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Experiments on Immunization with Haptens.

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It is known that the specific substance contained in Forssman's antigen which as such is only slightly antigenic¹ can be restored to high antigenic activity by the admixture of proteins foreign to the animal immunized. Recently a second method of producing the same result has been found, which consists in the injection of the hapten along with kaolin.² Similar effects have been described by Zozaya³ with mixtures of a polysaccharide from *B. anthracis*, and collodion particles.

We had no difficulty in corroborating the findings of Gonzalez and Armangué, and in addition we observed that hemolysins for sheep blood could be produced by injecting the Forssman hapten mixed with a suspension of collodion particles. These observations suggested the possibility that other ways of increasing the slight antigenic activity of the hapten might be found. In fact, in some animals we obtained higher titers than in the controls, on injecting the specific substance and at the same time trypan blue or turpentine, but the results were quite irregular. A single attempt to produce precipitins and bacterial agglutinins by Zozaya's method was not successful. However, it was possible to produce agglutinins and precipitins of moderate titer by the injection of a specific substance prepared from *V. cholerae* which was adsorbed to charcoal. This substance was prepared by extraction with 75% alcohol followed by treatment with alkali according to the method of Landsteiner and Levene.⁴ (The sera of 5 rabbits after 5 intraperitoneal

¹ Landsteiner, K., and Simms, S., *J. Exp. Med.*, 1923, **38**, 136.

² Gonzalez and Armangué, *Comp. Rend. Soc. Biol.*, 1931, **106**, 1006.

³ Zozaya, J., *Science*, 1931, **74**, 270.

⁴ Landsteiner, K., and Levene, P., *J. Exp. Med.*, 1927, **46**, 213.

injections of the specific substance from *V. cholerae* adsorbed to charcoal gave, after 2 hours at 37°C., agglutinin titers of (1) 1:1600, (2) 1:100, (3) 1:50, (4) 1:100, and (5) 1:50, respectively. Precipitation reactions, made by adding 2 drops of the immune serum to 0.2 cc. of a 1:5000 dilution of the specific substance were distinctly positive in 2 cases, and weakly positive in 2 others.)

Control animals injected with the substance alone produced no precipitins, and the sera showed only traces of agglutination in a dilution of 1 to 10. A solution of the specific substance still gave a biuret reaction, and on hydrolysis with acid a precipitate was formed which contained alcohol soluble acids.

In one experiment in which an azodye made from diazotized tartranilic acid and resorcinol⁵ was adsorbed to aluminum hydroxide and injected into guinea pigs, a certain degree of sensitization seemed to be brought about, since some of the animals showed mild anaphylactic symptoms and one of them died in acute shock on the injection of a corresponding azoprotein after an appropriate interval.⁵ It was, however, not possible to reproduce this result in a second experiment.

The observations reported show in confirmation of those of Gonzalez and Armangué that the hapten of the Forssman substance can exhibit distinct antigenic activity, and one may reasonably assume that this will hold for other sorts of haptens, without the aid of antigenic proteins. On the other hand, the experiments do not disprove the idea that in the high activity of natural complex antigens the proteins play a significant rôle.

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Single Cell Dissociation of the Mycobacterium of "Rat Leprosy."*

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An acid-fast organism isolated by Chapin¹ from a leprous rat in 1912 has been kept in the culture collection of the National Tubercu-

⁵ Landsteiner, K., and Levene, P., *J. Exp. Med.*, 1930, **52**, 347.

* This experiment is part of a group investigation being carried on in conjunction with the Medical Research Board, National Tuberculosis Association.

¹ Chapin, *U. S. Treas. Dept., Pub. Health Rep.*, 1912, **27**, 161.