

peristaltic augmentation became manifest also in parts of the colon and not infrequently even in the otherwise inert cecum. The augmented waves of the stomach are not very pronounced but the pyloric part of the stomach often contracts strongly as a whole. The vagus nerves were stimulated within the thorax in their course upon the lower part of the esophagus. Ergotoxine unmistakably increases the motor responsiveness of all parts of the gut to stimulation of the nerves even when their cardiac action is in no way involved.

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An allergic skin reaction to diphtheria bacilli.

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While immunity in diphtheria may be regarded as being principally antitoxic in nature, it is highly probable that antibodies of a lytic nature may be concerned. With this in view, we have applied an allergic skin reaction in addition to the toxin test of Schick, in studying immunity in diphtheria to the following persons:

1. To 123 persons of various ages, most of whom were healthy and well and had never had diphtheria or received an injection of diphtheria antitoxin.
2. To 61 persons receiving curative or prophylactic doses of diphtheria antitoxin.

The antigen for the allergic tests was prepared of 45 recently isolated cultures of diphtheria bacilli of various types; each culture was grown in glucose broth for four days and all mixed in a single flask and shaken mechanically with glass beads to break up clumps. To each 100 c.c. of the emulsion was added 5 c.c. of sterile horse serum antitoxin (2,500 units) and the whole shaken at room temperature for four hours. After this time the emulsion was placed in sterile centrifuge tubes and the bacilli separated and

washed twice with large volumes of sterile salt solution. After the final washing the bacilli were re-suspended in sufficient sterile salt solution to make, after thorough shaking, about two billion bacilli per cubic centimeter. This emulsion was heated at 60° C. for an hour; cultured for sterility and preserved with 0.2 per cent. tricresol. Subcutaneous injection of 1 and 2 cubic centimeters into 250 gram guinea-pigs showed absolutely no evidences of local reaction or general toxemia. In conducting the test, 0.1 c.c. of the emulsion which we have called *diphtherin*, was injected intracutaneously in the arm.

Reactions with the *diphtherin* were usually well marked and of two types, papular and pustular reactions. The latter were more severe than the former and both occurred with well-defined zones of erythema. These reactions usually reached their height within seventy-two hours and then began to recede.

The toxin tests were conducted with one-fortieth the M. L. D. of toxin diluted with sufficient normal salt solution containing 0.2 per cent. tricresol to render the dose 0.1 c.c. which amount was injected intracutaneously.

The throats and noses of a large number of persons were cultured to study the relation between the occurrence of positive reactions and the presence or absence of diphtheria bacilli in the upper air passages.

The bacteriolytic power of the sera of persons reacting positively and negatively to the *diphtherin* test, for living diphtheria bacilli were conducted toward throwing more light upon the nature of the allergic antibody. Complement fixation and agglutination tests were likewise conducted.

The following is a summary of the results of this investigation:

1. An allergic skin reaction was observed in about 70 per cent. of children and 35 per cent. of adults following the intracutaneous injection of a polyvalent antigen of washed, neutralized and heat-killed diphtheria bacilli.

2. These reactions were regarded as allergic in character and therefore entirely distinct from the toxin reaction of Schick.

3. About 53 per cent. of persons of various ages yielded positive *diphtherin* and negative toxin (Schick) reactions. About 10 per cent. yielded negative *diphtherin* and positive toxin reactions,

both tests agreeing therefore in about 63 per cent. of persons; 12.5 per cent. reacted positively and 24.1 per cent. negatively to both tests.

If a positive *diphtherin* reaction may be regarded as an index of lytic immunity, only 10 per cent. of persons were found who did not show the presence of either an antitoxic or lytic immunity, while 53.3 per cent. showed both types of antibodies; 24.1 per cent. showed antitoxic immunity only and 12.5 per cent. allergic, but no antitoxic antibody.

4. The percentage of positive *diphtherin* reactions was slightly greater among those who were convalescent from diphtheria.

5. There is no relation between the occurrence of positive and negative *diphtherin* and toxin reactions and the presence or absence of diphtheria bacilli; a negative toxin reaction in a person presenting clinical evidences of infection indicates that the individual does not require antitoxin but nothing more; he may be infected with virulent diphtheria bacilli capable of disseminating the disease.

6. The sera of persons yielding positive *diphtherin* reactions were not found to possess demonstrable bacteriolytic properties for diphtheria bacilli.

7. The sera of persons yielding positive *diphtherin* reactions yielded weakly positive or negative complement fixation and agglutination reactions with *diphtherin* as antigen.

8. Whether or not the *diphtherin* reaction will prove of practical value in handling outbreaks of diphtheria from the standpoint of passive immunization and diagnosis will depend upon future experiences under such conditions and also upon the results of experimental work bearing upon the broad question of allergic reactions as an index of immunity; it would appear at least that more attention should be paid the question of bacteriolytic immunity in diphtheria.