

Summary. A bacterium, pathogenic for the roach, *Blatta orientalis*, was isolated in pure culture from the hemolymph of this insect, and proved to be *Staphylococcus albus*, as described in Bergey's Manual. Infections

could be established in normal roaches by inoculation with diseased hemolymph or with broth cultures. Death was preceded by a characteristic progressive paralysis.

13820

Protective Action of Sulfanilamide Against Liver Cirrhosis from Chronic Poisoning with Carbon Tetrachloride.*

J. C. FORBES, B. E. LEACH AND G. ZUR WILLIAMS.

From the Departments of Biochemistry and Pathology, Medical College of Virginia, Richmond.

In a previous article¹ it was reported that oral administration of sulfanilamide, sulfathiazole or sulfapyridine prior to exposure reduced markedly the mortality of rats following acute poisoning by inhalation of carbon tetrachloride. Additional work on this problem dealing with the effect of sulfanilamide against chronic poisoning from carbon tetrachloride, as well as results obtained by use of other possible protective substances, is presented at this time.

These chronic poisoning experiments confirmed our previous observations. In preliminary experiments in which sulfanilamide was incorporated in the diet, (100 mg per 100 g of food) it was found that the animals ate well when no carbon tetrachloride was administered, but as soon as the periods of anesthesia were begun they practically refused to eat and consequently became more susceptible than the controls. This necessitated the administration of the drug by stomach tube in all subsequent experiments. One cm³ of solution per 100 g of body weight was always used, the drug being either completely dissolved or with undissolved material in fine suspension in the water. Approximately 3 hr were allowed to elapse from the time of sulfanilamide administration before each period of anesthesia was begun. A summary of the experimental results is pre-

sented in Table I. It will be seen that there is a certain amount of overlapping but the general protective tendency is evident. In experiments 4 and 5, records of the daily food consumption were made. During the first few weeks no significant difference was noted between control and treated animals, but as the experiment progressed the food consumption of those receiving sulfanilamide was definitely greater than that of control animals.

The possible protective action of a variety of other substances has been studied in a number of acute poisoning experiments, but no protective action was obtained in any case. These substances included the following vitamin preparations, thiamine hydrochloride, riboflavin, pyridoxin hydrochloride, calcium pantothenate, nicotinic acid, inositol, para-aminobenzoic acid and ascorbic acid, and the following amino acids, *dl*-alanine, glycine, *l*-tyrosine and *dl*-methionine. Since para-aminobenzoic acid is known to inhibit the action of sulfanilamide against microorganisms, acute poisoning experiments were carried out in which this vitamin was administered simultaneously with sulfanilamide. No evidence of inhibition of the protective action of the sulfanilamide was obtained.

Discussion. The mechanism for the protective action of the sulfonamide drugs against carbon tetrachloride is obscure. Mackenzie and Mackenzie² have recently reported that

* Acknowledgment is gratefully made to the John and Mary R. Markle Foundation for its financial aid.

¹ Leach, B. E., and Forbes, J. C., *Proc. Soc. Exp. Biol. and Med.*, 1941, **48**, 361.

² Mackenzie, J. B., and Mackenzie, C. G., *Proc. Fed. Am. Soc. f. Exp. Biol.*, 1942, **1**, 122.

TABLE I.

Effect of Sulfanilamide on Production of Liver Cirrhosis from Chronic Carbon Tetrachloride Poisoning.

Exp. No.	No. of rats showing liver cirrhosis†				No. died	Remarks
	None	Mild	Moderate	Severe		
1	8	3	1	0	0	7.5 mg* sulfanilamide daily. CCl ₄ daily except Sundays for 22 days, then every other day for 25 days. Controls for above.
	0	0	1	3	8	
2	6	0	0	0	2	7.5 mg* of drug daily for 54 days. CCl ₄ daily for 14 days, then 3 or 4 times a wk for 40 days. Controls for above.
	0	3	5	1	5	
3	4	4	1	0	0	7.5 mg* of drug daily for 52 days. CCl ₄ daily for 8 days, then every other day for 44 days. Controls for above.
	0	3	3	0	2	
4	2	4	1	1	0	30 mg* of drug every other day for 15 days, then 3 times per wk for 32 days. CCl ₄ given 3 hr after each sulfanilamide adm. Controls for above.
	0	0	3	0	7	
5	5	4	0	0	0	30 mg* of drug 3 times per wk for 75 days. CCl ₄ given 3 hr after each sulfanilamide adm. Controls for above.
	2	2	3	2	4	

*Per 100 g of body weight, administered by stomach tube.

†The grading of cirrhosis was determined as follows:

Mild = Definite round cell infiltration with increased connective tissue but no pseudo-lobule regeneration.

Moderate = Definite and numerous pseudo-lobule regeneration with much intervening connective tissue.

Severe = Entire liver made up of pseudo-lobules with marked and interlobular scarring.

certain sulfonamide drugs cause marked enlargement of the thyroid gland in rats, with loss of colloid material and reduction in the basal metabolic rate. Administration of crystalline thyroxine to rats has been shown by McIver³ to increase their susceptibility to chloroform. The possibility exists that the protective action of sulfanilamide against carbon tetrachloride might be due to inhibition of thyroid activity. Experiments to test

this possibility are contemplated for the near future.

Summary. Administration of sulfanilamide to rats retards the development of liver cirrhosis from chronic poisoning with carbon tetrachloride. A number of vitamins and amino acids were tested for possible protective action in acute poisoning experiments, but none was found to increase the animal's tolerance. Administration of para-amino-benzoic acid did not inhibit the protective action of sulfanilamide against acute poisoning by carbon tetrachloride.

³ McIver, M. A., Proc. Soc. Exp. Biol. and Med., 1940, **45**, 201.