

Effect of Sodium Salicylate Treatment on Antibody Titers in Rats Infected with *Trypanosoma lewisi*. (20552)

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An increased parasitemia and a prolongation of the reproduction phase of *T. lewisi* in salicylate-treated rats has been described by Becker and Gallagher(1). The mode of action of salicylates, as it affects the immune response, has not been adequately explained. Two possible mechanisms of salicylate activity have been postulated, namely, an ACTH-like effect(2), or an interference with antigen-antibody reaction(3,4). This present investigation is an attempt to show that the circulating antibody concentration is lowered by salicylate treatment, lending support to the former viewpoint.

Materials and methods. Male Wistar rats 6 weeks old were infected intraperitoneally with the Becker strain of *T. lewisi* and divided into 2 groups: (A) untreated; (B) sodium salicylate in distilled water (90 mg/ml) administered daily from the day of infection via a stomach tube (45 mg/100 g body wt). Treatment was discontinued the day before sacrificing. The animals were sacrificed at various intervals (Table I) by exsanguination under anesthesia. Each antiserum was titrated for agglutinins using trypanosomes collected from untreated rats with an 8-day infection. The organisms were suspended in a phosphate buffered (pH 7.4) saline solution containing 0.002 M glucose and used at a concentration of 120×10^5 trypanosomes per ml in the titrations. All tubes were read at the end of a 2-hour incubation at room temperature. Antisera salicylate levels were determined by the method described by Keller(5).

Results. As may be seen in Table I demonstrable agglutinins appeared in untreated animals in most instances after the 8th day of infection. A parallel series of salicylate-treated animals did not develop agglutinins until the 30th day with the exception of a low titer in one animal at the 16th day. Many of the salicylate-treated animals died during the

course of the experiment showing a high parasitemia at the time of death.

The concentrations of salicylate in the antisera were found to be low and unrelated to the agglutinin titers. Levels of salicylate ranged from 0.02 to 0.85 mg/ml in individual animals. To check the possibility of inhibition of the antigen-antibody reaction *in vitro* by these levels of salicylate, varying amounts of sodium salicylate were added to several antisera from untreated animals. No lowering of the agglutinin titers of these antisera was observed at concentrations of 0.3, 0.6, 1.2, 2.4, 4.8, and 9.6 mg/ml.

Discussion. The typical course of infection as described by Taliaferro(6) in untreated animals, and as altered by salicylate treatment(1) was observed in this study. Increased output of ACTH in animals receiving salicylate has been given as an explanation for the specific direct or indirect effect of the drug. Adrenal ascorbic acid depletion was not found in hypophysectomized animals receiving salicylate(2). The evidence that ACTH and cortisone treatment reduces antibody concentration seems to be adequate (7-9).

In this study a direct determination of the concentration of circulating antibody was carried out. Inhibition of antibody production or its increased catabolism, or both, could account for the lower agglutinin titers found in salicylate-treated animals. Lysenko has demonstrated a lowered total serum nitrogen and gamma-globulin in salicylate-treated infected animals(10). The progressive nature of the infection in treated animals may be the result of lowered antibody concentration.

Friend(11) and others have shown that salicylates inhibit antigen-antibody reactions *in vitro*. Friend obtained only 4% inhibition of an egg albumin-anti-egg albumin system using 80 mg of sodium salicylate per ml. This property of the drug was shown not to be operative in this investigation since salicylate

ANTIBODY TITERS IN SALICYLATE TREATMENT

TABLE I. Agglutinin Titers of Untreated and Salicylate Treated Animals.

Day of infection	Neg.*	Serum dilution									Avg mg sal./ml antiserum
		1:2	1:4	1:8	1:16	1:32	1:64	1:128	1:256	1:512	
Untreated											
2	3										
4	4										
6	4										
8	2	1	1								
10		1	1	1							
12	1			3							
14	2		2								
16				1	1		1	1			
18		1				1	1		1		
20					1						
22			2	1		1					
26							1			1	
30							2	1		1	
35						2	1	1			
50						1					
60					1	2					
80				1							
90							1				
120								2			
170					1	1					
Salicylate treated											
2	2										.83
4	4										.10
6	4										.09
8	4										.09
10	4										.27
12	5										.27
14	4										.23
16	3		1								.25
18	4										.41
20	2										.35
22	4										.28
26	2										.15
30	1		1					1			.43
35	3					1	1				.15
50					1	1	1				.23
60											
80					1	1					.12
90			1								.03

* No. of animals showing no agglutination.
 Figures represent No. of individual rats tested.

levels in antisera were comparatively very low and the addition of salicylate to antisera from untreated animals showed no agglutination inhibition.

Summary. Daily treatment with sodium salicylate reduced the concentration of circulating antibody in rats infected with *T. lewisi*. Possible modes of action are discussed.

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