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The fate of injected protein in an animal immunized against it.

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Proteins have been selected as antigens capable of reproducing the reactions of immunity and the attempt has been made to determine if immunization by repeated injection modifies their absorption. In the normal rabbit proteins such as horse serum and egg albumin are absorbed with no conspicuous inflammatory reaction, whereas in the rabbit immunized by six or seven injections of the antigen at intervals of five days a subsequent injection produces an intense inflammatory reaction associated with necrosis at the site of introduction of the antigen (Arthus phenomenon). A former study[1] has shown that the injected horse serum, egg albumin or crystalline egg albumin introduced into an immunized animal fails to enter the blood in quantities demonstrable by the precipitin reaction, whereas, in the normal animal the antigen enters the blood and is demonstrable in considerable concentration. The present experiments were undertaken to determine the fate of the antigen at the site of injection. The first experiments were made with crystalline egg albumin. The presence of the protein in an extract of tissue removed from the site of injection was determined by the precipitin reaction and its concentration in a weighed amount of tissue determined by comparison with precipitin reactions obtained when the precipitating serum used in the tests was mixed with known concentrations of the antigen. Concentration of antigen at the site of injection in normal and immune animals at varying intervals after injection of 0.5 cc. of a 5 per cent solution of crystalline egg albumin is shown in the following table:

	Normal Animal	Immune Animal
1 day	1/200	1/20
2 days	1/500	1/50
3 days	0	1/250
4 days	....	1/750
5 days	....	0

[1] Opie, E. L., *J. Immunol.*, 1923, viii, 55.

In the immune animal antigen was still demonstrable at the end of five days in the necrotic skin at the site of injection (Arthus phenomenon) but was absent in the surrounding indurated tissue as indicated in the table.

The foregoing figures show that a readily diffusible antigen such as crystalline egg albumin in an immune animal is fixed at the site of injection and for this reason fails to enter the circulating blood.

Similar experiments performed with horse serum showed that it had disappeared from the site of injection both in the normal and in the immune animal at the end of three days, but the evidence that the immune animal holds the protein at the site of injection is readily obtained by estimating the quantity of protein still present at the end of twenty-four hours.

In one experiment twenty-four hours after intradermic injection of 0.5 cc. of horse serum into a normal animal the amount obtainable at the site of injection was 0.17 cc. and the antigen was present in considerable quantity in the blood serum. After the same injection into an immune animal 0.449 cc. was recovered from the site of injection and none was found in the blood serum.

The experiments indicate that the immune animal differs from the normal in its ability to fix the antigen at the site of injection. It is probable that this fixation is brought about by specific precipitation. Associated with this precipitation there is an acute inflammatory reaction (Arthus phenomenon) and the precipitate formed by antigen and precipitate which is strongly chemotactic is probably destroyed by leucocytic digestion.