?
7. Imagine that you are a doctor at a free clinic in Bangladesh that provides health services to many rural villages in the area. In the past couple of weeks, many of the people have been coming in with symptoms similar to cholera. What might those symptoms be? How can you treat these patients?
8. Now imagine that you are a World Health Organization representative visiting a rural village in Southeast Asia that has recently had a cholera outbreak. What are some possible solutions you can propose to the UN that can prevent an outbreak like this from ever happening again?

References

[1] World Health Organization. 2007. Cholera Fact Sheet. [online] <http://www.who.int/mediacentre/factsheets/fs107/en/> [Accessed 2 April 2018].

[2] Das, B., J. Bischerour, and F.-X. Barre. 2011. Molecular mechanism of acquisition of the cholera toxin genes. *The Indian Journal of Medical Research* 133(2): 195–200.

[3] Interpro. *n.d.* Cholera toxin. [online] <https://www.ebi.ac.uk/interpro/potm/2005_9/Page2.htm> [Accessed 2 April 2018].

[4] Centers for Disease Control and Prevention. *n.d.* Cholera – *Vibrio cholerae* infection | Vaccines. [online] <https://www.cdc.gov/cholera/vaccines.html> [Accessed 2 April 2018].

[5] Centers for Disease Control and Prevention. *n.d.* Cholera – *Vibrio cholerae* infection | Treatment. [online] <https://www.cdc.gov/cholera/treatment/index.html> [Accessed 2 April 2018].

[6] Centers for Disease Control and Prevention. *n.d.* Five basic cholera prevention steps. [online] <https://www.cdc.gov/cholera/preventionsteps.html> [Accessed 2 April 2018].

[7] Centers for Disease Control and Prevention. *n.d.* Safe water system | slow sand filtration. [online] <https://www.cdc.gov/safewater/sand-filtration.html> [Accessed 2 April 2018].

[8] Centers for Disease Control and Prevention. *n.d.* Safe water system | solar disinfection. [online] <https://www.cdc.gov/safewater/solardisinfection.html> [Accessed 2 April 2018].

[9] Centers for Disease Control and Prevention. *n.d.* Safe water system | chlorination. [online] <https://www.cdc.gov/safewater/chlorination.html> [Accessed 2 April 2018].

[10] Cavallaro, E.C. *et al.* 2011. Evaluation of pot-chlorination of wells during a cholera outbreak, Bissau, Guinea-Bissau, 2008. *J Water Health.* 9(2): 394–402.

[11] Centers for Disease Control and Prevention. *n.d.* Cholera – *Vibrio cholerae* infection | rehydration therapy. [online] <https://www.cdc.gov/cholera/treatment/rehydration-therapy.html> [Accessed 2 April 2018].

[12] Centers for Disease Control and Prevention. *n.d.* Cholera – *Vibrio cholerae* infection | antibiotic treatment. [online] <https://www.cdc.gov/cholera/treatment/antibiotic-treatment.html> [Accessed 2 April 2018].