THE EFFECT OF SODIUM SALICYLATE ON VARIOUS TYPES OF EXPERIMENTAL ARTHRITIS*

DAVID JOHN DAVIS, M.D.
CHICAGO

The following experiments were made in order to determine the effect of salicylates in animals inoculated with various types of streptococci. These cocci were isolated from various sources, and their causal relation to certain clinical conditions, especially of the rheumatic types, is pointed out in its appropriate place with the several series of experiments reported below.

The experiments with the different organisms were all carried on in the same way. The animals used were rabbits. They were given, in some cases on the previous day, in other cases from one to two hours previous to inoculation, 5 grains of a synthetic preparation[1] of sodium salicylate subcutaneously or intramuscularly. They were then inoculated intravenously with suitable doses of living suspensions of twenty-four-hour cultures of the streptococci. On each subsequent day from 3 to 5 grains of salicylate were given to the animals, usually subcutaneously, for a period of two to three weeks if the animal lived, or until the animal died. Careful observations of the animals were made from day to day for evidence of infection, especially arthritis. In all experiments a series of six animals were inoculated with identical amounts of culture, three of which received the salicylate as above indicated, and three served as control animals. Young animals were used, since they are more susceptible to infection than old animals.

Experiment 1.—Six young rabbits were carefully selected, of approximately the same weight and age and about three-quarters grown. Their weight was about 1,100 gm. All were given, into the ear vein, equal amounts of Streptococcus 236 suspended in about 2 c.c. of salt solution. Three animals had received two hours previously 5 grains of sodium salicylate subcutaneously; this same amount was continued daily following the injection. Streptococcus 236 is an organism that was isolated from a person dying of an infection which began as a sore throat and which occurred during the Chicago milk epidemic in 1912. It was hemolytic and encapsulated and possessed the properties of the epidemic type of streptococci as described by Dr. Rosenow and myself previously.[2] The reasons for testing an organism of this type are readily appar-

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* From the Department of Experimental Medicine, University of Illinois, Chicago.

1. It has been shown by Waddell (ARCHIVES INT. MED., 1911, viii, 784) that the synthetic preparations of salicylates behave like the natural products.

2. Davis, D. J., and Rosenow, E. C.: An Epidemic of Sore Throat Due to a Peculiar Streptococcus, Jour. Am. Med. Assn., 1912, lviii, 773.

ent, since the use of salicylates, aspirin, etc., is so universal in cases of severe sore throat, especially when complicated by joint symptoms as not infrequently happens.

In this series all the animals died, each having developed multiple arthritis. The three receiving salicylates lived four, seven and three days, a total of fourteen days following inoculation. The controls lived eight, eleven and seven days, a total of twenty-six days. Two of the former and one of the latter showed slight lesions of endocarditis. From the joints in all the animals the streptococcus was recovered and in four of the six the heart's blood at necropsy yielded streptococci. It is evident from this experiment that the salicylates had no favorable influence on the course of the infection with this streptococcus. Indeed, the data indicate rather a slight unfavorable effect.

Experiment 2.—The next series of animals were inoculated with a hemolytic streptococcus of bovine origin isolated from the udder of a cow suffering with severe mastitis. It was very similar to Streptococcus 236 and was highly virulent to animals. The experiment was made exactly as was the previous one. All the animals developed multiple arthritis. The three receiving salicylates died after five, two and three days, respectively. Two of the controls died after five and three days and the remaining animal was still alive one month later though suffering from a large and badly deformed joint. One of the salicylate rabbits at necropsy revealed endocarditis. In the heart's blood of the five animals that died streptococci were found post mortem. Here again the salicylates had no favorable effect; if anything the reverse.

Experiment 3.—The next series of animals was treated exactly as in the previous experiments except that after the first dose of 5 grains, 3 grains of salicylates were given daily. This of course is still relatively a large dose. The streptococcus used was obtained from Dr. E. C. Rosenow, who shortly before had isolated it from the kneejoint of a person suffering with acute rheumatic fever. This organism had the general properties of the *Diplococtus rheumaticus* as described by Poynton and Payne. Since these organisms are less virulent for animals than the hemolytic streptococci, it was necessary to inject considerably larger doses, the growth from three blood-agar slants being given to each animal. All the animals without exception developed arthritis of greater or less intensity and multiple in character. Only one, an animal which was receiving salicylates, died; this occurred nine days after inoculation and the necropsy revealed multiple acute arthritis, endocarditis and fibrinous pericarditis. Cultures were positive from all these lesions. Three of the animals were killed after eleven days and cultures from joints yielded streptococci. The remaining two animals, one receiving salicylates daily for three weeks, and the other as control, were kept under observation for three months. No appreciable effect of the salicylates was evident. At the end of this time the joints in both animals were still distinctly and about equally enlarged. Otherwise the animals appeared normal and were not emaciated.

Experiment 4.—The next series of animals was inoculated with a streptococcus (256) isolated from the tonsil crypts in pure culture from an individual suffering with chronic tonsillitis and chronic rheumatoid arthritis. This organism was probably the causal agent in this condition. It was hemolytic and highly virulent for animals. The experiments were carried on exactly as with the other organisms. All animals developed multiple joint lesions within a few days. Those receiving the salicylates died after five, eight and nine days, respectively. No endocarditis. Two of the control animals died after four and five days; the third animal did not die, but developed multiple arthritis, the lesions becoming chronic and leading to marked enlargement and deformity of some of the joints. In connection with this experiment another rabbit was inoculated with a small dose of the same streptococcus (256). Joint lesions appeared after several days. Seven days after the inoculation and at a time when the arthritis was distinct, the animal was given 5 grains daily of sodium

salicylate. The lesions continued in a chronic state and showed no appreciable improvement after several weeks. The general course of the infection in this animal was almost identical with the outcome in the control animal that lived in the previous experiment, though it had a somewhat smaller dose of streptococci. It must be said, therefore, that the sodium salicylate had no appreciable effect on the course of the infection.

SUMMARY

It is clear from the several series of experiments here reported that sodium salicylate does not exert a favorable effect on infections in rabbits caused by various types of streptococci under the conditions detailed above. It does not prevent localization of the organism in joints, nor does it prevent the appearance of endocarditis. It would seem to have, therefore, no prophylactic value, nor does it alter the course of the infection after it has once become established.