Felix d'Herelle on the Discovery of Bacterial Viruses

“In 1910, I was in Mexico, in the state of Yucatan, when an invasion of locusts occurred; the Indians reported to me that in a certain place the ground was strewn with the corpses of these insects. I went there and collected sick locusts, easily picked out since their principal symptom was an abundant blackish diarrhoea. This malady had not as yet been described, so I studied it. It was caused by bacteria, the locust coccobacillus, which were present almost in the pure state in the diarrhoeal liquid. I could start epidemics in columns of healthy insects by dusting cultures of the coccobacillus on plants in front of the advancing columns: the insects infected themselves as they devoured the soiled plants.”

“During the years which followed, I went from the Argentine to North Africa to spread this illness. In the course of these researches, at various times I noticed an anomaly shown by some cultures of the coccobacillus which intrigued me greatly, although in fact the observation was ordinary enough, so banal indeed that many bacteriologists had certainly made it before on a variety of cultures.”

“The anomaly consisted of clear spots, quite circular, two or three millimeters in diameter, speckling the cultures grown on agar. I scratched the surface of the agar in these transparent patches, and made slides for the microscope; there was nothing to be seen. I concluded from this and other experiments that the something which caused the formation of the clear spots must be so small as to be filtrable, that is to say able to pass a porcelain filter of the Chamberland type, which will hold back all bacteria.”

“On my return to Paris in August, 1915, I was asked by Dr. Roux [then director of the Pasteur Institute] to investigate an epidemic of dysentery which was raging in a cavalry squadron, then resting at Maisons-Lafitte. I filtered emulsions of the faeces of the sick men, let the filtrates act on cultures of dysentery bacilli and spread them after incubation on nutritive agar in petri dishes: on various occasions I again found my clear spots.”

“At this time we often got cases of bacillary dysentery in the hospital of the Institut Pasteur in Paris. I resolved to follow one of these patients through from the moment of admission to the end of convalescence, to see at what time the principle causing the appearance of clear patches first appeared. This is what I did with the first case which was available.”
“The first day I isolated from the bloody stools a Shiga dysentery bacillus, but the spreading on agar of a broth culture, to which had been added a filtrate from the faeces of the same sick man, gave normal growth. The same experiment, repeated on the second and third days, was equally negative. The fourth day, as on the preceding days, I made an emulsion with a few drops of the still bloody stools, and filtered it through a Chamberland candle; to a broth culture of the dysentery bacillus isolated the first day, I added a drop of the filtrate; then I spread a drop of this mixture on agar. I placed the tube of broth culture and the agar plate in an incubator at 37°. It was the end of the afternoon, in what was then the mortuary, where I had my laboratory.”

“The next morning, on opening the incubator, I experienced one of those rare moments of intense emotion which reward the research worker for all his pains: at the first glance I saw that the broth culture, which the night before had been very turbid, was perfectly clear: all the bacteria had vanished, they had dissolved away like sugar in water. As for the agar spread, it was devoid of all growth and what caused my emotion was that in a flash I had understood: what caused my clear spots was in fact an invisible microbe, a filtrable virus, but a virus parasitic on bacteria.”

“Another thought came to me also: "If this is true, the same thing has probably occurred during the night in the sick man, who yesterday was in a serious condition. In his intestine, as in my test-tube, the dysentery bacilli will have dissolved away under the action of their parasite. He should now be cured." I dashed to the hospital. In fact, during the night, his general condition had greatly improved and convalescence was beginning.”
In 1917 d'Herelle published his first report of this discovery in a Short note entitled "On an invisible microbial antagonist of dysentery Bacilli."


From the feces of diverse patients convalescing from bacillary dysentery, and in one case from the urine, I have isolated an invisible microbe with the properties of antagonism to the bacillus of Shiga. This finding is particularly easy in the cases of common enteritis following dysentery; in convalescents who do not present this complication the disappearance of the anti-microbe quickly follows that of the pathogenic bacillus. In spite of numerous examinations, I have never found the antagonistic microbes either in the feces of dysenteritics during the disease period, or in the feces of normal subjects.

The isolation of the anti-Shiga microbe is simple: one inoculates a tube of bouillon with four to five drops of feces, incubates at 37°C for 18 hours, and then filters with a Chamberland L2 filter. A small quantity of the active filtrate added, either to a broth culture of Shiga bacillus, or to an emulsion of these bacillus in broth or even in physiological saline, provokes the arrest of the culture, the death of the bacillus then their lysis, which is complete after a period of time varying from hours to days depending on the amount of the culture and the quantity of the filtrate added.

The invisible microbe grows [cultive] in the lysed culture of Shiga bacillus because a trace of this liquid, placed in a new culture of Shiga, reproduces the same phenomenon with the same intensity: I have carried this out up to the present time with the first stock isolated for more than fifty successive transfers. The following experiment gives, moreover, the visible evidence that the antagonistic action is produced by a living germ: if one adds to a culture of Shiga a dilution of approximately one to a million of an already lysed culture, and if, immediately after, one spreads out on an agar slant a droplet of this culture, one obtains, after incubation, a coat of dysentery bacilli showing a certain number of circles about 1 mm in diameter, where the culture is void; these points can only represent the colonies of the antagonistic microbe: a chemical substance would not be able to concentrate at defined points. In working with measured quantities, I have seen that a lysed culture of Shiga contains five to six million of these filterable germs per cubic centimeter. One three-millionth of a cubic centimeter of the preceding culture from Shiga, or a single germ, introduced into a tube of broth, inhibits the culture of Shiga even when liberally inoculated; the same quantity added to a 10 cm3 culture of Shiga sterilizes it and lyses it in five or six days.

The diverse stocks of the antagonistic microbe which I have isolated were originally active only against the bacillus of Shiga; through symbiotic culture [culture en symbiose] with the dysentery bacilli of Hiss or Flexner, I could, after several passages, render them antagonistic to these bacilli. I have not obtained any results working with other microbes: typhoid bacilli, paratyphoid bacilli, staphylococci, etc. The appearance of antagonism against the bacillus of Flexner or of Hiss is accompanied by a diminution followed by a loss of power against Shiga, this power being recoverable with its original intensity after several symbiotic cultures; the specificity of antagonistic action therefore is not inherent in the nature of the invisible microbe, but is acquired in the sick organism by symbiotic culture with the pathogenic bacillus. In the absence of dysentery bacilli the anti-microbe does not grow in any medium, it does not attack heat killed dysentery bacilli; in contrast it grows perfectly in an emulsion of washed bacilli in physiological salt solution: it results from these studies that the antidysentery microbe is an obligate bacteriophage [un bacteriophage obligatoire].

The anti-Shiga microbe does not show any pathogenic action on any of the animals tested. Cultures of Shiga lysed by the action of the invisible microbe, which are in reality cultures of the anti-microbe, possessed the property of immunizing a rabbit against a dose of Shiga bacilli which killed the controls in five days.
I have searched for evidence of such an anti-microbe from convalescents from typhoid fever: in two cases, one from the urine and the other from the feces, I have been successful in isolating a filterable microbe giving the clear lytic property with respect to bacillus of paratyphoid A, but always less marked than the anti-Shiga microbe. These properties are attenuated in successive culture.

In summary, in certain convalescents from dysentery, I have shown that the disappearance of the dysentery bacillus coincides with the appearance of an invisible microbe endowed with antagonistic properties with respect to the pathogenic bacillus. This microbe, the true microbe of immunity, is an obligate bacteriophage; its parasitism is strictly specific, but if it is limited to one species at a given moment, it may develop antagonism in turn against diverse germs by accustomization. It appears therefore that in bacillary dysentery, next to the anti-tonic [sic] homologous immunity, emanating directly from the organism under attack, there exists a heterologous antimicrobial immunity produced by the antagonistic microorganism. It is probable that this phenomenon is not special to dysentery, but of a more general order because I have shown it can be found likewise, though less marked, in two cases [sic] of paratyphoid fever.