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Alleged Protective Action of Colloidal Dyes in Anaphylactic Shock.*

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Protection with congo red and trypan blue against anaphylactic shock of guinea pigs has been claimed recently by Nikolaiev and Goldberg.[1] They used 7 sensitized guinea pigs treated with congo red and trypan blue, and 4 sensitized guinea pigs without protective dye-treatment. The dyes were injected intraperitoneally in total doses of from 10 to 50 mg., in from 10 to 30 minutes before injection of the antigen intraperitoneally; the dyes and the antigen were presumably mixed together in the abdomen. Of the 7 dye-treated guinea pigs, 3 showed symptoms of anaphylactic shock and 4 did not; the 4 controls showed symptoms. Such results on so small a group of animals are not impressive. Using a much larger group of animals from 2 species in a study of the same problem, approached from different angles, I obtained negative results 4 years ago and again recently. A record of my results at this time may be useful to others, for avoiding unprofitable experimentation along similar lines.

A total of 70 animals (51 guinea pigs and 19 pigeons) was used. The colloidal dyes tried were: congo red, mercurochrome, rose bengal, and vital red, which were always used in 1% strength in 6% dextrose solution. The following conditions were used with sensitized animals: intravenous injection of the dyes in from 5 to 27 minutes before injection of the antigen; daily intravenous injection for 3 days of the dyes before the antigen; intravenous injection of mixtures of the dyes and antigen, freshly made and after incubations for ½ hour and 1 hour; intravenous injection of mixtures of the dyes and antigen freshly boiled together (the mixtures did not coagulate[2]). In these experiments, the total dosage of the dyes was 40 mg. per kilo, and of the antigen 0.2 cc. (horse serum). Normal animals were injected hypodermically with the following mixtures of the dyes and horse serum to see if the process of sensitization

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[1] Nikolaiev and Goldberg, *Z. f. d. ges. exp. Med.*, 1930, **73**, 475.

[2] Hanzlik, PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 364.

could be influenced: fresh mixtures; mixtures incubated for ½ hour and 1 hour; boiled mixtures (no coagulation). In some cases, 0.2 cc. of the serum was used with 4 cc. of dye solution per kilo, and in others equal parts of serum and dye solution. At the end of 2 weeks, 0.2 cc. of horse serum as antigen was injected intravenously. At least 3, and sometimes 5, animals were used for each experimental condition. A total of 15 animals (9 guinea pigs and 6 pigeons) served as untreated controls for both groups of experiments.

The results obtained may be stated briefly: 82% of the 51 treated guinea pigs and 100% of the 19 treated pigeons showed the typical signs and symptoms of anaphylactic shock, in variable degree; about one-half of these animals died, the same being true of the controls. All the guinea pigs showed the typical pulmonary distention. Collectively, the vast majority, or 87%, of all the animals used failed to be protected by the colloidal dyes used. Accordingly, an intrinsic cellular reaction (antigen-antibody) was not prevented by colloidal dyes, some of which could prevent the effects of drugs and toxins.[3] This difference points to fundamental differences in the tissue reactivities of proteins and of drugs and toxins, the latter perhaps acting more in the cell exterior (humoral and cell-surface mechanisms), in accordance with certain postulates and evidences of pharmacology.

Conclusions. The colloidal dyes congo red, vital red, rose bengal, and mercurochrome, tried under a variety of conditions, failed to protect the majority of guinea pigs and pigeons against the typical symptoms of anaphylactic shock. These negative results do not support the positive claims of Nikolaiev and Goldberg, who used congo red and trypan blue. It is suggested that the results with these colloidal dyes point to fundamental differences in the tissue reactivities of proteins and of drugs and toxins.

[3] Hanzlik and Butt, *J. Pharm. Exp. Therap.*, 1928, **33**, 260.