Phage In The Time Of Cholera

By Julianna LeMieux — February 8, 2017

Although they don't generally make headlines, *Vibrio cholerae* infections wreak havoc in areas of the world with poor sanitation, causing millions of cases of cholera and over 100,000 deaths each year.

A cholera infection can range from mild to a severe diarrheal disease with profuse watery diarrhea and vomiting, rapid loss of fluids, dehydration, shock and death within a few hours.

When these outbreaks occur, there is a rapid increase in the number of cases, and transmission is frequently seen among people sharing a household. Therefore, a drug that could quickly and easily be administered to people living in close proximity to a cholera outbreak, to contain the spread of the bacteria, would be incredibly useful in the fight against cholera.

A team at Tufts Medical School recently reported [1], in *Nature Communications*, that using viruses (phages) that infect the bacteria may be able to do just that. They found that giving animals (mice and rabbits) a cocktail of three phages that infect *V. cholerae*, before infecting with live bacteria, resulted in protection of the mice from the bacterial infection. When these viruses, or phages, infect a bacterial cell and replicate, they kill the bacterial cell in the process.

In order to test this, between 1 and 10 million phages were put into the mice's stomachs by orogastric inoculation (into the stomach through a tube.) Three hours later, a large dose of *V. cholerae* (500,000 bacteria) were administered the same way. After 24 hours, the mice were killed and the number of bacteria in the small intestine were counted.
As shown in the figure below, the number of surviving *V. cholerae* cells in the small intestine were drastically reduced in the mice that had received the phage prior to infection versus the mice that had not been given phage.

There are three types of phage (ICP1, ICP2, and ICP3.) The first column on the left (black circles) represents the amount of bacteria recovered from the intestines of the mice that were given no phage before infection with bacteria. The next three columns (yellow, blue and green circles) represent mice that were given one of the three phages before infection with bacteria. Lastly, the purple circles represent mice that received the cocktail of all three phages before infection. Administering each phage individually reduced the amount of bacteria in the intestine, but, none worked as well alone as a cocktail of all three together.

These data suggest that receiving the phage (and especially the cocktail of all three phage) prevents infection by the bacteria. In a real world scenario, this could be incredibly useful in the instance that a cholera case is confirmed in a crowded village. If everyone who is in close contact with the patient could take the phage cocktail even hours before exposure to the *V. cholerae*, transmission could be prevented.

Dr. Andrew Camilli, the lead investigator in the study says, "Seeing this project reach this point is incredibly exciting. We have been working on cholera phage in my lab for years and this result brings us one step closer to the reality of using phage therapy for the prevention of cholera."
One hallmark of a cholera outbreak is how quickly it spreads. For example, when the UN peacekeepers started a cholera epidemic in Haiti in 2010, the first cholera case was confirmed on October 21, 2010. Just one month later, during the week of November 27--December 3, the median daily number of deaths [2] was 41. That's per day.

That's not an outbreak - that's an explosion. With this level of transmission, antibiotics don't work quickly enough. What is needed to quell outbreaks is a therapy that can stop transmission in its tracks. And, although phage therapy is not going to stop outbreaks from occurring, it may make them smaller, acting as an important stop gap in the burden that cholera is on certain communities.

Notes:
Conflict of Interest: Dr. Andrew Camilli, the lead author of this study, was my PhD thesis advisor. Although it is a pleasure to highlight the work coming out of a lab that I worked in, I chose this topic based solely on its scientific merit.