

microbe under one condition an ordinary saprophyte, can raise itself not only to parasitic life, causing pathogenic action, but further to a parasitic action which is as specific as that of *B. anthracis* or *B. influenzae*, as, for instance, is the case with the streptococcus pyogenes, the pneumococcus, and possibly certain species of diphtheroid bacilli. If this be the correct interpretation of the above observations, we could not oppose the view that at a very early history in the evolution of bacteria the first branches were of the nature of "pure saprophytes," that gradually another branch became evolved out of the former, leading to the evolution of what we designated as "conditional parasites," and that to these latter the final and highest branch, the "specific parasites," owe their origin. We may further in this hypothesis find the explanation why many of the specific parasites so readily revert to the stage of conditional parasitism—loss of virulence and loss of specific pathogenicity—ultimately altogether losing the power of maintaining a parasitic life and of causing disease; and, finally, that conditional parasites may return to the state of pure saprophytes, as is the case with some varieties of staphylococcus aureus and albus, *B. coli* and streptococci.

There appears nothing improbable in the view that if the bacteria causing specific infectious disease, that is, the distinctly parasitic bacteria, were prevented from transmitting their species through, and maintaining their existence in, the animal body, that is to say, if they were reduced to a saprophytic mode of existence only, they would ultimately lose their power of parasitism altogether, and in consequence their power for further mischief, and specific diseases caused by them at present would spontaneously disappear in the future. We see an indication, at any rate, for this consummation in what actually occurs in those specific diseases which are imported into a country which is not endemic for the particular disease, for example, plague, cholera.

Symbiosis.

From a number of direct experiments made during the last ten or twelve years, it appears that a definite interaction between certain bacteria can be demonstrated. I am not referring to the fact that pathogenic bacteria distributed in water gradually diminish, and after many days and weeks (in proportion to their initial numbers), ultimately disappear, which is due, not to a destructive action on them by the saprophytic water bacteria themselves, but to entirely other causes, chief amongst them inanition, the pathogenic bacteria requiring for their maintenance highly specialized organic nutritive materials absent in the water or present only in insufficient amount.

Wherever saprophytic bacteria endowed with the power of rapid multiplication find the conditions suitable for their growth and multiplication, they naturally crowd out, as it were, the more specialized and more slowly-growing pathogenic bacteria, though the medium offers to the latter otherwise suitable conditions. It is a question of a "survival of the fittest in the struggle for existence." To the same cause are to be ascribed the well-known adverse effects which putrefaction and decomposition exert on pathogenic bacteria. The comparatively rapid disappearance of non-sporing pathogenic bacteria from the dead body, due to the rapid growth of putrefactive bacteria and their chemical products, has been established experimentally.

When I referred to a definite interaction between certain bacteria, I was not referring either to the indirect action which the products, generated in culture media by the growth of one species, are capable of exerting in some instances adversely, in others favourably on the simultaneous or subsequent growth and action of another species, either *in vitro* or *in corpore*, but to a direct influence which one species is capable of effecting on another species simultaneously present—that is, growing symbiotically either in artificial culture or in the animal body. The enhanced influence of streptococcus pyogenes on the virulence of *B. diphtheriae*, as also that of streptococci, proteus vulgaris and other putrefactive microbes on bacillus tuberculosis, may be inferred from the increase in virulence of the two diseases respectively in the noxious presence of the above species. This influence of symbiosis within the animal body of one microbe not necessarily other than saprophyte on a specific parasite, though in some instances shown to be *nil*, is in other instances distinct, in some it is antagonistic, in others enhancing.

From the experimental evidence already gained, it must be obvious that this branch of bacteriology—namely, the study of the effect of symbiosis—offers a fruitful and important field of research, important both in theory and practice. To

mention one consideration only: the greater or lesser susceptibility to infection with a particular specific disease of one person over another is justly considered a complex subject, for it must depend on the mode of contagion, on the virulence of the contagion itself, on the condition of the individual, on the presence or absence of protective substances in—that is, in the vulnerability of the individual—and probably on other at present unknown factors.

Taking a specific instance—for example, the now notorious typhoid oyster banquets at Winchester and at Southampton in November, 1902, investigated by Dr. Bulstrode. A considerable percentage of the consumers of the oysters were taken ill the next day with gastro-enteritis, which obviously was not typhoid, nor could it have been due to the ingested typhoid bacilli. In epidemics of typhoid by infected water such acute illness—namely, transitory gastro-enteritis—is not recorded. The initial acute transitory gastro-enteritis must have been, therefore, due to some cause other than that of *B. typhosus*, which latter, and in a percentage only of these cases, manifested itself in due course—that is, after the usual incubation period of ten to fourteen days. This other cause, producing the acute transitory gastro-enteritis, more abundantly present in the oysters than the *B. typhosus*, is probably to be sought in the simultaneous presence in those oysters of some pathogenic microbes belonging to the group of the *B. enteritidis* of Gaertner. As a matter of fact, in oysters which were taken at a subsequent date but from the same pit from which the above typhoid oysters were derived, I found in a percentage of them distinct evidence of the presence of bacteria belonging to the group of *B. enteritidis* of Gaertner. The ingestion of this microbe, producing the initial transitory gastro-enteritis, may have had an important influence not only in raising the susceptibility *per se* of the affected person towards the typhoid bacillus, but it may have directly been instrumental in enhancing the virulence of this latter. In the animal experiments such an enhancing of the virulence of the typhoid bacillus by the *B. Gaertner* was directly demonstrated. May not such symbiosis be at least one of the factors contributing to the consummation of infection?

Experimentally it has been proved that the symbiosis of *B. pseudo-tuberculosis* has an enhancing influence on the *B. tuberculosis*, and from a paper by Professor Hueppe, who collected the statistics from various observers, it appears that of persons considered to be free from either general or pulmonary tuberculosis there were, nevertheless, discovered, on the *post-mortem* table, in nearly 40 per cent. tubercle bacilli in the bronchial glands, or in one or the other organ, in slight lesions only discoverable on the *post-mortem* table. Is it not conceivable that the absence in these individuals of the other enhancing microbe is the real cause of this immunity to general tuberculosis? Is it not conceivable that the terms "predisposition to consumption" and "greater vulnerability of the tissues to tuberculosis" may include symbiosis of another microbe, which prepares the ground for, and enhances the activity of, the tubercle bacillus? These are questions which experimental pathology will be able to solve, and which, in the interest of practical medicine and of hygiene, are well worthy to be undertaken.

THE "MICROCOCOCCUS RHEUMATICUS": ITS CULTURAL AND OTHER CHARACTERS.

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IN their communication to the BRITISH MEDICAL JOURNAL, January, 1903, Beaton and Ainley Walker described with considerable detail the microscopical and cultural characters of the organism which they called the "micrococcus rheumaticus." Recently I have had the opportunity of repeating their work. My results, as will be seen, are in the main confirmatory, though there are a few points and conclusions in which we differ.

The organisms with which I worked were of two different strains. One obtained from the synovial membrane of a girl with acute rheumatism and recovered from the vegetations of an endocarditis in a rabbit. The second was from a culture very kindly sent to me by Dr. Paine.

The microscopical and cultural characters of the two were practically identical; the only difference noted being that the

coagulation of milk was more rapid and more complete with the organism obtained from Dr. Paine than with the other.

MICROSCOPICAL AND STAINING CHARACTERS.

The organism is a small micrococcus which occurs in the tissues and in cultures in pairs or in short chains. Grown in milk bouillon the chains are more definite, but I have never seen chains containing more than a dozen organisms. In size it is smaller than the ordinary streptococcus, and I have never been able to produce in any media the long chains which one so constantly finds in cultures of the streptococcus pyogenes. Many of the organisms, especially those seen in pairs, are rather oval in shape, and more resemble the pneumococcus than the streptococcus. No capsule could be demonstrated. Degeneration forms are fairly common, the coccus becoming swollen and elongated, but even in cultures of several days' growth the infrequency of degeneration forms as compared with those in a growth of streptococcus pyogenes of a similar period is a very striking feature.

It stains readily with all the ordinary aniline dyes. It retains the stain by Gram and in Weigert's modification of this method.

CULTURAL CHARACTERS.

The media used were all standardized according to Eyre's method to +10.

Bouillon.—In twenty-four hours at 37° C. there was a very slight turbidity in the fluid, with a slight flocculent deposit at the bottom of the tube. In forty-eight hours and still more markedly in three days, the fluid had again become clear, and at the bottom of the tube there was a very distinct deposit. The media became very distinctly acid. There was no formation of indol.

Glycerine Bouillon.—The growth was very slight, and in five days there was a slight flocculent deposit at the bottom of the tube. The fluid remained perfectly clear. The alkalinity was slightly diminished, but no acid reaction was present even after three weeks.

Peptone Solution.—The appearances were very much the same as in bouillon, but the acidity was more marked.

Gelatine (stab).—In two days minute colonies were made out along the needle track—there was no extension of growth on the surface. In five days the growth was slightly more apparent, but at later periods there appeared to be very little increased growth. There was no liquefaction of the media and no gas production.

Gelatine (streak).—In twenty-four hours there were minute whitish colonies. At later periods there was fusion of the colonies at places, but in the main the colonies remained small and discrete, even after three weeks. There was no liquefaction.

Gelatine Plates.—The colonies were small, rounded, and distinctly granular. The edges were quite regular. They attained their maximum size—that of a small pin's head—in five days. There was no liquefaction.

Agar (streak).—Small semitransparent colonies, slightly raised above the surface. There was very slight spread. The appearance in five days was not much altered from the appearance got in twenty-four hours. The growth in agar was rather more abundant at 20° C. than at 37° C.

Deep Agar.—There was no growth.

Blood Agar.—This is one of the most satisfactory media. In twenty-four hours there are minute whitish colonies, slightly raised above the surface. In forty-eight hours the colonies are slightly larger, and at places there may be fusion, giving rise to a uniform mass of growth. However, even after several weeks, at the edges, the colonies are still quite discrete. On this medium the growth gradually produces an alteration in the red blood pigment, producing a rusty-brown or chocolate colour. Not only does the organism grow well on this medium, but it has a very long existence. The culture Dr. Paine sent me was subcultured from a tube after eight and a half months, and I have subcultured from a blood agar tube after six months.

Blood Serum.—On human serum after twenty-four hours there are minute, small, slightly raised colonies. These, however, spread very considerably, and in three days there is a uniform whitish streak on the surface of the medium.

Milk.—In twenty-four hours—no acidity, no coagulation. In forty-eight hours—acid reaction, no coagulation. In three days—acid reaction, coagulation.

Milk rendered distinctly alkaline to litmus paper gave similar results, the acidity being quite marked in forty-eight hours.

Litmus Milk distinctly Blue.—Began to assume a lighter blue in twenty-four hours; in forty-eight hours it was a distinct pinkish tint, and in three days it was a rose pink and was coagulated.

Milk with Bouillon slightly Acidified with Lactic Acid.—With the organism got from Dr. Paine there was distinct coagulation in twenty-four hours. With the organism isolated by me the coagulation was only slight in twenty-four hours but was quite marked in forty-eight hours.

Potato.—No visible growth.

Anaerobic Cultures.

Deep Glucose Agar.—There was a slight growth along the needle track; no surface spread. The medium seemed to be unfavourable.

Formate Bouillon.—No growth was obtained.

RESULTS OF INOCULATION.

My results have been absolutely confirmatory of those pub-

lished by Paine and Poynton and others. These have already been published elsewhere,¹ and I need only say that intravenous injections in animals produces endocarditis, polyarthritis, and chorea. The polyarthritis usually develops in about three days after the inoculation. With subcutaneous injections, even in large doses, I have not seen any suppuration, but Beaton and Walker have twice seen the formation of a subcutaneous abscess, and have produced a suppurative peritonitis. They do not, however, state whether or not from the pus they recovered the micrococcus in pure culture.

It will be seen from the above that, except in some minor points, my results correspond with those got by Beaton and Walker.

As to whether this organism is to be classed as a streptococcus or not is a matter of very little practical importance. If we use the term in its generic sense, then no fault can be found with it, but, fortunately or unfortunately, the term streptococcus has to most people a specific meaning, and the organism which we find in acute rheumatism produces by inoculation results which are entirely different from those produced by an inoculation of the 'streptococcus' in its ordinarily accepted sense. Therefore it seems to me it is essential to designate this organism by a special term, such as the "micrococcus rheumaticus," as proposed by Beaton and Walker. This seems all the more important since it has been maintained that this micrococcus which we have isolated is not causal of acute rheumatism, but is probably a streptococcus causal of the terminal infection.

Besides, there are points in the cultural characters and vitality of the organism which seem to distinguish it as absolutely from the streptococci as the pneumococci are distinguished from them. The growth on gelatine appears earlier, and is more abundant in the micrococcus rheumaticus. Its more abundant and earlier growth on ordinary agar at 20° C. than at 37° C. is quite unlike what is seen with the streptococci. The very marked acid production in bouillon and in milk, the early coagulation of the milk, and the length of time the organism lives in suitable culture media are features which distinguish it absolutely from the streptococcus.

The results of inoculation in animals are, as I have already indicated, entirely different. Even if we admit that the organism can produce suppuration, though I feel considerable doubt on this point, yet ordinarily it does not give rise to pus, but causes in rabbits non-suppurative polyarthritis, endocarditis, etc. These conditions have not been produced by inoculation of what we ordinarily call streptococci. We do not claim that because this organism produces endocarditis therefore it is the causal organism of morbus cordis. What, however, we do claim, is that it can be isolated from cases of typical acute rheumatism; that it can be grown outside the body, there showing characters which are in some respects specific; that in inoculation in animals it produces a combination of lesions which are similar to those of acute rheumatism in the human subject sometimes specially affecting the joints, sometimes specially the heart, sometimes producing chorea, sometimes producing a combination of these conditions, and that from these lesions the organism can be recovered in pure culture.

On these grounds there seems but one conclusion, that this "micrococcus rheumaticus" is a special organism, and is causal in acute rheumatism.

REFERENCE.

¹ *Journal of Pathology and Bacteriology*, March, 1904.

AFEBRILE ENTERIC FEVER.

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THE following notes of a case of this variety of enteric fever which was complicated by thrombosis of the left femoral vein may be of interest. The patient was a young woman, aged 20, who was nursing her married sister during a sharp attack of enteric fever. I saw her on the fourth day of illness, when she complained of headache and pains in her limbs, loss of appetite, and lassitude. There was also slight abdominal pain. On examination her tongue was moist and coated, pulse 90, and temperature 98.4° F. Her abdomen was slightly distended and tender. The spleen was not markedly enlarged, and there were no rose spots. The mucous membranes of the lips and eyelids were well coloured. The bowels were constipated. The heart and lungs were normal. A provisional diagnosis was made that the patient was probably suffering