

EXPERIMENTAL ARTHRITIS IN THE RABBIT, PRODUCED WITH STREPTOCOCCUS MITIS.*

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Arthritis has been produced in animals by means of various microorganisms. Those persons who advocate the specificity of *Micrococcus rheumaticus* in acute rheumatic fever find much positive support in the results obtained from the inoculation of animals in which arthritis, endocarditis, or pericarditis occur. In view of this consideration we have been led to inject rabbits with *Streptococcus mitis* isolated *intra vitam* from cases of subacute bacterial endocarditis, with the results to be described in this paper.

This communication does not deal with the etiology of rheumatism. Clinicians and pathologists must first decide what shall be termed acute articular rheumatism. However, as we¹ have pointed out, one group of cases of rheumatism exists in which there is a characteristic myocardial lesion (Aschoff bodies) associated with a verrucous endocarditis and unattended by embolic phenomena. Bacteriological examination in these cases is negative. There is a large second group comprising the bacterial infections of the endocardium, and a third group of bacterial or toxic arthritides with or without endocarditis.

It is possible to produce arthritis in rabbits by means of *Bacillus pyogenes fetidus liquefaciens*, staphylococci, hemolytic streptococci, the streptococcus of epidemic sore throat, Achalme's bacillus, *Micrococcus rheumaticus* isolated from the throat, blood, and joints, *Streptococcus salivarius* and *fecalis* (Horder), the pneumococcus, and *Streptococcus viridans*. Rosenow has reported the production of arthritis with *Streptococcus viridans* in a small percentage, and of endocarditis in a large percentage of rabbits. Our figures have been quite the reverse; that is, 50 per cent. of our rabbits developed

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¹ Thalhimer, W., and Rothschild, M. A., *Jour. Exper. Med.*, 1914, xix, 417.

arthritis and 7 per cent. endocarditis. We have employed nine different strains of *Streptococcus mitis* (table I). By reference to the table it will be seen that there is a slight variation in the ability of the different strains to produce arthritis.

TABLE I.

| Organism. | No. of rabbits. | Arthritis. | Endocarditis. |
|-----------|-----------------|------------|---------------|
| 4,110 | 10 | 7 | 2 |
| 4,147 | 9 | 3 | 0 |
| 4,206 | 7 | 3 | 1 |
| 4,275 | 6 | 5 | 0 |
| 4,170 | 3 | 2 | 0 |
| 4,342 | 3 | 1 | 0 |
| 4,357 | 2 | 1 | 0 |
| 2,524 | 1 | 0 | 0 |
| C | 1 | 0 | 0 |
| | 42 | 22 | 3 |
| | | 50% | 7% |

CHARACTER OF THE ARTHRITIS.

The rabbits described here are the same as those reported in our communication² in which the method of injection, the media used,

TABLE II.³

Rabbit 53. Organism 4,275. Injected May 26, 1913. 5 Injections.

| Date. | Left fore foot. | Right fore foot. | Left hind foot. | Right hind foot. |
|------------------|--------------------------------|------------------|-----------------|------------------|
| June 9. | + ⁴ | - | + | + |
| June 14. | ++ | - | ++ | ++ |
| June 16. | ++ | - | + | ++ |
| June 24. | +++ | - | - | + |
| June 29. | +++ | - | - | + |
| July 3. | +++ (Elbow) + (Wrist) | + | - | + |
| July 7. | + | - | + | + |
| July 9. | + | - | + | + |
| July 21. | ++ | - | - | ++ |
| July 28. | ++ | - | + | ++ |
| Aug. 25. | - | + | + | + |
| Sept. 3. | + | + | - | + |
| | Killed | | | |

² Thalheimer, W., and Rothschild, M. A., *Jour. Exper. Med.*, 1914, xix, 429.

³ Beattie (*Jour. Path. and Bacteriol.*, 1910, xiv, 436, table VI) shows in a graphic manner the involvement of the joints of a rabbit that was injected with a streptococcus resembling *Streptococcus rheumaticus*. His table corresponds closely to tables II, III, IV, and V in our series.

⁴ In the tables, + = joint affected; - = joint not affected.

and the doses are given. The production of arthritis appears to be independent of the doses of the streptococci and the media employed.

By reference to tables II, III, IV, and V the evanescent and mi-

TABLE III.

Rabbit 10. Organism 4,147. Injected December 10, 1912. 6 Injections. Killed January 24, 1913.

| Date. | Left fore foot. | Right fore foot. | Left hind foot. | Right hind foot. |
|--------------|-----------------|------------------|-----------------|-------------------------|
| Dec. 26..... | — | — | — | Limps; ankle swollen. |
| Dec. 27..... | — | — | — | No limp; ankle swollen. |
| Dec. 28..... | — | — | — | — |
| Dec. 29..... | — | — | — | Ankle swollen. |
| Dec. 31..... | — | — | — | Ankle swollen. |
| Jan. 6..... | — | — | — | Ankle swollen. |
| Jan. 13..... | — | — | — | Swelling smaller. |
| Jan. 17..... | — | — | — | Swelling smaller. |
| Jan. 22..... | — | — | — | Swelling smaller. |
| Jan. 24..... | — | — | — | Swelling smaller. |

TABLE IV.

Rabbit 18. Organism 4,110. Injected December 22, 1912. 4 Injections. Died February 20, 1913.

| Date. | Left fore foot. | Right fore foot. | Left hind foot. | Right hind foot. |
|--------------|----------------------|------------------|-----------------|------------------|
| Dec. 25..... | — | — | Limps | — |
| Dec. 27..... | — | — | Ankle swollen | — |
| Dec. 31..... | — | Stiff | Stiff | — |
| Jan. 13..... | — | — | — | — |
| Jan. 18..... | Limps; ankle swollen | — | — | — |
| Jan. 25..... | — | — | — | — |

TABLE V.

Rabbit 70. Organism 4,357. Injected June 24, 1913. 2 Injections. Died July 13, 1913.

| Date. | Left fore foot. | Right fore foot. | Left hind foot. | Right hind foot. |
|--------------|-----------------|------------------|-----------------|------------------|
| June 27..... | — | — | Stiff | Stiff |
| June 28..... | — | — | + | + |
| June 29..... | — | — | + | + |
| July 3..... | — | — | Knee + | Knee + |
| July 7..... | — | — | + | ++ |
| July 9..... | — | — | + | + |
| July 13..... | — | — | — | — |

gratory character of the arthritis is seen. Authors have used these characters as an argument for the specificity of a special organism

in causing acute articular rheumatism. The fact that the joints after extensive involvement return to a normal condition has been emphasized by Poynton and Paine, Beattie, and others. The arthritis produced by *Streptococcus mitis* has the same general characteristics. In some of the animals a chronic type of arthritis arises, the joint cartilages being eroded, the articular surfaces proliferated, and a partial ankylosis of the joint resulting. Poynton and Paine have seen the same results follow from *Micrococcus rheumaticus*. For control experiments we injected a number of rabbits with streptococci obtained from the sore throat epidemic in Chicago. Our results agreed with those of Davis who produced arthritis in every animal inoculated with organisms from the Chicago and Boston epidemics of sore throat. We injected a series of rabbits with hemolytic streptococci, and our results agreed with those of Cole who states: "In most cases the pathological changes in the joints are mild, consisting mainly of edema about the joint, the fluid becoming turbid, sticky, and tenacious, injection of the capsule and slight infiltration, mainly of the villi, with polymorphonuclear leucocytes." The arthritides which developed in our series were acute in their development, almost purulent in nature, and accompanied by some destruction of the surfaces of the articular cartilages. A series of rabbits (eleven) was injected separately with five different strains of *Streptococcus rheumaticus*, one strain isolated by Poynton and Paine, one by Beattie, one by Lintz, and two by Rosenow. 45 per cent. of the animals developed an arthritis; and the character of the arthritis was identical with that caused by *Streptococcus mitis*.

CHARACTER OF THE JOINT EXUDATE.

The exudate was of the same character as that described by the observers working with *Streptococcus rheumaticus*. It was of a thick, sticky, gelatinous consistence and contained many large endothelial cells with distinct phagocytic properties, a moderate number of polymorphonuclear leucocytes, and a large quantity of homogeneous material. The exudate is both articular and periarticular, having a decided tendency to extend down the tendon sheaths, and in one rabbit it extended from the knee joint to the ankle. In only

one instance was there any tendency towards decided pus formation.

Bacteriological studies of the exudate (table VI) show that we were able to demonstrate microorganisms in a comparatively small

TABLE VI.

| Organism. | No. of rabbit. | Blood cultures. | Joints. | |
|-----------|----------------|----------------------|---------|-----------|
| | | | Smears. | Cultures. |
| 4,147 | 1 | o | o | + |
| 4,147 | 10 | o | o | o |
| 4,142 | 42 | o | o | + |
| 4,170 | 27 | Not taken | o | o |
| 4,170 | 43 | o | o | o |
| 4,357 | 70 | o | o | o |
| 4,110 | 18 | o | o | o |
| 4,110 | 36 | + | + | + |
| 4,110 | 37 | o | o | o |
| 4,110 | 38 | + | o | o |
| 4,110 | 47 | o | o | o |
| 4,110 | 48 | o | + | o |
| 4,110 | 49 | Autopsy records lost | | |
| 4,206 | 39 | o | + | o |
| 4,206 | 57 | o | o | o |
| 4,206 | 59 | + | + | + |
| 4,275 | 35 | o | + | + |
| 4,275 | 41 | o | o | o |
| 4,275 | 51 | o | o | o |
| 4,275 | 52 | o | o | o |
| 4,275 | 53 | o | + | o |
| 4,342 | 55 | o | + | o |

percentage. In smears the organisms are almost always found intracellularly both in the large endothelial cells and in the polymorphonuclear leucocytes. The organisms can be recovered in cultures in only about one third of the animals. In one rabbit with a positive blood culture both smears and cultures from the joint were negative. Two of the rabbits having a vegetative endocarditis with positive blood cultures gave cultures from the joints. In the table bacteriological studies of the joints which have subsequently returned to normal are included; consequently the figures may not give a true index of the relative finding of streptococci in the affected joints. Meyer claims as one of the characteristics of the arthritis produced by *Streptococcus rheumaticus* that organisms can not be recovered from the joints. Other observers, however, have isolated the organism in the joints of cases of rheumatism and in arthritis produced experimentally in animals.

CONCLUSIONS.

1. We have produced arthritis in 50 per cent. of the rabbits injected with *Streptococcus mitis*.
2. The character of the arthritis is identical with that produced by *Micrococcus rheumaticus*.
3. The exudate in and about the joints partakes of the same nature as that caused by *Streptococcus rheumaticus*.
4. Bacteriological studies show that *Streptococcus mitis* can be recovered from about one third of the affected joints.
5. Arthritis produced by other types of streptococci differs by reason of greater destruction of tissue, by being more permanent in character, and by the exudate containing large numbers of polymorphonuclear leucocytes.
6. The deduction of a distinct variety or species of streptococcus based upon the power to cause arthritis in rabbits is unwarranted.

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