REVIEW OF THE BACTERIOLOGY OF ACUTE
ARTICULAR RHEUMATISM.*

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The view that regards acute rheumatism as an infectious disease has now gained such general acceptance and has so completely superseded the older "chemical" and "neurotrophic" theories as to its nature that time need not be taken to review the facts which have led to such a general belief.

With the growth of this idea of the infectious nature of the disease it was but natural that a search for the infectious agent should begin and but natural also, considering the importance of the disease, that the search should be both eager and persistent.

To trace in detail the history of this search for the microbic cause would take us far beyond the scope of this brief paper. A great amount of work on this subject has been done during the past ten years and we can hope only to review briefly the results of this work.

As was perhaps to be expected, these results are far from being uniform and consistent. Different investigators have reached very different and conflicting conclusions, which, however, may be grouped under the following heads: 1. That acute rheumatism is not caused by any one organism, but is a particular reaction to various infections. 2. That the disease is only an attenuated pyemia resulting from infection by the common pyogenic streptococci and staphylococci. 3. That the disease is due to a specific anaërobic bacillus. 4. That it is due to a specific diplococcus or streptococcus. 5. That acute rheumatism is a specific infectious disease whose microbic cause has not yet been discovered. Thus it will be seen that there is disagreement not only as to the special organism causing the disease, but also as to whether it is a definite and specific disease at all.

IS ACUTE RHEUMATISM A SPECIFIC DISEASE?

Obviously the first point to be decided, if possible, is whether acute rheumatism is a distinct and specific disease. To most of us, I fancy, the answer will seem so simple and clear as hardly to warrant a serious discussion of the question, and it will come to us as something of a shock to find so sound a man as Chvostek¹ willing to make such a statement as the following:

A separation of the so-called genuine articular rheumatism from the pseudo-rheumatic or rheumatoid affections is not possible. The small group of cases in which we do not know the exciting agent and its portal of entrance, and which for this reason we class together as a single disease, is constantly growing smaller, and the time may not be distant when acute articular rheumatism, as a distinct disease, will find its well-deserved end.

The view that acute rheumatism is not a disease *sui generis* has been advocated also by Birch-Hirschfeld,² Sahli,³ Singer,⁴ Menzer⁵ and others. Birch-Hirschfeld, Sahli and Singer are convinced that the disease is only a modified and attenuated pyemia caused by the common pyogenic cocci. Singer especially has been aggressive in upholding this idea and insists that further search for a specific agent is merely a waste of time. Menzer re-

gards the disease as the result of infection through the tonsils by the ordinary parasites of the mouth (chiefly streptococci), which for some reason have become pathogenic.

Against the view of these few investigators must be set the almost unanimous belief in England and America and that of the great majority of observers on the Continent that rheumatic fever, not only in its clinical picture, but in its pathogenesis as well, is a single and specific disease. The frequency of the disease; its seasonal relationship and epidemic character; its distinct and characteristic clinical course; the frequency and specificity of its visceral and other abarticular manifestations; the tendency to complete recovery, as well as the proneness to subsequent attacks; its specific reaction to the salicylates—all these and many other facts point toward the view that rheumatic fever is a distinct clinical and pathologic entity and not merely an atypical form of sepsis of heterogeneous origin.

Singer bases his belief chiefly on the postmortem bacteriologic findings in cases of rheumatism or rheumatic chorea in which he found now streptococci, now staphylococci, in the blood and tissues. The very fact that different organisms were recovered from different cases would suggest strongly that he must have been dealing with cases in which there had been a secondary or terminal infection such as is so commonly found in various other infectious diseases. The idea that acute rheumatism is only a clinical syndrome which may be produced by the action of any of the ordinary pyogenic cocci can, it seems to me, be dismissed from further consideration.

HAS ITS MICROBIC CAUSE BEEN FOUND?

Assuming, then, that it is a specific disease, we have now to consider whether or not its microbic cause has been found. In 1897 Achalme⁶ described a large, spore-bearing anaërobic bacillus which he found in the postmortem examination of cases of rheumatism and which he believed to be its cause. This view was endorsed by Thiroloix and others in France. Further investigations, however, have demonstrated that this was almost certainly a contaminating organism and Achalme's claims have been almost universally rejected.

The assertion that the bacterial cause of acute rheumatism is a specific diplococcus or streptococcus can not be dismissed so readily. As early as 1894 von Leyden⁷ found in the inflamed endocardium of several cases of rheumatism a fine diplococcus. A similar diplococcus was found by Triboulet⁸ and others in France. In 1899 Wassermann,⁹ in a fatal case of post-rheumatic chorea recovered from the heart blood, from the heart valves and from the brain a fine streptococcus which grew with difficulty, but which in a series of eighty rabbits regularly produced joint inflammations.

The Work of Fritz Meyer.—This work was soon followed by that of Fritz Meyer.¹⁰ Meyer examined in some thirty cases of rheumatism, during life, the blood and joint contents with absolutely negative results. As a result of these negative findings he was led to examine the inflamed tonsils in cases of rheumatism with the idea that the organism might be found only there and that the joint symptoms might be caused by its toxin alone. After making broth cultures of the mixed growth of bacteria found in such inflamed tonsils he injected this

* Read in the Section on Practice of Medicine of the American Medical Association, at the Fifty-seventh Annual Session, June, 1906.

1. Wien. klin. Wochschr., 1895, p. 469.

2. Verhand. VII Congress. Inn. Med., 1888, p. 346.

3. Deutsch Arch. f. Klin. Med., 1892, vol. II, p. 451.

4. Verhand. XIX Congress. Inn. Med., 1901, p. 441.

5. "Die Aetiologie d. Acute Gelenksrheumatismus," Berlin, 1902.

6. Ann. de l'Inst. Pasteur, 1897, p. 845.

7. Deutsch. med. Wochschr., 1894, p. 913.

8. Compt. rend. de la Soc. de Biol., 1898, vol. V, p. 214.

9. Berliner klin. Wochschr., 1899, No. 29, p. 638.

10. Ztschr. f. klin. Med., 1902, vol. XLVI, p. 311.

culture intravenously into rabbits, and in the exudate of the inflamed joints which resulted he found only one kind, a diplococcus, and this only in small quantities.

In this way he isolated the same organism from the throats of 25 cases of rheumatism. This diplococcus produced in rabbits very characteristic joint inflammations, in which the lesions were confined solely to the synovial membrane. The organisms could be found in the mononuclear leucocytes and in the endothelial cells, but not in the blood nor in the serous effusions of the joints. On the other hand, if he injected the ordinary streptococci and staphylococci he produced much more severe and destructive lesions of the joints and the organism could always be recovered from the blood. In another series of rabbits he injected the specific diplococci and some staphylococci together, and in a few days the animal showed in the blood only the staphylococci and in the joints only the diplococci. He then sought to determine if this organism possessed any special tendency to excite endocarditis, and in a series of 100 rabbits, without previously injuring the heart valves, he produced endocarditis twenty-one times. In these the blood, and sometimes also the valve vegetations, were sterile. In a control series of 100 rabbits, using other bacteria, he produced endocarditis only twice. Meyer's work impresses one as careful and thorough and, because of the large number of control experiments, seems entitled to serious consideration.

The Work of Poynton and Paine.—During the past five years the idea that a special diplococcus might be the exciting cause of rheumatism has received considerable support from the work of Poynton and Paine¹¹ and their followers in England. The results of their work is briefly as follows:

In 32 cases of acute rheumatism they have isolated a diplococcus which they believe to have specific characteristics and to be the cause of rheumatism. They have recovered the organism in culture from the heart blood after death, from fragments of the valve granulations, from the throats of rheumatic patients, from the urine in rheumatic pericarditis and three times from the circulating blood. They have demonstrated the diplococcus in tissue from the heart valves, pericardium, tonsils, pleura and from a subcutaneous fibrous nodule. Inoculated into animals the organism produces polyarthritis, endocarditis, bursitis and teno-synovitis. Moreover, in four fatal cases of rheumatism, in three of which there was chorea at the time of death, they isolated and cultivated the diplococcus from the cerebrospinal fluid; three times in chorea they demonstrated the organism in the cerebral pia mater and once in the brain. They are inclined to believe that rheumatic chorea is due to a slight meningo-encephalitis caused by the local action of the specific diplococcus. Poynton and Paine emphasize the fact that the diplococcus is not to be found in the circulating blood nor in the joint effusions of ordinary cases of rheumatism. It is only in the very severe and fatal cases that it can be readily discovered. In the joints the organism is found in the areolar tissue beneath the synovial membrane, but, because of the phagocytic action of the cells lining the membrane, it is not usually to be found in the joint fluid. They believe that, while there is no single specific test by which the organism can be distinguished from the ordinary streptococci, it nevertheless possesses a number of qualities which together differentiate it from them. These features are

briefly: its minute size, its greater tendency to grow in pairs, its feeble retention of Gram's stain, its greater resistance to drying, its earlier and greater production of acid, its ability to grow readily in filtered cultures of *Streptococcus pyogenes* (Marmorek's test), and, finally, its more constant tendency to produce polyarthritis and endocarditis in rabbits, its low grade of virulence and its freedom from the production of pyemic abscesses. They believe their diplococcus to be identical with the diplococcus of Triboulet and Meyer and the streptococcus of Wassermann and to be the specific agent in the causation of rheumatic fever, and they suggest for it the name *Diplococcus rheumaticus*.

Their work has been supported by that of a number of other observers in England. Beaton and Walker¹² isolated a similar organism in 15 cases of rheumatism, chorea and rheumatic endocarditis. Walker and Ryffel¹³ found that this diplococcus had a hemolytic action greater and more rapid than that of any streptococcus they examined and suggest that the rapid development of anemia in rheumatism may find its explanation here. They also showed that the organism was peculiar in that it produced relatively large amounts of formic acid, and this acid was present in considerable amounts in the urine of those suffering from rheumatism. Shaw¹⁴ procured from Poynton, Walker and Wassermann cultures of their respective organisms and, after studying them culturally and experimentally, concludes that all three organisms are identical. All of them produced in rabbits and monkeys arthritis, pericarditis, endocarditis and myocarditis. He believes that this organism is the causal agent in rheumatism. Beattie,¹⁵ who also confirmed Poynton and Paine's work, believes that he has produced in rabbits chorea as well as polyarthritis and endocarditis.

In this country Lewis and Longcope¹⁶ report the finding of a streptococcus in the blood, during life, of a fatal case of rheumatism, endocarditis and chorea, which in rabbits produced constantly a very characteristic polyarthritis and which they believe to be identical with the coccus described by Wassermann, Meyer and Poynton and Paine.

Whether the bacterium under discussion should properly be classed as a diplococcus or as a streptococcus is of much less practical importance than is the question whether the cocci described by Triboulet, Wassermann, Meyer, Poynton and Payne and others are one and the same organism. While a positive answer to this question is not possible, it may be said that the morphologic and cultural features agree very well in the main; that the results of animal inoculation are surprisingly consistent and uniform and that the writers themselves seem to be in very general agreement as to the identity and unity of these organisms.

Arguments of Opponents.—Turning now for a moment to those who believe that the infective agent of rheumatism has not yet been found, it must be said that to this number belong the great majority of those who have carefully investigated the subject. The arguments against the claims of the *Diplococcus rheumaticus* are chiefly four:

1. That many careful investigators (Pribram,¹⁷ Phil-

12. Brit. Med. Jour., 1903, vol. i, p. 237.

13. Brit. Med. Jour., 1903, vol. ii, p. 659.

14. Jour. Path. and Bact., 1904, p. 158.

15. Brit. Med. Jour., 1904, vol. ii, p. 1510.

16. Amer. Jour. Med. Sciences, 1904, vol. cxxviii, p. 601.

17. "Der Acute Gelenksrheumatismus," Nothnagel Series, vol. v. Part I, p. 3:2.

11. Lancet, 1900, II, p. 861; also Brit. Med. Jour., 1901, II, p. 779; Zentralbl. f. Bact., 1902, xxxi, p. 502; Lancet, 1905, II, p. 1760.

lip,¹⁸ Menzer,⁵ Lenhartz,¹⁹ Canon,²⁰ Cole²¹ and others) have had uniformly negative results from the bacteriologic examination of the blood and joint fluid during life in large series of cases of undoubted rheumatism.

2. That the morphologic and cultural characteristics for *D. rheumaticus* are not sufficient to differentiate it certainly from other varieties of the streptococcus.

3. That the ability to produce in rabbits arthritis and endocarditis is by no means peculiar to this organism, but is shared by the common types of streptococci and staphylococci.

4. That the finding of a coccus in the blood or tissues shortly before death, or postmortem, may be readily explained by assuming either that the case has been one of septic disease and not of true rheumatism, or that to the rheumatic infection has been added a terminal streptococcus infection, such as is often seen in such other infectious diseases as scarlet fever, diphtheria, smallpox, etc.

The fact that most observers have failed to isolate any organism from the circulating blood or joint fluid should not, in itself, I think, be given much weight in opposing the claims of the diplococcus. It was just such negative results that led Meyer to direct his attention to the tonsils, with the idea that the germs might be localized there and that the joint symptoms, in many cases at least, might be due to their toxin alone. Poynton also insists that the organism is rarely to be found in the circulating blood or in the serous joint effusions, and both writers believe that the germs should be sought for in the periarticular tissues rather than in the contents of the synovial sac.

Whether the diplococcus possesses at present morphologic and cultural peculiarities sufficient to separate it with certainty from other streptococci is open to doubt. Even those who believe in the specificity of the organism are not in accord on this point. The English workers, for the most part, believe that it can be so differentiated. Meyer, on the other hand, could separate his organism from the various other cocci of the throat only by the inoculation into rabbits. The question is one of much complexity and difficulty and must be left for further bacteriologic study to settle.

That the common forms of pyogenic cocci are capable of producing joint inflammations in animals has been repeatedly demonstrated. Cole,²¹ especially, has shown recently that various strains of streptococci, when introduced intravenously into rabbits, are able to produce an arthritis similar to that described as resulting from the *D. rheumaticus*. In two instances out of twenty-one the inoculated rabbits showed endocarditis as well, and Cole concludes that one is not warranted in describing a distinct species of streptococcus merely on the basis of this property of producing arthritis and endocarditis in animals. On the other hand, most of the workers with the diplococcus have been impressed with the constancy and fidelity with which the inoculated animals have reproduced the lesions of rheumatism in man. Meyer especially offers a large series of control experiments to show the marked differences between the lesions produced by the diplococcus and those excited by the common pus-forming organisms.

The only effective answer to the fourth argument against the claims of the diplococcus can be that the or-

ganism found in the blood and tissues of these severe and fatal cases is not any of the usual pyogenic cocci, but is a specific diplococcus and is identical with that found in the inflamed tonsils only, in the milder cases. It will be seen, therefore, that the whole case for the *D. rheumaticus* rests on the proofs of its specificity and identity. Thus far the evidence offered can hardly be said to be convincing on this point. Nevertheless, the fact that so many workers, in different countries, should have obtained results so strikingly uniform and similar is interesting and impressive and can not be dismissed lightly. These results justify and demand, it seems to me, further careful investigation along these same lines.

CONCLUSIONS.

We are justified, I think, in believing:

1. That acute rheumatism is a specific, infectious disease, and is not merely an attenuated pyemia resulting from the common pyogenic organisms.

2. That the bacillus of Achalmé has no etiologic relation to acute rheumatism.

3. That while there is considerable evidence in favor of the view that the disease is caused by a specific diplococcus or streptococcus, positive proofs of the specificity and identity of this organism and of its causal relation to rheumatism are still lacking.

DIFFERENTIAL DIAGNOSIS OF RHEUMATOID JOINT AFFECTIONS.*

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The title of this paper, if liberally interpreted, might lead one to discuss the differential diagnosis of a great variety of joint affections that present certain features resembling those of true rheumatism and which might, therefore, be called rheumatoid.

Rather arbitrarily, perhaps, I shall narrow the discussion and not consider such conditions as sarcoma of the joint, ordinary monarticular tuberculosis, sprains and other traumatic arthritides, though, as is well known, there is often a necessity for differentiating between rheumatism and these conditions. Nor shall I do more than mention the arthritides occurring in connection with definite infectious diseases, such as scarlatina, pneumonia, epidemic meningitis, septicemia, pyemia, etc. Here diagnosis is comparatively easy if the existence of the primary disease is known, though in some instances, e. g., during convalescence from a mild and ambulatory scarlet fever, diagnosis may not be simple.

In epidemic meningitis, too, joint pains with articular and periarticular swellings may be early and somewhat confusing, though the equally early cerebral and spinal symptoms usually give the clew. Mistakes in regarding as rheumatism an arthralgia or arthritis, even a suppurative arthritis, or septicemia are made, but it is generally due to hasty study of a case rather than to any inherent difficulty in differentiation. The fact that just preceding an arthritis there has been a definite infectious disease should lead one to hesitate before deciding on true rheumatism. And the arthralgias, etc., following injection of diphtheria antitoxin and other therapeutic sera should be thought of.

Laying these affections aside, therefore, there still remain a goodly number of joint troubles more or less

18. Deutsch. Arch. klin. Med., 1903, vol. lxxvi, p. 150.

19. "Die Septischen Erkrankungen," Nothnagel Series, p. 187.

20. "Bacteriologie des Blutes bei Infect. Krankh.," Jena, 1905, p. 53.

21. Jour. of Infectious Diseases, 1904, vol. 1, p. 714.

* Read in the Section on Practice of Medicine of the American Medical Association, at the Fifty-seventh Annual Session, June, 1906.