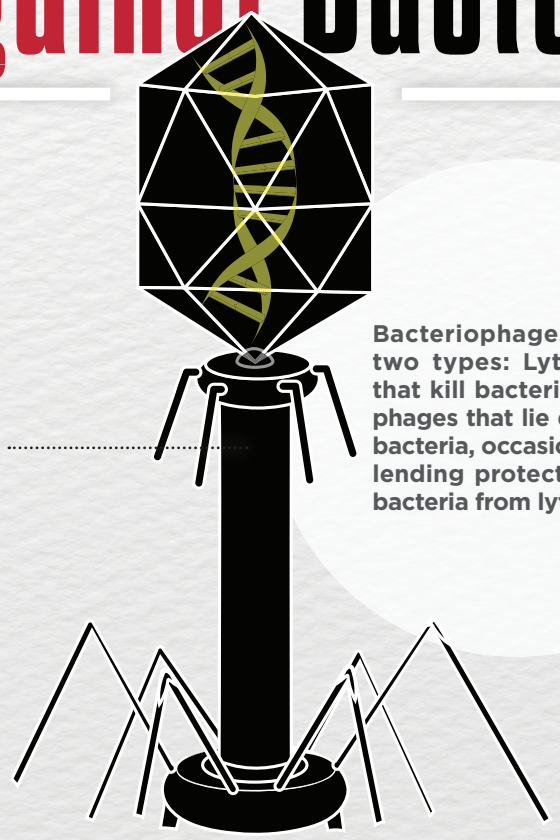
Viruses Against Bacteria

By Danielle Gerhard, PhD
Designed by Erin Lemieux

In 1915, the English bacteriologist Frederick Twort published his findings on an "ultra-microscopic" virus that appeared to kill bacteria that he cultured from contaminated smallpox vaccines.[1] Shortly after, the French-Canadian microbiologist Félix d'Hérelle coined the term bacteriophages, or bacteria-eaters, from the Greek word phagein, meaning "to devour."

While studying the stool of dysentery patients, d'Hérelle isolated an "anti-Shiga" agent and tested its lytic potential in a culture of the illness-causing bacterium.[2] The promising results of this experiment and others inspired d'Hérelle to test a phage therapy in a boy suffering from severe dysentery. The treatment was a success.



Bacteriophages come in two types: Lytic phages that kill bacteria and prophages that lie dormant in bacteria, occasionally even lending protection to the bacteria from lytic phages.

The promise of phage therapy drew global interest, and d'Hérelle traveled the world, isolating phages from patients recovering from illnesses. However, mixed results from phage therapy trials combined with Alexander Fleming's discovery of penicillin caused researchers in the West to abandon research into bacteriophage.

Although scientists in the Soviet Union continued phage research, very little made its way across the iron curtain. The Cold War further divided the scientific community, keeping antibiotic research from the Soviet Union and phage therapy work from the West. Now in the face of rising rates of antimicrobial resistance, scientists show a renewed interest in these bacteria-eaters.

Antimicrobials are broad-spectrum, killing both pathogenic bacteria and good commensal bacteria. In contrast, bacteriophages tend to be specific, making them useful for phage therapy.

To gain access to the cell, a bacteriophage first has to bind to a specific receptor on the cell membrane. If there is a receptor mis-match between the phage and bacterium, infection does not occur.

Some bacteria like the multidrug-resistant bacterium *Pseudomonas aeruginosa*, which is found in health care settings and in the lungs of patients with cystic fibrosis, like to stick together in a slimy layer called a biofilm. Biofilms, described as cities for microbes, begin development following a successful attachment to a surface, such as a lung, where they continue to put down roots. Although bacteria living in biofilms show strong antimicrobial resistance,[3] tiny bacteriophages can successfully infect these cities.[4]

References
1. Twort, F.W. An investigation on the nature of ultra-microscopic viruses. *Lancet* 186, 1241-1243 (1961).
2. Stone, R. Stalin's forgotten cure. *Science* 298, 728-731 (2002).
3. Mah, T. *et al.* A genetic basis for Pseudomonas aeruginosa biofilm antibiotic resistance. *Nature* 426, 306-310 (2003).
4. Harper, D.R., *et al.* Bacteriophages and biofilms. *Antibiotics* 3, 270-284 (2014).
5. Luong, T., *et al.* Phage therapy in the resistance era: where do we stand and where are we going? *Clinical Therapeutics* 42, 1659-1680 (2020).