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An Immunological Study of the Relation Between Pernicious Anemia and Anemia Due to Welch B. Toxin.

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Chronic anemia was produced in rabbits by the injection of Welch B. toxin. The blood picture was characterized by (1) low color index, (2) anisocytosis without distortion of the shape of the cells, (3) rarity of nucleated red corpuscles. The histological examination of the organs showed changes consistent with blood destruction from any cause. Study of the spinal cord for degenerative changes, such as are frequently found in pernicious anemia, were negative.

The anemia which developed, however, was characterized by remissions when the injections were continued over long periods of time. The blood picture in rabbits which were given non-fatal doses returned to the normal despite the continuance of injection of the toxin. If large doses were then given the resistance could be broken down and anemia once more produced. This phenomenon could be repeated. It seemed, therefore, theoretically possible that the remissions in pernicious anemia were due to a varying immunity on the part of the human organism to the Welch B. toxin, and that, furthermore, the protoplasm of the rabbit was not designed to produce the typical changes of pernicious anemia as it occurred in man. For this reason it seemed important to determine the immunologic reactions associated with anemia due to Welch B. toxin, and compare them to those observed in pernicious anemia.

A study of the anti-hemotoxin furnished a method for making comparison between the clinical and the experimental anemia. As shown by Bull and Pritchett,¹ Welch toxin when mixed with serum containing anti-hemotoxin and injected intravenously into an ani-

mal does not result in destruction of red cells, whereas the toxin injected alone causes severe anemia and death. Lyall² developed a technique for measuring the hemolytic activity of the toxin *in vitro*, and the titre of the anti-hemotoxic serum used. In this test varying amounts of toxin are mixed with 0.1 cc. of serum, a 5 per cent suspension of red blood cells is added and the mixture incubated for two hours. The absence of hemolysis measures the amount of anti-hemotoxin present in the serum.

The sera of 7 rabbits in whom chronic anemia was produced gave complete inhibition of hemolysis against 0.1 to 0.7 cc. of toxin. Anti-hemotoxin was present both in the periods of severe anemia and in the periods of remission. The first appearance of anti-hemotoxin occurred 3 weeks after the first injection in small amounts and was synchronous with the beginning of an elevation in blood count. The sera of 3 rabbits who were rendered acutely anemic in less than 3 weeks did not inhibit hemolysis. The development of anemia for the second or third time did not appear to be due to the disappearance of anti-hemotoxin, but to the fact that the resistance of the animal was broken down by large doses of toxin.

Eight cases of pernicious anemia, representing various stages of the disease from the severely anemic patient to the patient in remission, were tested. In none was there inhibition of hemolysis. Negative results were also obtained in 9 normal individuals, 3 normal rabbits and 2 patients with severe secondary anemia.

The complete absence of anti-hemotoxin in the pernicious anemia patients studied offers no evidence that this disease has any relation to experimental anemia in the rabbit due to the toxin of the Welch bacillus.

¹ Bull, C. G., and Pritchett, I. W., *J. Exp. Med.*, 1917, **xxvi**, 129.

² Lyall, H. W., *J. Med. Res.*, 1914, **xxx**, 515.