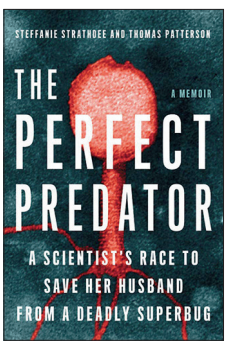
Books

The Darwinian dance



Published Online
September 2, 2019
http://dx.doi.org/10.1016/S1473-3099(19)30471-2

The Perfect Predator: A Scientist's Race to Save Her Husband from a Deadly Superbug: A Memoir
Steffanie Strathdee, Thomas Patterson, Teresa Baker
Hachette Books, 2019
pp 352, £20
ISBN-13:978-0316418089

When Steffanie Strathdee's husband, Thomas Patterson, started vomiting and experiencing intense stomach pains on their vacation in Egypt, they assumed that he could be cured with an overnight course of antibiotics. Instead, they returned home to learn that he had a pancreatic pseudocyst that had been infected with *Acinetobacter baumannii*, a multidrug-resistant infection that their doctor described as "the worst bacteria on the planet". Patterson was dying and with no treatment options left, Strathdee put her training as an epidemiologist into action and set to find an alternative approach that might save her husband. In the end she found phage therapy and saved Thomas. In *The Perfect Predator: A Scientist's Race to Save Her Husband from a Deadly Superbug: A Memoir,* Strathdee tell their story.

Phages are viruses that replicate by infecting and multiplying within a specific bacterium until the bacterium is destroyed. Although phages were discovered in 1915, and were briefly popular as an antimicrobial treatment, they soon fell out of favour in western medicine while remaining comparatively popular in the Soviet bloc. The phage preparations that reached the mass market were not targeted to specific infections, were often either mistakenly sterilised or dangerously impure, and were wrongly marketed as a treatment for non-bacterial conditions such as herpes. Penicillin quickly replaced phage therapy in western medicine, but was slower to catch on elsewhere due to the difficulties involved in manufacturing it in sufficient quantities. The fact that phage research continued in the Soviet bloc only added to the marginalisation of the field, as it was now associated with the Union of Soviet Socialist Republics. Ironically, research into phage enzymes launched the fields of molecular biology, genetic engineering, and cancer biology even as phage therapy became marginalised.

Despite the long history of phage therapy, Strathdee faced several obstacles to use phage therapy that would not apply to a more conventional novel drug treatment. Phages need to be well matched to the bacteria they are intended to attack, which in Patterson's case meant working with a sample of Patterson's bacteria rather than just matching genus and species. Furthermore, because bacteria mutate, a single phage would be useless because the infection would quickly become immune to it; instead cocktails of three or four different phages were used.

Beyond these basic biological issues, the couple also faced organisational difficulties: treating Patterson required the skills of phage experts, many of whom felt that their work was not yet ready for use in humans. Further setbacks came when they discovered that the US military had been working on phage therapy for infected service personnel, but refused to share their phages with a civilian—until informed that the Belgian military were doing similar work and had already agreed to help. The team also had to apply to the US Food and Drug Administration (FDA) for an experimental investigational new drug, which would grant them permission to use the procedure on an otherwise untreatable patient. The protocol they applied under was designed specifically for testing drugs because there was no regulatory mechanism for treatments like phage therapy, which might play a role in preventing further research in this area. Even once these issues had been addressed, there was no established protocol or even a rough draft on how to apply the treatment. The team had to decide whether the phages should be administered intravenously or injected at the source of the infection, how to prepare them, the correct dosage, and length of treatment. There were also concerns about endotoxin exposure, because the debris from the destroyed bacteria could drive Patterson's immune system into septic shock.

Despite these difficulties, Patterson recovered and was released from the hospital after 9 months. However, the implications of his experience were only starting to become clear. Patterson's treatment provided an impetus for the FDA to reconsider their regulatory model so as to allow for treatments like phage therapy. Strathdee also found herself receiving calls for help from others with multidrug-resistant infections, and she attempted to help coordinate the network of researchers, which eventually led to Strathdee becoming Director of the UC San Diego Center for Innovative Phage Application and Therapeutics.

Strathdee's story highlights the seriousness of antibiotic resistance. By 2050, one person could die from an antibiotic-resistant infection every 3 seconds, and roughly one-fifth of infections in Europe, North America, and Australia are believed to be resistant to antibiotics. Despite being an infectious disease epidemiologist, Strathdee "wasn't…going around sounding alarm bells" about the problem until her husband was nearly killed by an antibiotic-resistant infection. Although it is important to address the overuse and misuse of antibiotics and to continue searching for new antibiotics, phage therapy offers some intriguing possibilities. Treating resistant bacteria is a Darwinian dance—with each treatment, the bacteria mutates, rendering the current treatment ineffective, but these mutations can also open up new vulnerabilities. Strathdee admits that "we don't know if phage therapy will be shown to be efficacious in clinical trials", but between the seriousness of the situation and the possibilities that phage therapy offers, it seems likely that the resistance to phage research is coming to an end.

Robert Stirrups