



## Nina Chanishvili—keeping bacteriophages in the limelight



For more on the trial on phage therapy in urinary tract infections see *Lancet Infect Dis* 2021; 21: 427–36

Nina Chanishvili remembers clearly visiting the laboratory where her uncle worked on bacteriophages—viruses that kill bacteria—in the Eliava Institute of Bacteriophage, Microbiology & Virology in Tbilisi, Georgia, as a young girl. Today, she is head of research and development at that very same institute, a position she has held since 2012 after working her way up through various positions.

Despite being discovered in 1917, bacteriophages were rapidly overtaken by the discovery of penicillin in 1928, and interest in high-income countries fell sharply. However, in eastern Europe, Russia, Georgia, and other former states of the Soviet Union, the popularity of bacteriophages endures until this day. Now, with antimicrobial resistance rising everywhere, scientists are prepared to look again at alternative methods for treating infections.

Such is her devotion to this field, that Chanishvili has written a book about the early use of bacteriophages, *A literature review of the practical application of bacteriophage research*. “They are used to treat all kinds of conditions, including common ear, nose, and throat infections”, says Chanishvili. “Cocktails of bacteriophages were also created to treat sepsis, but there was reluctance to use them intravenously.”

Bacteriophages are more expensive and time-consuming to produce than penicillin, and come in two types (virulent or temperate), and only the virulent ones can be used in preparations, complicating their use. Another key factor in killing their early popularity was the actions of Howard Florey, who shared the 1945 Nobel Prize for Medicine for discovering penicillin. “As part of a knowledge sharing project, he visited the former USSR”, explains Chanishvili, “and when he returned to the USA, his report questioned the efficacy of bacteriophages. This was like the kiss of death, someone so eminent saying this”. Florey’s negative comments came despite a huge number of reports from Russian doctors on the success of bacteriophages in treating wounds and other war injuries.

In the 1970s, even after successful animal studies with bacteriophages, the reluctance to use them intravenously continued. Then Chanishvili’s uncle actually treated, after special permission from a hospital director, a young doctor (aged mid-20s) whose sepsis was resistant to last-line antibiotics, and he made a near-complete recovery. “This case provided great confidence to treat another 900 patients for sepsis using bacteriophages in different hospitals across the USSR, mostly very young children and with mainly positive outcomes. This continued until the end of the Soviet era”, she explains.

Even after this, western countries like the USA could not be persuaded of the safety of bacteriophages, because scientists believed that the presence of temperate bacteriophages risked horizontal gene transfer that could promote microbial resistance. Thus, until the 1990s, virtually no-one was

interested in following up bacteriophage treatment. “It was then that the journalist Peter Radezky contacted our institute, wanting to know the ‘life story’ of bacteriophages for a book he was writing”, she explains.

It was an extremely difficult time for the Eliava institute in the mid-1990s and 2000s after the USSR broke up. However, following Radezky’s interest, more and more journalists wanted to come and learn about bacteriophages, including the BBC and the New York Times. This continues today. “In many cases, journalists bring a patient who wants treatment with bacteriophages, and they will film or document the patient’s journey”, explains Chanishvili. The patients mostly have infections resistant to last-line antibiotics, such as urogenital infections or, more commonly, cystic fibrosis. “Inhalation of bacteriophages can help extend the time between exacerbations”, she explains. “However, randomised controlled trials are very expensive.”

Chanishvili and colleagues recently published, in this journal, a randomised controlled trial of intravesical bacteriophage therapy to treat urinary tract infections (UTIs) in patients undergoing transurethral resection of the prostate (TURP). The study, done entirely in Georgia, showed bacteriophage therapy was non-inferior to standard-of-care antibiotic treatment, but was not superior to placebo bladder irrigation, in terms of efficacy or safety in treating UTIs in patients undergoing TURP. However, the bacteriophage safety profile seemed to be favourable, making future trials with a larger cohort feasible. Indeed, teams in Switzerland are following up these results and Chanishvili is collaborating on a new publication with them.

Her team is also working on restoration of the microbiome of asthma patients with bacteriophages, in collaboration with teams from the UK, Greece, Poland, and Switzerland. The UK team has shown that patients with asthma have certain phage genomes missing compared with the microbiome of healthy individuals, and the collaborators are conducting studies to isolate the bacteriophages that can balance the number of the target dominant bacteria (*Staphylococcus aureus*, *Acinetobacter baumannii*) in these “defective” microbiomes. “The results we have seen with cystic fibrosis suggest it is possible to treat asthma with bacteriophages and extend the time between exacerbations”, explains Chanishvili.

For the future, she worries about the lack of young people coming into science in Georgia. Yet she is still grateful for the beauty of her surroundings in Tbilisi, and her extended family whom she loves cooking for and entertaining. She looks forward to post COVID-19 times, hoping the economic crisis won’t endure, and to the more simple things in life like going to the theatre again.

Tony Kirby