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Anaphylactic Detoxication of Specific Proteins.*

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In the preceding paper[1] we report evidence that marked chemical alterations take place in specific foreign proteins on injection into the animal body, and that certain important immunological adaptations are due to these altered or denaturized proteins, rather than to the primary proteins originally injected. We have obtained further evidence in support of this by a study of the altered anaphylactic toxicity of specific foreign proteins on intravenous injection into normal, hypersensitive and immune dogs.

Measured quantities of horse serum were injected intravenously into these animals, and at varying intervals after this injection quantitative blood transfusions were made into partially exsanguinated anaphylactic recipients. The following is a summary of our results to date:

(1) *Normal Dogs.* Quantitative transfusions into anaphylactic recipients at any time within 6 hours after intravenous injection of 2 cc. horse serum per kg. of body weight into normal dogs invariably show the circulating blood to have a greater anaphylactic toxicity than that of control amounts of unaltered horse serum. This increase suggests the possibility that the initial change in the injected horse serum in normal dogs is an increase in the number of specific protein molecules by hydrolysis or colloidal dispersion, though other explanations of this increased toxicity are of course possible.

Transfusions at the end of 24 hours show a toxicity approximately equal to that of the control horse serum dose. A slight reduction in toxicity is noted by the end of 48 hours. A toxicity equal to about a quarter of the control dose is noted at the end of 3 days. There is no recognizable anaphylactic toxicity at the end of 4 days.

Quantitative titrations with rabbit precipitin show that there is little or no reduction in the amount of circulating horse protein in the injected normal dog at the end of 4 days.

(2) *Hypersensitive Dogs.* Quantitative transfusions at any time within 4 hours after intravenous injection of 2 cc. horse serum

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per kg. of body weight into hypersensitive dogs show an increased toxicity similar to that observed with normal dogs. At the end of 6 hours the toxicity is approximately that of the control horse serum dose. By the end of 10 hours the toxicity is reduced to about a quarter of the control dose. By the 15th hour the circulating blood usually becomes completely nontoxic.

Precipitin titrations show no reduction in the amount of circulating horse protein in the injected hypersensitive dog at this time.

In so far as a complete anaphylactic detoxication of horse proteins takes place by the end of 4 days in normal dogs, there is no reason to believe that the hypertrophy of this detoxicating function observed in hypersensitive dogs is necessarily due to specific antibodies.

This is a preliminary report.

[1] Manwaring, W. H., Marino, H. D., McClure, T. C., and Boone, T. H., PROC. SOC. EXP. BIOL. AND MED., 1927, xxiv, 553.

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Toxic Substances in Friedlander's Bacillus Cultures.

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Two substances, toxic for rabbits, were produced in cultures of a strain of Friedlander's bacillus, originally isolated from an epidemic of pneumonia among guinea pigs.

The organism is highly pathogenic for guinea pigs and rabbits by any route of injection. Mice are also readily infected by intraperitoneal injection; a dilution of 1 :10 billion of a 24-hour old broth culture (5-20 bacteria) produces the characteristic sticky mucoid exudate. Culturally, the organism forms acid but no gas in glucose, lactose, saccharose, maltose, mannite, and salicin, but not dulcite. It also reduces nitrates to nitrites, and gives a negative methyl red and Voges-Proskauer reaction.

Toxic Substance A. Procedure: The organism was grown in Huntoon's hormone broth containing 2 per cent peptone, in shallow layers in pint bottles, 20 cc. to a bottle giving a depth of 3/8 inch. The bottles were shaken once a day. The cultures were finally filtered through Berkefeld (N) candles. The pH and M.L.D. of the toxin for rabbits were determined at regular intervals.

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