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Autore	Abedon Stephen T
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Sommario/riassunto

Historically, the first observation of a transmissible lytic agent that is specifically active against a bacterium (Bacillus anthracis) was by a Russian microbiologist Nikolay Gamaleya in 1898. At that time, however, it was too early to make a connection to another discovery made by Dmitri Ivanovsky in 1892 and Martinus Beijerinck in 1898 on a non-bacterial pathogen infecting tobacco plants. Thus the viral world was discovered in two of the three domains of life, and our current understanding is that viruses represent the most abundant biological entities on the planet. The potential of bacteriophages for infection treatment have been recognized after the discoveries by Frederick Twort and Felix d'Hérelle in 1915 and 1917. Subsequent phage therapy developments, however, have been overshadowed by the remarkable success of antibiotics in infection control and treatment, and phage therapy research and development persisted mostly in the former Soviet Union countries, Russia and Georgia, as well as in France and Poland. The dramatic rise of antibiotic resistance and especially of multi-drug resistance among human and animal bacterial pathogens, however, challenged the position of antibiotics as a single most important pillar for infection control and treatment. Thus there is a renewed interest in phage therapy as a possible additive/alternative therapy, especially for the infections that resist routine antibiotic treatment. The basis for the revival of phage therapy is affected by a number of issues that need to be resolved before it can enter the arena,

which is traditionally reserved for antibiotics. Probably the most important is the regulatory issue: How should phage therapy be regulated? Similarly to drugs? Then the co-evolving nature of phage-bacterial host relationship will be a major hurdle for the production of consistent phage formulae. Or should we resort to the phage products such as lysins and the corresponding engineered versions in order to have accurate and consistent delivery doses? We still have very limited knowledge about the pharmacodynamics of phage therapy. More data, obtained in animal models, are necessary to evaluate the phage therapy efficiency compared, for example, to antibiotics. Another aspect is the safety of phage therapy. How do phages interact with the immune system and to what costs, or benefits? What are the risks, in the course of phage therapy, of transduction of undesirable properties such as virulence or antibiotic resistance genes? How frequent is the development of bacterial host resistance during phage therapy? Understanding these and many other aspects of phage therapy, basic and applied, is the main subject of this Topic.