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On an invisible microbe antagonistic toward dysenteric bacilli: brief note by Mr. F. D'Herelle, presented by Mr. Roux ☆

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I have isolated, from stools and, in one case, from the urine of patients recovering from bacillary dysentery, an invisible microbe endowed with antagonistic effects toward the Shiga bacillus. It is particularly easy to isolate in the case of common enteritis following dysentery. In convalescing patients who do not have this complication, the anti-Shiga microbe disappears very rapidly following the disappearance of the pathogenic bacillus. Despite numerous attempts, I have never found antagonistic microbes either in the stools of dysenteric patients who are still contaminated or in the stools of normal healthy subjects.

Isolation of the anti-Shiga microbe is simple: a nutrient broth tube is inoculated with 4–5 drops of stool, placed in the incubator at 37 °C for 18 h and then filtered using a Chamberland L_2 candle. A tiny quantity of active filtrate added either to a broth culture of Shiga bacilli or to an emulsion of the bacilli in broth or saline solution causes arrest of culture, death of the bacilli and then lysis, which is completed after a lapse of time varying from several hours to several days depending on the amount of culture and the quantity of added filtrate.

The invisible microbe is grown in lysed Shiga culture, since a trace amount of this liquid transferred to a new Shiga culture will reproduce the same phenomenon with the same intensity: up to the present time, and using the same initially isolated strain, I have carried out over 50 consecutive re-inoculations. Moreover, the following experiment provides visible proof that the antagonistic effect is produced by a live germ: if we add to a Shiga culture a dilution of a previously lysed culture, such that the Shiga culture only contains around one millionth, and if, immediately following this, we spread a drop of this culture onto a slant of gelose, we obtain, after incubation, a layer of dysenteric bacilli exhibiting a certain number of circles of around 1 mm in diameter on which the culture is non-existent; these points can only represent colonies of the antagonistic microbe: a chemical substance would not concentrate at defined points. By using measured quantities, I was able to observe that lysed Shiga culture contains from 5 to 6 billion filterable germs per cubic centimeter. One three-billionth of a cubic centimeter of a previous Shiga culture, i.e. one germ alone, when introduced into the nutrient broth tube, will prevent Shiga culture growth even if it has been heavily inoculated. The same quantity, when added to 10 cm^2 of a Shiga culture, will sterilize and lyse it in 5 or 6 days.

The various strains of the "anti-" microbe that I isolated were initially active only against the Shiga bacillus. Via culture in symbiosis with Hiss- or Flexner-type dysenteric bacilli, I was able, after several passages, to render them antagonistic toward these bacilli. I obtained no result when attempting this with other microbes such as typhoid and paratyphoid bacilli, staphylococci, etc. The onset of an antagonistic effect against the Flexner and Hiss bacilli was concomitant with a decrease

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in, and then a total loss of, an effect against Shiga, but this effect was restored to its initial intensity after several cultures in symbiosis. The specificity of the antagonistic action is thus not inherent to the nature of the invisible microbe, but is acquired within the patient's organism by culture in symbiosis with the pathogenic bacillus.

In the absence of dysenteric bacilli, the ''anti-'' microbe cannot be cultured in any medium. It does not attack heat-killed dysenteric bacilli. In contrast, it can be perfectly cultured using a saline emulsion of washed bacilli. This indicates that the anti-dysenteric microbe is an obligate bacteriophage.

The anti-Shiga microbe exerts no pathogenic effects upon laboratory animals. Shiga cultures lysed under the effect of the invisible microbe, which, in reality, are cultures of the ''anti-'' microbe, are endowed with the capacity to immunize rabbits against a dose of Shiga bacilli, which would kill controls in 5 days.

I tried to discover an ''anti-'' microbe in patients recovering from typhoid fever. In two cases, once in the urine and once in the stool, I succeeded in isolating a filterable microbe clearly possessing lytic properties against paratyphoid A bacillus, but these properties were nonetheless not as strong as those of the anti-Shiga microbe and they became less and less pronounced in the cultures which followed.

In summary, in certain patients recovering from dysentery, I observed that the disappearance of the dysenteric bacillus coincided with the appearance of an invisible microbe endowed with antagonistic properties toward a pathogenic bacillus. This microbe, which is a veritable ''microbe of immunity'', is an obligate bacteriophage. Its parasitism is strictly specific, but although it is limited to one species at a given time, it may in turn have an effect upon diverse germs via acclimatization. It would thus appear that in bacillary dysentery, along with homologous antitonic immunity emanating directly from the patient's organism, there also exists heterologous antimicrobial immunity produced by an antagonistic microorganism. It is probable that this phenomenon is not specific to dysentery, but that it is more widespread, since I was able to observe similar results, though less accentuated, in two cases of paratyphoid fever.

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