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15238 P

Sodium Salicylate Inhibiting Anti-Rh Immunization in Animals.

F. HOMBURGER. (Introduced by G. R. Minot.)

From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital, and the Department of Medicine, Harvard Medical School, Boston.

The inhibition of anti-RH agglutinins by ethylmercuri-thiosalicylate *in vitro* has been shown by Waller[1] and sodium salicylate is known to impair the formation of antipneumococcic immune antibodies in rabbits.[2] The present preliminary study suggests that sodium salicylate inhibits the formation of anti-Rh agglutinins in guinea pigs and in rabbits.

Experimental Procedure. Forty guinea pigs and 20 rabbits were used. All animals were immunized by the injection of red blood cells from rhesus monkeys. Guinea pigs received intraperitoneal injections of 1 cc of washed rhesus cells suspended in saline on the third and on the eighth day of the experiment. Rabbits were given intravenous injections of 0.01 cc of citrated rhesus blood in 1 cc of saline on the 4th, 5th, 6th, 11th, 12th and 13th days of the experiment. Half of the number of the animals received 0.16 g of sodium salicylate per kg of body weight daily by stomach tube (guinea pigs) or by subcutaneous injection (rabbits) starting the first day of the experiment and continued up to 48 hours before the blood was examined, 7 days after the last injection of rhesus blood. Anti-Rh agglutinins were looked for by the method of Landsteiner and Wiener[3] in the case of the guinea pigs* and by a modification of Diamond's[4] method, using human albumin† in the case of the rabbits. Negative readings were confirmed by microscopic examination. Serum salicylate levels were measured by the method used by Coburn.[5]

Results and Discussion. Of 21 animals‡

1 Waller, K., *Am. J. Clin. Path.*, 1944, **8**, 116.

2 Swift, H. F., *J. Exp. Med.*, 1922, **36**, 735.

3 Landsteiner, K., and Wiener, A. S., *J. Exp. Med.*, 1941, **74**, 309.

4 Diamond, L. K., and Denton, R. L., *J. Lab. and Clin. Med.*, 1945, **10**, 821.

* Some of these sera were examined by Dr. L. K. Diamond whose cooperation is gratefully acknowledged.

† The albumin used was a sample prepared by the Harvard Fractionation Laboratory and obtained through the courtesy of Prof. E. J. Cohn.

5 Coburn, A. F., *Bull. Johns Hopkins Hosp.*, 1943, **73**, 435.

‡ An epizootic described elsewhere[6] destroyed 9 of the guinea pigs and 12 rabbits died from aspiration pneumonia.

6 Homburger, F., Wilcox, C., Barnes, M. W., and Finland, M., *Science*, 1945, **102**, 449.

that had not received any sodium salicylate, 15 showed anti-Rh agglutinins following the injection of rhesus blood. In the case of the rabbits these were stronger which suggests that the methods used on these animals were better suited for such experiments.

Of 18 animals which had received sodium salicylate during the period of immunization only 2 showed microscopic agglutination of Rh positive cells.

No free salicyl radical was found in any of the sera tested which suggests that *in vivo* salicylate inhibits the formation of agglutinins rather than their effect in the plasma.

These findings call for confirmation and salicylate prophylaxis for erythroblastosis fetalis is not suggested here. On the contrary, the toxicity of this drug is again[7] emphasized. However, these experiments intimate the possibility of a chemotherapeutic approach to the subject of iso-immunization.

Summary. In guinea pigs and in rabbits the formation of anti-Rh agglutinins following the injection of rhesus monkey blood cells appears to be diminished when sodium salicylate has been administered 3 days prior to and during the period of immunization.

[7] Homburger, F., *Am. J. Med. Sci.*, in press.

15239 P

Biochemical Changes Following Poisoning of Rats by Alpha-naphthylthiourea.

K. P. DUBOIS, L. W. HOLM, AND W. L. DOYLE.
*From the University of Chicago Toxicity Laboratory.**

Alphanaphthylthiourea (ANTU) has been proposed as a rodenticide because of its effectiveness against Norway rats. Richter[1] has shown that poisoning by this compound is characterized by (a) development of intense pulmonary edema and pleural effusion, (b) marked resistance of herbivores in comparison to carnivores, (c) greater resistance of younger animals, (d) a rapid development of tolerance after repeated sublethal doses. These factors are individually significant in the action of many drugs. The present study indicates that ANTU profoundly alters the carbohydrate metabolism in poisoned animals and that the administration of cysteine counteracts these effects in rats.

Experimental. Purina Chow was used as diet for adult albino rats. ANTU was administered intraperitoneally in propylene glycol (5 mg ANTU per ml solvent). The solvent alone produced no observable effects. Under these conditions the LD-50 was approximately 3.0 mg per kilo. A dose of 10 mg per kg killed all rats between 6 and 24 hours after injection. Glucose was determined by the method of Folin and Malmros[2] and glycogen according to Good *et al.*[3] Our initial experiments consisted blood glucose determinations on rats prior to and 2.5 hours after injection of 10 mg per kg of ANTU. In 6 rats the average normal blood glucose rose from 68 ± 2 mg % to an average of 173 ± 18 mg % in 2.5 hours after poisoning. It was later observed that this initial hyperglycemia was followed by hypoglycemia which might be due to depletion of liver glycogen. Eight rats were fasted for 7 hours after which time 4 received 10 mg per kg of ANTU intraperitoneally. Food was withheld from both groups for another 8 hours after which

* This work was carried out under contract with the Medical Division of the Chemical Warfare Service.

[1] Richter, C. P., *J. Am. Med. Assn.*, 1945, **129**, 927.

[2] Folin, O., and Malmros, H., *J. Biol. Chem.*, 1929, **83**, 115.

[3] Good, C. A., Kramer, H., and Somogyi, M., *J. Biol. Chem.*, 1933, **100**, 484.