ON THE RESULTS OF CULTURES MADE WITH MATERIAL OBTAINED FROM THE JOINTS IN TWENTY-EIGHT CASES OF RHEUMATIC FEVER.¹

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In a previous communication² I produced arguments in favour of the view that, apart from well-recognized diseases, like gout, gonorrhoea and septicæmias, the symptom group commonly named "rheumatic fever" may be due to a variety of different causes. In the same paper I reported the complete failure of my attempts to isolate the Streptococcus rheumaticus of Poynton and Paine from the joint fluid of patients suffering from "rheumatic fever." In the course of these attempts I came across other organisms which I have thought it might be of interest to put on record. The material was usually taken from the knee-joint as soon as possible after its appearance and, as a rule, it was mixed with sterile citrate of soda solution (1 per cent) in order to delay clotting during the subsequent investigation; at the same time smears were made and stained by Leishman's stain, by Gram's method, by iron haematoxylin and in other ways, while many specimens were examined under dark ground illumination; this last, however, without any result. Aerobic and anaerobic cultures were made on many different media, varying these as I found that one or other medium failed to give results; in all cases among the media tried were peptone broth, milk broth, and blood agar, in order to ensure that quite simple organisms such as the S. rheumaticus were not overlooked.

The cases in which positive results were obtained were as follows:

1) A small Gram-negative diplococcus was seen inside one or two of the leucocytes of an exudate; from its position and staining properties one might have thought that it was a gonococcus, but it was much smaller than a gonococcus, about half the usual size, and quite round. In growth on blood agar it gave very fine colonies resembling those of a streptococcus; the cocci on this medium were very small and round, and they showed no tendency

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to the production of involution forms; when cultures were made in peptone serum water containing glucose, maltose, or lactose, none of these sugars were fermented. The culture died out after the second subculture, and I was unable to pursue it further. Clinically, the condition of the knee suggested gonorrhoeal arthritis, though the patient had no history of gonorrhoea and he recovered very rapidly indeed under a vaccine of his own germ. It is quite possible that this germ was an unusual form of gonococcus, though its appearance and cultural characters were against this view; while the absence of a history of gonorrhoea and the very rapid recovery also supported the idea that the organism was not a gonococcus.

(2) A patient (Private S.) had what appeared to be a typical attack of acute rheumatism without heart lesions; among the stained slides of the fluid from his left knee one, which had been stained by Leishman's stain, showed a small group of extra-cellular cocci. The citrated joint fluid, after an incubation period of six days, showed a few flocculi on the surface; these were found to be composed of masses of Gram-staining cocci with flattened sides, mostly in pairs, but occasionally in fours. Sub-culture on agar gave a dull white, very sticky growth of cocci arranged in tetrads and in pairs, growth in broth was diffuse and in this medium the arrangement of the cocci in tetrads was well marked. Anaerobic cultures in broth grew feebly after four days' incubation. The patient's opsonic index to the germ was found to be 0.27. He recovered rapidly from this attack, being ill only about four days; but a fortnight later he had a return of pain and swelling, this time in the right knee, and cultures from this joint gave a growth of the same organism as had been obtained from the left knee. This relapse lasted only three or four days, during which his opsonic index to the original culture was found to be 0.74. He was eventually invalided on account of repeated short attacks in other joints. Clinically, the onset resembled that of a moderately acute attack of rheumatic fever, and the patient stated that he had had a previous illness of the same kind some two years before. It may be added that in view of the clinical appearances salicylates were administered, but they seemed to have no effect in staving off the recurring attacks of arthritis. This case might be classed as a tetragenus septicæmia; it was, however, extremely mild for a septicemia, the patient was never very ill, and his invaliding was due more to the frequency of his relapses than to the severity of the symptoms.

(3) From another case I obtained a culture of a germ similar to
that found in Private S.'s joints. This man had been ill for three days before admission to hospital; he had slight fever only and had arthritis in both knees. The heart was not affected. This was the second attack of the same kind from which the patient had suffered, it only lasted for a very short time, and the man left hospital at the end of ten days, so that I missed the opportunity of taking his opsonic index to the germ, which did not develop in the joint fluid till the eleventh day of incubation. The delay in growth was probably due to the action of a small amount of sodium taurocholate which I had added to the joint fluid with a view to inhibit its bactericidal action. It was noted, however, that, compared with its development in other media, there was a considerably slower growth of this germ in joint exudates. This seems to be the case with other germs also, and joint fluid appears to be a poor culture medium for most bacteria.

(4) In two cases I found streptococci in joint exudates, once microscopically only and once after culture. I have already referred to these cases in a previous paper. The case in which the streptococci were found on microscopical examination of the joint fluid was one of moderately severe polyarthritis, but the heart escaped and the patient left hospital fit for duty after a month's stay. The organisms were only found after a very prolonged search, such as I gave to all smear specimens, and I only found two short chains. Cultures of the same fluid were sterile. The case from which I obtained a culture was that of a soldier who was admitted in the first place for fever of an indefinite type, which the officer in charge of the case labelled "influenza." He had been in hospital three or four days before he developed multiple arthritis with pericarditis and valvulitis. He recovered from the clinical symptoms but was left with a damaged heart, and was eventually invalided on this account. In my previous paper I gave reasons for thinking that the streptococcus which I isolated from this case was not identical with that described by Poynton, Paine, Beattie and others.

(5) Lastly, I would refer, with all reserve, to an organism which I have found microscopically under varying conditions and in attempts at culture from six joint fluids and one pleural exudate. All the cases were apparently undoubted rheumatic fever, and in three of them there were heart lesions. These were especially marked in the case from which the pleural exudate was obtained; this patient had multiple transient arthritis, pericarditis and endocarditis, while both pleura were inflamed at one time or another. He recovered from the acute symptoms, but was left with a badly
crippled heart. The organism in question is a rod somewhat resembling the diphtheria bacillus in shape, it is generally slightly curved, with rounded ends, and it stains in a beaded fashion; it is usually decolorized by Gram's method, but occasionally, when alcohol has been somewhat sparingly used, a few of the rods may retain the stain. In size it varies from that of a short to that of a medium diphtheria bacillus, and it is almost always found in clumps of five or six bacilli arranged in the same fashion as diphtheria bacilli. In one case I found a small clump of these organisms in a smear from a flake in the joint fluid; they were arranged as described above; there was just one fairly large clump from which a few individuals had apparently broken away when the smear was made. They were somewhat shorter than those found in cultures and, as the film in which they were found happened to be stained by Leishman's stain, I am unable to say whether, in their original condition, they retained Gram's stain or not. In a culture in hydrocele water, peptone, dextrose and glycerine, from the same exudate, the organisms increased for about ten days, apparently growing in the clot at the bottom of the tube; subcultures failed. Seven months later this same patient returned to hospital with a mild attack of "rheumatism," accompanied by inflammation in the tendon sheaths in front of the ankle. I was able to get a small quantity of fluid from the tendon sheaths and again obtained a scanty growth in the clot which formed at the bottom of a tube of peptone broth; subcultures again failed. In a second case the patient was admitted with a sore throat, so severe that quinsy was diagnosed, and an incision was made without, however, finding any pus. The culture from the throat consisted almost entirely of streptococci. He developed an acute arthritis in one knee which, in view of the throat condition, I was inclined to suspect was streptococcal in origin. I failed to obtain any growth of streptococci from the fluid in the joint, but I found, in a specimen taken from the surface of an agar slope, one clump of the bacteria which I have described. I am inclined to think that the germs had not grown, but were simply lying on the surface of the agar slope, which had been inoculated with a fairly large quantity of the exudate. Other cultures from this case failed. This patient passed through a mild attack of "rheumatic fever," the joints affected being the knees, wrists, fingers and shoulders, but the heart was not involved. He had a history of an attack of rheumatic fever four years previously, which lasted two months, and two years later he had a relapse which lasted a week. He recovered
completely from the present attack in twelve days. I have found the same organism in the following cultures taken from a pleural exudate and from four joint effusions:

(a) An aerobic culture on Loeffler's serum which had been incubating for a month, and in a subculture from this into a hydrocele water medium containing haemoglobin and glycerine, in which it was found after 72 hours.

(b) On a blood agar slope after a month's incubation, in a subculture from this into the hydrocele water medium, and in a blood broth tube after a month's incubation.

(c) In cultures from two joints and one pleural exudate in a hydrocele water medium containing dextrose, peptone and glycerine. The cultures had been incubated from fourteen to seventeen days, aerobically, and it was in them that I got the nearest approach to a real growth, but even in these the organisms were very few in number and I failed to get subcultures from them.

This communication is, of course, only preliminary in character; I think I have definitely excluded the possibility of the organisms last described being in the dyes or in the media; it is impossible, however, to say more about them until a culture material is found on which they will grow properly. I thought, however, that it might be useful to put the findings on record, since circumstances render it probable that shortly I shall not be in a position to pursue the subject myself. In any case the results of the whole series seem to lend support to my proposition that the term "rheumatic fever" is probably applied to a group of diseases due to a variety of causes rather than to a single disease owning a single causation.