

76 (486)

A study of the origin of the immune bodies by the method of organ transplantation.By **ARNO B. LUCKHARDT.** (By invitation.)*[From the Hull Physiological Laboratory of the University of Chicago.]*

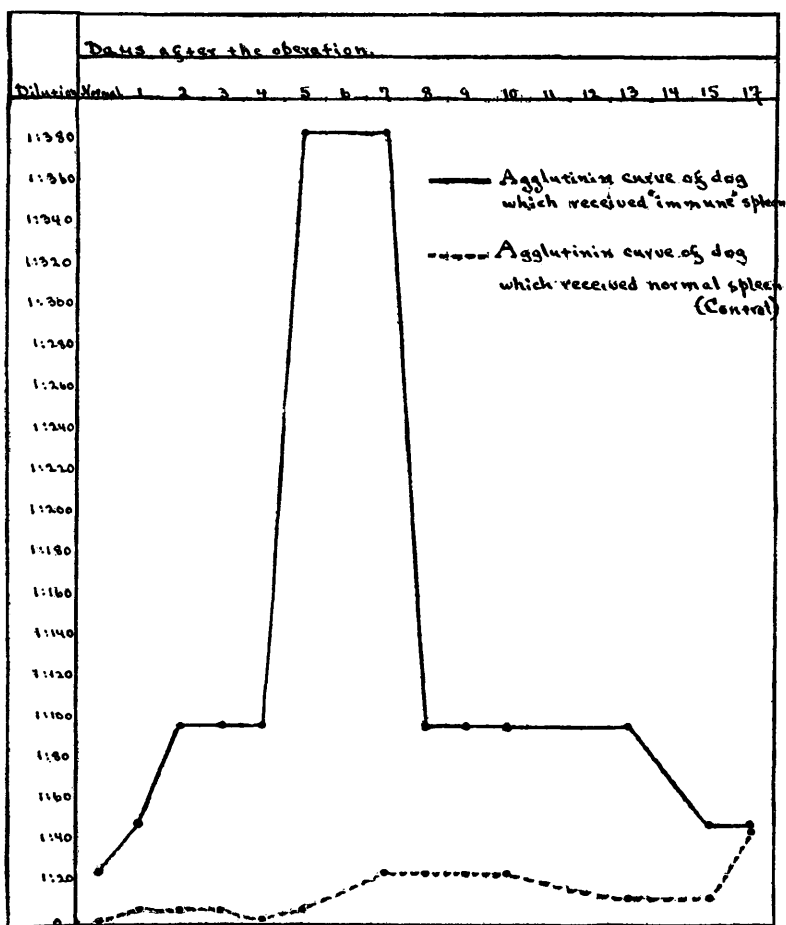
The interesting facts recently published by Prof. Hektoen and Prof. Carlson on antibodies and their formation indicate strongly that the blood takes no direct part in the fixation of antigen (goat's and rat's corpuscles) or in the production of antibodies (lysins and agglutinins) for these corpuscles. What tissue or tissues, if not the blood, fix the antigens as early as three hours after intravenous injection?

The organs which fix the antigens are undoubtedly also the organs intimately concerned with the production of the specific immune bodies for these antigens. Previous work on the origin of the antibodies, in general, strongly suggests that the hemopoietic organs (spleen, lymph glands, and bone marrow) are the source of the immune bodies. If, therefore, the antigens are fixed in part by the spleen, successful transplantation of that organ from one dog immunized 24 hours previously with goat's blood into a normal dog ought to cause the appearance of the specific lysins and agglutinins in the blood and body fluids of the latter. The technical difficulties involved in the transplantation of the spleen are great and so far the operation has not been performed by me as successfully as has recently been reported by Dr. Carrel.

In the meantime the following indirect method of attacking the problem was chosen. The spleen of a dog immunized 24 hours previously by an intravenous injection of goat's corpuscles is removed aseptically and ground up by means of a sterile meat grinder. The mass is suspended in warm physiological salt solution and introduced into the peritoneal cavity of a normal dog. The dog is bled at regular intervals for about three weeks. The sera kept in the ice chest are tested under the same conditions and on the same suspension of goat corpuscles at the end of that period.

The following considerations form the basis for this procedure. If the splenic tissue fixes the antigen either, or both, of two things

may happen when the macerated "immune" spleen is introduced into the peritoneal cavity of a normal dog. The splenic cells may escape death and give rise to the antibodies in the second dog; or the antigen may be split off again on the death of splenic cells (on Ehrlich's conception of antigen fixation) and reaching the cir-



ulation may again attach itself to suitable receptor and thus stimulate to specific antibody production.

With this method the spleen has given results so striking that I shall include the specific agglutinin curve of a single experiment on a dog which had received intraperitoneally emulsified spleen of another dog immunized 24 hours previously with an intravenous

injection of 1 c.c. of a 10 per cent. suspension of washed goat's corpuscles per kilo body weight. The control animal received intraperitoneally an emulsion of spleen from a normal dog (see curve).

Never does the serum of the control dog cause agglutination in greater dilution than 1:48. The agglutinating power is, on the whole, less than 1:24. The serum of the dog which received the immunized dog's spleen showed an increase in agglutinin from the start. Rising from a normal of 1:24 the serum agglutinates on the fifth and seventh day in a dilution of 1:384. From the eighth to the thirteenth day the serum agglutinates in a dilution of 1:96; and on the seventeenth day, the day of testing the fluids, the serum possesses an agglutinating value of only 1:48.

A future paper will give in greater detail this and other experiments which have yielded similar results with respect to antigen-fixation by the spleen. The mechanism of subsequent antibody formation in the recipient, whether by growth of the living cells or a second fixation of antigen liberated by the dead or dying splenic cells remains an open question. The results so far obtained warrant the conclusion that the spleen fixes antigen; and that this organ is, therefore, necessarily concerned with antibody formation.

The same method has been used with lymph glands and bone marrow with negative results. The work is being continued along this line with the hope of proving the point directly and conclusively by the successful transplantation of the spleen.

77 (487)

The concentration of ammonia in the blood of dogs and cats necessary to produce ammonia tetany.

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The importance of this subject rests in its relation to the markedly increased ammonia content of the blood of animals in parathyroid tetany. In a recent paper,¹ evidence was presented which indicates that this increased ammonia is apparently asso-

¹ Carlson and Jacobson : *American Jour. of Physiol.*, 1910, xxv, 403.