Conclusion.

From the cases investigated it was to be concluded that, whilst the injection of subcutaneous oxygen in pneumonia is without effect on the death rate, there is an immediate improvement in symptoms, with a curtailment of fever. The actual course of the disease itself is shortened by six or seven days. The reduction in the febrile period, and in the course of the disease, is more definite in broncho-pneumonia.

The definite alleviation of the toxæmia is not peculiar to pneumonia and seems quite apart from any specific action on the lung tissue *per se*. The toxæmia in a case of severe diphtheria was greatly relieved after injection of oxygen.

As a whole the pathological processes are apparently expedited. Possibly the stages of hepatization are hastened by an early formation of hydrogen peroxide in the pulmonary tissues.²

To the medical superintendent, Dr. J. D'Ewart, my thanks are due for permission to make use of the cases investigated.

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BACTERIOLOGY OF THE TONSILS IN RELATION TO RHEUMATISM IN CHILDREN.*

BY

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It has often been suggested that the infective agent in rheumatism, in regard to which streptococci have more often been incriminated than any other organism, is to be found in the tonsil. Whether it exerts its toxic influence from there, or whether it enters the body by that portal, and is then disseminated to other parts, has not yet been decided. If, however, specific streptococci are to blame, and their *locus* of rest or passage is in the tonsil, one would expect to find some difference in the streptococcal flora of the tonsil in rheumatic and non-rheumatic cases. To determine this point a number of rheumatic and non-rheumatic tonsils were investigated. The rheumatic tonsils came from out-patients with articular rheumatism, chorea, and heart conditions, all of whom had some degree of enlargement or sepsis in their tonsils. The non-rheumatic patients were those in whom the tonsils were enlarged or septic, and from whom no history of any rheumatic manifestation could be elicited. In each case an endeavour was made to isolate all the varieties of streptococci present in each tonsil so that the types might be compared.

Analysis of Streptococci from the Tonsils of Rheumatic and Non-Rheumatic Children.

	Rheumatic.	Non-Rheumatic.
Total tonsils	50	48
Total streptococci	190	157
Streptococci per tonsil	3.80	3.27
Haemolytic	14.1%	14.03%
Non-haemolytic	85.9%	85.97%
Green	46.3%	45.86%
Non-green	51.0%	53.51%
Doubtful	2.7%	0.63%
Mitis	44.2%	37.0%
Salivarius	26.3%	28.0%
Faecalis	4.2%	3.18%
Pyogenes	12.6%	11.5%
Other streptococci	12.7%	20.0%

From this table it will be seen that the streptococci from the rheumatic tonsils do not differ materially, as regards the characteristics investigated, from those of the non-rheumatic. There is at present no really satisfactory classification of non-haemolytic streptococci, and this makes it difficult to draw a hard-and-fast line between varieties. Classification by means of sugar fermentation is not much to be relied on, and therefore, though we put in comparative differences in this particular, we fully realize its limitations. As, however, the conditions were always identical for cultures from the rheumatic and non-rheumatic series, even these variable tests should be of some assistance.

* The investigations upon which this paper is based were carried out by one of us (R. A. M.) during tenure of the Ida Sebag-Montefiore Research Fellowship at the Hospital for Sick Children.

The appearance of the culture plates showed no marked difference, and even on Crowe's medium,¹ which shows the minutest changes in colony appearance, we were unable to tell a rheumatic from a non-rheumatic plate. As regards the number of streptococci isolated per tonsil, this is rather low, owing to the fact that in one case in each series there were no streptococci found, in one or two almost a pure growth of one variety, and also that in a few cases the organisms died before any of their reactions could be carried out. This, however, was the same for both series.

Most observers—Poynton and Paine,² Small,³ and Birkhaug,⁴ to mention only a few—who have described "rheumatic streptococci," have placed them in the non-haemolytic and non-green-producing group. Without trying to isolate any of these recognized varieties, it might be expected that rheumatic tonsils would show a higher percentage of inert streptococci. There was little difference in our series, the rheumatic being slightly lower. This is in agreement with the work of Hitchcock,⁶ who found no greater incidence of inert streptococci in rheumatic fever throats.

Discussion.

For many years tonsillectomy in rheumatism has been advocated. Poynton and Paine (1900)² demonstrated their diplococcus in rheumatic tonsils, and in 1913 Poynton⁷ says that unhealthy tonsils are very frequent in rheumatism. Again in 1925⁸ he says that he believes successful removal of unhealthy tonsils to be a valuable prophylactic step in rheumatism when viewed on broad lines. Schichold (1910)⁹ claimed that removal of the tonsils cures the attack and prevents recurrence, and Hutchison (1911)¹⁰ upholds his view, if not quite so emphatically. Pybus (1915),¹¹ Morris (1916),¹² and Langmead (1920)¹³ all consider that tonsillectomy is advantageous, and in more recent years the British Medical Association report (1926),¹⁴ Robey and Freedman (1927),¹⁵ Kaiser (1927 and 1929),¹⁶ and Wilkinson and Ogilvie (1928)¹⁷ all recommend tonsillectomy.

From the observations of the above-named authors it would seem that rheumatic infection has a close connexion with the tonsil, and certainly any workers who have described definite streptococci as possible causes of rheumatism have been able to isolate the organisms from the tonsil. A number of different varieties are described, none of which seems definitely established, or is regularly isolated from every case. Birkhaug⁵ made a considerable advance when he succeeded in preparing a soluble exotoxin from his non-methaemoglobin-forming streptococcus, and he published some interesting results of skin tests which gave a much higher incidence of positives in rheumatic than in non-rheumatic children. This finding has not, however, been definitely corroborated in this country. Indeed, Mackie and McLachlan (1927)¹⁸ state that "the ability to produce toxic filtrates seems to rest in some peculiarity of this type of micro-organism" (streptococci), "rather than in a specific etiological role in respect of rheumatic fever."

To review briefly some of the results of earlier experiments, Cole, in 1904,¹⁹ produced arthritis and endocarditis in rabbits by inoculation of streptococci from various sources, not necessarily rheumatic; and in 1913 Harrison²⁰ states that inoculation of "non-rheumatic" streptococci will produce arthritis, at times indistinguishable from that produced by *Streptococcus rheumaticus* (Poynton and Paine). Faber in 1915²¹ produced a sensitization by giving more than one injection, and obtained arthritis in animals with a comparatively non-pathogenic green-producing streptococcus. Rosenow (1914)²² isolated three different types of streptococci from joint fluids in fourteen rheumatic cases. Swift and Kinsella²³ showed in 1917 that there were considerable immunological and cultural differences in streptococci isolated from their series of rheumatic fever cases. Clawson (1925)²⁴ isolated green-producing streptococci from twenty cases of well-defined acute rheumatic fever, and Andrewes, Derick, and Swift (1926)²⁵ found haemolytic, non-haemolytic, and *viridans* streptococci in acute throats in association with rheumatic fever. The researches of these workers show a considerable diversity of possible causal agents in rheumatism, and they have isolated in most cases streptococci which are to be found

normally as saprophytes (so-called) in various parts of the body. It is difficult, on the supposition of a specific bacterial cause of rheumatism, to correlate this conflicting work, and indeed it seems reasonable to suppose that the soil is more important than the seed, and that any streptococcus present in a given patient may, in suitable circumstances, become the infecting agent. What these circumstances are has not yet been determined, but the sensitization by small doses of streptococcal toxin over long periods is a point of importance. Swift, Wilson, and Todd²⁶ suggest that patients may be made more sensitive to toxins by repeated skin test doses, and also that hypersensitivity seems to increase with age. They also think that type specificity does not exist. Swift, Derick, and Hitchcock²⁷ have gone a step further in this direction. They produced a hypersensitive state in rabbits, when a comparatively small dose of streptococci would produce a disproportionately severe result. Their conclusions represent an interesting hypothesis for the etiology of rheumatic fever.

"The theory is advanced that the pathogenesis of rheumatic fever can be explained by the existence in certain individuals of a condition of hypersensitiveness (allergy or hyperergy) to streptococci, resulting from repeated low-grade infections or from the persistence of foci of infection in the body. When under suitable circumstances streptococci or their products are disseminated to the tissues, these tissues over-react and the characteristic picture of the disease results. When, on the other hand, a state of immunity exists" (which they say may be developed by different dosage among other things) "the dissemination of streptococci results in a minimum of injury to the tissues, and the characteristic phenomena of the disease fail to appear."

To return to the tonsils, they may well be one of the foci in which these "repeated low-grade infections" occur, which would account for the undoubted advantages to be obtained from tonsillectomy in rheumatism. If, as has been suggested, the type of streptococcus is unimportant, then the fact of there being little difference between the rheumatic and non-rheumatic tonsils as regards their streptococcal flora is not of much importance, and cannot be used as an argument against tonsillectomy, as *prima facie* it might seem to be.

Conclusions.

1. Streptococci isolated from rheumatic tonsils do not differ materially from those isolated from non-rheumatic tonsils.

2. This absence of difference fits in with the theory that there is no specific streptococcus which is the cause of rheumatism, but that the condition is due to a hypersensitiveness resulting from repeated small doses of toxin.

3. The tonsil is probably one of the foci from which these toxins may be absorbed.

4. For this reason, in spite of the lack of difference mentioned above, tonsillectomy in rheumatic cases is probably a valuable prophylactic and therapeutic measure.

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AN UNUSUAL INFECTIVE CONDITION OF THE BLADDER.

BY

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THE case of cystitis here recorded, in which an atypical bacillus was apparently the infecting organism, is of considerable bacteriological interest. The clinical details were as follows.

The patient, a man aged 65, had an acute attack of cystitis about ten years ago; since then he had been troubled with a mild degree of frequency of micturition at various times; he continued to pass a very turbid urine, and a diagnosis of prostatic abscess had been made. He reported that his urine had been examined bacteriologically on several occasions during the past ten years, and it had always contained much pus and, as he stated, *B. coli*. He was referred to me for the possibility of vaccine treatment.

Examination of the urine showed numerous pus cells and non-motile bacilli, which in stained films proved to be Gram-negative. Cultures on all the usual media were sterile. These results were repeatedly obtained, whether attempts were made to grow the organism aerobically or anaerobically. Finally, after numerous attempts, a small growth was obtained on agar to which human oxalated blood had been added. After several subcultures on this medium it became possible to grow it fairly readily on ordinary agar, and its cultural characteristics were further investigated, with the following results: gelatin was not liquefied; indol was produced in broth in overnight cultures; litmus milk was turned acid but was not clotted. When the organism was grown in sugar media—dextrose, maltose, dulcitol, mannite, lactose, and cane sugar—they became acid, but no gas was produced.

At the time the organism was thought to be *B. coli anaerogenes*. Later on my attention was called to a paper by Bamforth,¹ in which an organism with very similar cultural characteristics, which was associated with a small outbreak of dysentery, is described, and related to the bacilli described by Sonne. Later still Nabarro's observations² on the relation between *B. coli anaerogenes* and Sonne's bacillus were noted; accordingly, further observations were made on my cultures. On plating the agar culture it was found that the colonies could be divided into rough and smooth forms. On litmus lactose agar plates both red and blue colonies were noted. On further forty-eight to fifty-two hours' incubation the colourless colonies showed central red papillae. The red colonies were thus coloured in twenty-four hours, and, as Nabarro points out, are not to be distinguished on plates from *B. coli*.

Both Dr. Bamforth and Dr. Nabarro very kindly sent me some of their antiserum, which they had prepared from their bacilli. Considerable difficulty was experienced in making stable emulsions, since, as White³ points out, spontaneous agglutination is very apt to occur in rough forms of this group, and therefore emulsions in distilled water were used. In each case agglutination took place up to the end point of the two serums employed. Both were pooled serums, and were used on agar subcultures of mixed types of colonies.

The interesting features of this case are the unusual infecting organism and the curious fact that many times no growth could be obtained, although the urine was swarming with bacilli. No lysis of the cultures subsequently obtained was ever noted.

I might mention that recently I saw a similar case. The patient had cystitis, and microscopical examination showed very numerous pus cells and masses of Gram-negative bacilli, but no growth could be obtained; I was informed that a previous examination had given a similar result. Unfortunately I had no opportunity of examining this second case again.

At the present time the first patient's symptoms remain the same in spite of all treatment. The urine still contains numerous pus cells and masses of Gram-negative non-motile bacilli. The curious fact that has arisen now is that the bacilli described previously can be isolated without difficulty, so that one is uncertain whether the organism now isolated with ease is the same bacillus noted in every examination, but which could not be obtained by culture in many of the previous examinations. Morphologically it appears to be exactly similar. The patient's serum does not agglutinate this organism obtained from his urine.

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