Felix d'Hérelle: His Life and Work and the Foundation of a Bacteriophage Reference Center

Hans-W. Ackermann, Mario Martin, Jean-F. Vieu, and Pierre Nicolle
Department of Microbiology
Faculty of Medicine
Laval University
Quebec 10, Quebec, Canada G1K 7P4
and
Institut Pasteur
Services des Entérobactéries et de Pathologie exotique
75724 Paris, France

The Natural Sciences and Engineering Council of Canada has provided funds for a reference center for bacterial viruses, to be named after Félix d'Hérelle. The center is located at Laval University, Quebec City, Quebec, Canada.

Life and Scientific Work of Félix d'Hérelle
Biographical Notes

Félix d'Hérelle was born in 1873 in Montreal, Quebec, Canada. His father, a French Canadian, died 6 years later and his mother, of Dutch origin, took the boy to Paris, France. Little is known of his youth. He married in 1893 and reportedly studied medicine in Paris; Lille, France; Leiden, The Netherlands; and Montreal, where he graduated.

In 1901 d'Hérelle went to Guatemala City, Guatemala, as a hospital bacteriologist and became a professor of bacteriology at the local medical school. He later recounted that he had learned his science while making the trip (14). In 1907 d'Hérelle went to Merida, Mexico, and worked on the fermentation of sisal and also as a government bacteriologist. While there, he also studied an infectious enteritis of locusts that offered great potential for biological pest control. d'Hérelle isolated the agent of the disease and named it "Coccobacillus acridiorum" (now a subspecies of Enterobacter aerogenes [19]).

The Mexican government sent d'Hérelle to the Pasteur Institute in Paris (in 1909?), where he became an assistant to Salimbeni and, later (from 1914 to 1921), head of a laboratory. By his own account, he was back in Mexico in 1919 (7, 12). His exact whereabouts in these years are uncertain. Between 1911 and 1915, he went on missions to Argentina, Turkey, and Tunisia, organizing locust control by means of his coccobacillus. According to Charles Nicolle, then director of the Pasteur Institute of Tunis, Tunisia, the latter campaign was a failure.

It was in 1915 in Tunisia that d'Hérelle saw his first "toches vierges," or phage plaques. He showed them to Nicolle, who suggested that they were due to a virus (12, 16). Phages were actually discovered sometime in August 1916. Back in France, d’Hérelle found plaques again, in cultures of a dysentery bacillus. Their principle was infectious, and they destroyed agar and broth cultures of the bacilli. d'Hérelle concluded that the agent was an invisible, parasitic microorganism, and he published his findings in a famous note in September 1917 (8). He was then 44 years old, not exactly a young man.

d'Hérelle became instantly famous and began a period of frenzied activity. He went on a mission to Indochina and, in 1921, abruptly left the Pasteur Institute of Paris. During the next 12 years, he taught in Leiden, headed a bacteriology department in Egypt, went to Assam at the request of the British government, taught "protobiology" at Yale University (New Haven, Conn.) and founded the Laboratoire du Bactériophage in Paris. The latter was devoted to the production of phages for therapeutic use.

In 1934, on the invitation of the Russian government, d'Hérelle founded bacteriophage research institutes in Tiflis, Kiev, and Kharkov. This activity ended in near catastrophe, when his friend and collaborator of long standing, G. Eliava, was shot for political reasons (14). Word has it that Eliava had...
poisoned wells with bacteriophages." It seems that here is a martyr of science waiting for rehabilitation. d'Hérelle left Russia and thus escaped the Great Purge in 1937. He went back to Paris, was interned in Vichy during the German occupation, and died in 1949, still a Canadian citizen.

The life of Félix d'Hérelle has been recounted by various biographers (1–5, 14–16, 18). Some questions, however, remain open to speculation. Did he graduate in medicine? It is generally admitted that he graduated around 1900 in Montreal, yet we find no mention of d'Hérelle in the records of the University of Montreal, then a branch of Laval University in Quebec City, nor in the records of the latter. Then there is a curious paper in the *Naturaliste Canadien* of 1901, signed by a "Félix d'Hérelle, chemist," which claims that plants produce carbon instead of extracting it from the atmosphere (6). d'Hérelle's later writing shows considerable medical knowledge, which strongly suggests that he studied medicine.

If he did not graduate, this might explain why he went to Guatemala, considered a very remote place at the time. It could also be a clue to his rather itinerant life. Similarly, the circumstances surrounding his departures from the Pasteur Institute and Yale University remain to be elucidated.

**Contributions to Science**

d'Hérelle worked very hard and was an extremely productive writer. Besides his scholarly and interesting papers on "Cocobacillus acridorum" and locust disease (7), he produced no less than 97 papers, books, and monographs on bacteriophages (17). He coined the term *bacteriophage* (8) and studied phages of dysentery, typhoid, plague, and cholera bacilli, of staphylococci, and of Pasteurella. Fully 26 papers were on the role of phages in disease. Others were dedicated to phage techniques, phage antiserum, phage ecology, and even the behavior of phages in leukocytes. Some 30 papers were on the nature of bacteriophages. This was part of the "Twort-d'Hérelle controversy," a subject discussed in detail by Nicolle (16) and Duckworth (13).

In 1915 the English bacteriologist Frederick William Twort (1877–1950) described transmissible lysis in micrococci. He offered several explanations, none of which was "viral" in a modern sense (20). His now famous note went unnoticed at first, but the viral nature of bacteriophages was doubted by others, and a controversy ensued that was to last 20 years. It is a major riddle of microbiology why Twort, although retelling the story of his discovery as late as 1949 (21), quit phage research. However, this does not diminish his historical merit, and we believe that bacteriophages were discovered twice at a short interval.

d'Hérelle centered his career on bacteriophages. As early as 1921, he published an astonishing book (9) which contains much of his later thinking. He described techniques that are still in use, phage-bacterium interactions, properties of phages, and the role of phages in human and animal disease. There was only one phage, "Bacteriophagus intestinale." It was a living organism—an antigenically complex virus—and infection was a struggle between phages and bacteria. In retrospect, it is most interesting for the history of science that phages were defined as obligate parasites that entered bacteria and multiplied in these or became latent and conferred antiphage immunity on their hosts. To our knowledge, d'Hérelle was the first to have postulated the concept of intracellular multiplication of viruses.

A further major book was published in 1926 (10). It reviewed an already considerable body of knowledge (643 references). d'Hérelle followed the outline of his previous book and maintained and amplified his earlier hypotheses and conclusions. The bacteriophage corpuscle, or "Protobios bacteriophagus," was a virus which played a central role in infectious disease and could be used for cure and prevention. This idea was further developed in a book published in 1938 (11).

The main reason for the existence of the Félix d'Hérelle Reference Center for Bacterial Viruses is the growing confusion in bacteriophages. In addition to some 1,500 typing phages, over 2,000 bacterial viruses have been studied by electron microscopy, and "new" phages are described at the pace of 150 per year. There is no agreement on nomenclature, and synonyms are plentiful. Worse, many "phages" may actually be isolates of the same virus or have been lost or destroyed. They are thus no longer available for comparative studies. This situation impedes future research and makes descriptions of new phages increasingly meaningless. Clearly, a collection of type phages, specifically
devoted to phage taxonomy, is needed.

The situation is not much better with typing phages. In fact, only phages of major sets, for example of *Salmonella typhi*, *Salmonella paratyphi* B, or *Staphylococcus aureus*, are certain to be preserved. Other sets are constantly endangered, because loss of a single phage invalidates the whole scheme. Finally, it may be desirable to have a repository for phages that are harmful to industrial microorganisms or otherwise interesting.

The center is a nonprofit organization, intended as an instrument of the International Committee on Taxonomy of Viruses (R. E. F. Matthews, Intervirology, in press). It collaborates with laboratories specializing in phages of mycoplasmas and cyanobacteria. The center is essentially a taxonomical collection, backed by a Philips EM 300 electron microscope and over 3,000 literature files, mainly on morphology and physicochemical properties.

Which phages will be collected? It seems pointless to collect everything, for example, all 60 isolates of T-even-type phages or the over 100 variants of typhoid phage Vi II. Likewise, mutants or typing phages maintained by other institutions, such as the Enteric Reference Laboratory in Colindale, London, England, will not be collected.

Prime targets are type viruses of phage species, their propagating bacteria, and, if applicable, lysogenic hosts and antisera. They will be requested from their original investigators. Other "collectibles" are phages of minor typing schemes not maintained elsewhere, phages of industrial microorganisms, and phages used in teaching or specific for antibiotic resistance plasmids.

Upon receipt, every phage is studied in the electron microscope, and depositors will receive a courtesy micrograph. Phages are stored in lyophil and as lysates at 4°C. Bacteria are usually kept in lyophil, as stab cultures, and at −70°C in glycerol broth. Phages will be distributed without charge to scientists and research institutions (it is hoped that this policy can be maintained). Before distribution, their identities will be checked by electron microscopy.

The potential benefits of the center are many. In addition to the preservation of type viruses, the very fact of collecting many different phages offers unique opportunities for comparative studies, both for graduate students and guest workers. There would also be an increase in knowledge of the preservation of phages (a problem that is still not completely solved). Another natural task would be to provide references and expertise on the identities of new phages, usually limited to electron microscopy. The principles of the center may be summarized as follows:

1. The center is a taxonomically oriented depository for bacteriophages and an instrument of the International Committee on Taxonomy of Viruses.  
2. The center collects and preserves type viruses of phage species, certain typing and teaching phages, viruses of industrially important bacteria, phages specific for resistance plasmids, and propagating and lysogenic bacteria.
3. Mutants and typing phages which are distributed by internationally acknowledged institutions are not collected.
4. The main collection is located in Quebec City. Phages for mycoplasmas and cyanobacteria are kept in collaborating laboratories located in Rochester, N.Y., and Cincinnati, Ohio, respectively.
5. Deposits are requested from the original investigators. Each phage should be deposited with information on its history, maintenance conditions, references, and, if possible, antiserum.
6. Phages are authenticated by electron microscopy and are kept as lysates and in lyophil. Morphology is checked at each propagation. Depositors receive a complimentary micrograph.
7. Phages and their hosts are available without charge to scientists and scientific institutions. Bacteria which are the subject of patents or patent applications will not be distributed or used without permission of the depositor.
8. On request, the center provides literature references and morphological expertise on the identities of new phages.
9. Guest workers are welcome.
10. A catalog is published at each International Congress of Virolgy.

Literature Cited


ASM News