3154

Effect of reticulo-endothelial blockade on agglutinin formation.

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The reticulo-endothelial system is considered at present to be the possible place of antibody formation. Several observers[1] have offered proof that the physical blocking of this system diminished the production of hemolysin and precipitin. Reports, however, differ on the effect of blocking the system on the production of agglutinin. In our experiments, therefore, we have limited our observation to the effect of reticulo-endothelial blockade on typhoid agglutinin formation in rabbits. Colloidal iron, a saccharated iron-oxide solution, 35 grams per 100 cc. of water, was used for the indifferent non-protein material. It was injected intravenously in 2 to 6 cc. amounts, depending on the weight of the rabbit, almost daily until nine to nineteen injections were given. In most of the rabbits the iron was given preliminary to the typhoid vaccination. In several rabbits, however, it was continued throughout the period of immunization; in several rabbits the antibody titre was permitted to drop, and then the iron injection resumed.

The rabbits stood the iron injections well, and there was no loss in weight. The blood picture was little changed; the hemoglobin and red blood cells were practically unchanged, and the leukocytes only slightly increased. The differential blood count showed a tendency toward an increased number of large mononuclear cells. The typhoid vaccine used for injection was an attenuated washed suspension of a twenty-four hour agar culture standardized to 5 billion bacteria per cc. In the first series of experiments a single dose of 1 cc. was injected intravenously, and the agglutinin titre examined after a week. However, many

[1] Gay, F. P., and Clark, A. R., *J. Am. Med. Assn.*, 1924, lxxxiii, 1296. Isaacs, M. L., PROC. SOC. EXP. BIOL. AND MED., 1925, xxiii, 185. Jungeblut, C. W., and Berlott, J. A., *J. Exp. Med.*, 1926, xliii, 613. Gay, F. P., *Arch. Path.*, 1926, i, 590.

of the rabbits did not survive this dose; and other methods of immunization, such as a preliminary subcutaneous dose or small gradually increasing intravenous doses, were given. Fatalities also occurred when these methods of immunization were used.

Forty-one rabbits were used in these experiments; eight normal controls, seven glucose controls used to rule out the possible effect of the sugar in the colloidal iron, and twenty-five injected with iron oxide. Agglutinin titres were obtained on twenty-six of the rabbits. Eight normal controls, four glucose controls, and fifteen injected with iron.

The agglutinin titres of the normal rabbits were as follows: one, with a titre of 1:80; three with 1:640; one with 1:1280; and three with 1:2560. The titres of the glucose rabbits were as follows: two with a titre of 1:160, and two with 1:640. The titres of the rabbits injected with iron were as follows: one with a titre of 1:20; one with 1:80; one with 1:160, three with 1:320; two with 1:640; two with 1:1280, and four with 1:2560. The typhoid agglutinin formation was apparently not inhibited in any degree by the physical blocking of the reticulo-endothelial system.

All the rabbits that had received iron were autopsied, whether they died accidentally or were killed at the end of the experiment. Microscopically the large cells of the reticulo-endothelium were loaded with iron. There was little difference in the microscopic appearance of the tissues of the rabbits receiving nine injections and of those receiving nineteen injections. The continuation of the injection of iron during immunization had no perceptible effect on agglutinin formation. When the agglutinin titre dropped in rabbits that had preliminary iron injections, the titre could be restimulated by another injection of iron. The different methods of immunization elicited the same response in the normal controls, in the glucose controls, and in the iron oxide rabbits.

Conclusion: The blockade of the reticulo-endothelial system of rabbits with saccharated iron oxide had no apparent effect on typhoid agglutinin formation.