

THE THERAPEUTIC USE OF BACTERIOPHAGE¹

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Since D'Herelle described the phenomenon known as bacteriophage a great interest has been manifested in its use as a therapeutic agent.

The bacteriophage, as is well known, is an agent which has the capacity of lysing bacterial cells and at the same time reproducing itself; so that a phage lysed culture may then induce lysis in a second culture and so on indefinitely. D'Herelle establishes a very strong argument supporting his belief that the bacteriophage is an ultra-microscopic parasite of the bacterium. Most bacteriologists, however, hold to one of several hypotheses centering around the conception of bacteriophagic activity as a manifestation of some dissociative or abnormal normal physiology of the bacterium itself.

Regardless of one's acceptance of these concepts as to its nature, the use of the bacteriophage in the control of infectious diseases appears as a definite possibility. Certainly numerous experiments and studies seem to indicate that it is a factor which is naturally present. And it appears to be significant in the mechanism of resistance to and recovery from many epidemic and some non-epidemic diseases.

With these considerations in mind, a number of infections of various types were treated with bacteriophage or with filtrates of cultures thought to contain bacteriophage. In previous publications a series of cases of streptococcus septicemias were reported detailing the method of treatment and results obtained. Of forty such cases, only eleven resulted fatally, and these eleven were complicated by various factors which might properly exclude them from an experimental study. It must be admitted, however, that upon critical analysis of the character of the strains of streptococci isolated from these patients who recovered spontaneously without treatment, it could be presumed that other factors, generally considered under the term microbial dissociation, were responsible for the favorable results. However, it is by no means improbable that bacteriophagy and microbial dissociation are but different manifestations of the same fundamental thing, or that one is either the cause or the result of the other. Theoretical considerations concerning this appear in an earlier paper.

In other types of infections I have been able to establish more definitely that the filtrates used actually fulfilled the requirements for the identification of bacteriophage. In these cases results at times have been so remarkably favorable that it is impossible to escape the conviction that the bacteriophage is a valuable therapeutic aid.

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In seven of fifteen cases of typhoid fever convalescence has been induced in about forty-eight hours.

In two cases of staphylococcus septicemia the blood stream has become sterile promptly after use of the phage. In numerous localized infections due to streptococci, staphylococci, and other organisms there has been a very prompt and unusually rapid improvement. The details concerning these later cases will appear in the near future in another publication.

The term bacteriophage used in this connection actually denotes a filtrate of a phage lysed broth culture. Such a filtrate contains not only lytic principle, but also dispersed bacterial protein and the metabolic products of the organism. I have made no attempt to evaluate the influence of these other factors on the results obtained. It would appear that such a filtrate would be a more effective immunizing agent than the phage alone. The point is capable of experimental study as it is possible to free the filtrates of many of these other factors. Clinically, however, it is of no consequence as the end result is the important consideration.

During a period of four years no alarming results have occurred from subcutaneous injections. Filtrates of lysed typhoid culture, that have been prepared for less than one month, have proven toxic even in 1cc amounts. No alarming symptoms have developed, however, except a rather severe rigor and sharp elevation of temperature. I have not used amounts greater than 1cc. Results seem to be equally as good when two or three cubic centimeters are given subcutaneously. For this reason intravenous injections of typhoid filtrates have been discontinued.

I cannot escape the conviction that in many infectious diseases the bacteriophage or, more properly, phage lysed filtrates, of the offending organism may be a valuable therapeutic aid, and that in some cases it is a dominating factor in the recovery from diseases which are otherwise usually fatal.

BRIEF BIBLIOGRAPHY

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