

Experiments on Sensitization of Guinea Pigs with Simple Chemical Compounds.

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The sensitization of guinea pigs with simple compounds such as primulin,¹ salvarsan,² and p-phenylene diamine³ has been studied by several authors, but the development of the subject has been somewhat hindered by difficulties encountered in reproducing some of these experiments.⁴

As already observed by Mayer, we found that guinea pigs rubbed repeatedly with salve containing p-phenylene diamine showed increased redness and scaling, in comparison to controls. Furthermore, increased sensitivity was obtained by the administration of a salve containing p-nitroso-dimethylaniline and by repeated intracutaneous injections of a saline solution of p-phenylene diamine, and some such effects were noticed, also, after injecting p-nitroso-dimethylaniline and p-amino-phenol, using approximately 1 mg. of the substances per injection.

Following this, smaller doses of 0.02 mg. were injected on the back twice a week over a longer period, a method similar to that advocated by Kolle⁵ for the production of hypersensitiveness to salvarsan, in animals. With this method definite sensitization effects were obtained, besides salvarsan, with other compounds such as p-phenylene-diamine and p-nitroso-dimethylaniline. Thus, on reinjection on the sides about 7 days after the last injection of a course consisting of up to 20 injections at one or 3 day intervals, a number of the guinea pigs showed pinkish, more or less

¹ Bloch, B., and Steiner-Wourlish, A., *Arch. f. Dermat. u. Syph.*, 1926, **152**, 283; 1930, **162**, 349.

² Swift, H., *J. A. M. A.*, 1912, **59**, 1236; Frei, W., *Klin. Wochenschr.*, 1928, **7**, 1026; Sulzberger, M., *Arch. Dermat. and Syph.*, 1929, **20**, 669; Nathan, E., and coworkers, *Klin. Wochenschr.*, 1929, **8**, 1714; Mayer, R. L., and Sulzberger, M., *Arch. f. Dermat. u. Syph.*, 1931, **163**, 245.

³ Mayer, R. L., *Arch. f. Dermat. u. Syph.*, 1931, **163**, 223.

⁴ Sulzberger, M., *Arch. Dermat. and Syph.*, 1930, **22**, footnote p. 849; Meyer, K., *Biochem. Z.*, 1925, **166**, 202; Bock, G., *Münch. Med. Wochenschr.*, 1929, **76**, 915.

⁵ Kolle, W., *Reale Accademia d'Italia*, Convegno "Volta," Rome, Sept. 25, 1933.

elevated areas within 24 hours, averaging $\frac{3}{4}$ -1 cm. in diameter. Likewise, with 1:2:4 dinitro-chlorbenzene* distinctly increased reactions, noticeable even after less than 10 injections, were observed in most of the guinea pigs after daily intracutaneous injections of the substance. In a preliminary experiment with suberanic-resorcine dye,⁶ 2 out of 6 animals treated in the manner described showed definite reactions, so that one may assume that sensitization is possible with this substance, also. White guinea pigs were used throughout. Intracutaneous injections of 1/50 mg. of the compounds in 0.1 cc. saline were used for the tests as well as for sensitization except in the case of dinitro-chlorbenzene, where doses of 1/400 mg. were injected. Normal animals used as controls showed no definite or much weaker reactions than those described.

In a limited number of specificity tests with the substances named, in animals that gave marked homologous reactions there was, as a rule, no difficulty in recognizing reactions with the homologous compound by their greater intensity. The guinea pigs sensitive to p-phenylene diamine, in addition to the homologous reaction, gave a smaller but distinct reaction with nitroso-dimethylaniline.

Injections of aminoazobenzene, aminoazobenzene disulphonic acid, and the carbohydrate dextran have, so far, yielded negative results.

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Relationship Between Complement and Prothrombin.

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Bordet was the first to recognize a relationship between thrombin and complement. Fuchs¹ has recently claimed that the *mid-piece* of complement is identical with prothrombin. Since the complement content of plasma and serum are apparently the same, the change of prothrombin to thrombin does not seem to influence complement. A close association of prothrombin and thrombin with complement is indicated by:

* The experiments with this substance were suggested to us by Prof. Zangger in Zürich. See Wedroff, N. S., *Arch. Gewerbepath. u. Gewerbehyg.*, 1932, **3**, 509.

⁶ Landsteiner, K., and van der Scheer, J., *J. Exp. Med.*, 1932, **56**, 399.

¹ Fuchs, H. J., *Z. f. Immunitätsfor.*, 1929, **62**, 107.