CONCLUSIONS

By means of the Schick test we are in a position to tell definitely who is susceptible to diphtheria and when an epidemic breaks out can inject those and those only, paying no further attention to the ones giving a negative reaction.

By it the danger of cross-infection is greatly decreased. Children with diphtheria that have had scarlet fever and are therefore immune from scarlet fever can be placed in scarlet fever wards when the inmates yield negative Schicks, etc.

It permits a great reduction in antitoxin bills. Much needless pain and annoyance of patients is avoided, and the possibility of anaphylactic shock is greatly minimized.

City Hall.

SOME OBSERVATIONS OF THE
SCHICK TEST

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Among the studies which have, from time to time, helped us toward a better understanding and more effective treatment of nose and throat conditions, those concerned with diphtheria command a prominent place. The introduction of antitoxin of course revolutionized the treatment of this disease, and numerous investigations of its value, dosage, possible sequelae, the immunity produced, etc., have since added much to the literature of the subject.

A feature of especial interest and value which stands out among these is the fact, now well established, that certain persons have a natural immunity to diphtheria and will not take it, however much exposed. Many of these, indeed, become carriers of the Klebs-Loeffler bacilli, and infect others, although themselves safe from the disease.

Finding the diphtheria organism in the throats of such persons is of uncertain diagnostic value unless supplemented by a test to show whether immunity is present or absent. In such cases sore throats due to other organisms may easily be confounded with diphtheria, the diagnosis being established by the laboratory finding the Klebs-Loeffler organisms.

These are among the cases which puzzle and worry the doctor. He finds, for instance, a case of slight tonsillitis (clinically), sends a swab for examination, ordering a mild gargle and perhaps an iron mixture meantime; back from the laboratory comes the report, "Diphtheria positive," and he hurries back to his patient with antitoxin only to find that in the brief interval everything has cleared up and the patient appears normal. The next patient showing a similar picture he decides to treat in the same way, but in place of clearing up it progresses to a virulent case of diphtheria in which he now finds himself disappointed in the use of antitoxin, late injections of this being of comparatively less value.

From such experiences he argues that either the laboratory is of little use to him, or antitoxin is an overrated remedy; or still more likely, concludes that thereafter whenever there is the possibility of diphtheria being present he will do best to inject promptly the antitoxin and not wait for any laboratory report. He feels that the injection will do no harm, and if it

turns out to be diphtheria he has gained so much in time and effect. In the last he is certainly right, and yet every medical man would prefer to avoid the use of this remedy in any case in which he might safely do so.

The Schick¹ test for immunity offers a promising aid in this matter. If by a simple injection into the skin we can determine who is, and who is not, liable to infection, a long step is taken toward simplifying the handling of these situations.

1. The use of immunizing doses of antitoxin will not be necessary if persons exposed to infection are found to be naturally immune.

2. Even when bacilli are found in the throats of such persons, no injection of antitoxin need be given when they suffer from tonsillar or other pharyngeal infections.

3. Nurses in institutions, when proved immune, can safely care for diphtheria patients while susceptible nurses are kept away and employed on other cases.

4. Much aid can be had in solving the puzzle of why one patient recovers without antitoxin while the next, apparently an exact counterpart, dies in spite of the use of this valuable remedy.

Park² has given an interesting and very complete description of the Schick test, its technic, etc., and for the benefit of the reader who has not access to such information part of the matter is included here.

It has been shown that only persons who have either no antitoxin or but a minute amount in their blood and tissue are liable to contract diphtheria. With this fact before us we have but to estimate the amount of antitoxin present in any individual to know whether he will be safe from infection or liable to it if exposed.

Methods of doing this previously proposed have been too troublesome for practical use, but Schick's test is at once simple and safe, and seems to be reliable.

It is not more difficult to make than the Pirquet test made with tuberculin for tuberculosis, and consists of the intracutaneous injection of a prepared solution containing minute quantities of diphtheria toxin. This will produce a positive reaction in twenty-four or forty-eight hours if antitoxin is absent, or present in amount insufficient for protection.

The reaction consists of redness and slight swelling over the injected area. It continues for a week or more and leaves a brownish pigmentation with superficial scaling for a time after this.

In a small percentage of older children and adults there is a pseudoreaction even when large amounts of antitoxin are present, and these must be carefully distinguished from the true reactions.

The pseudoreaction can be recognized by its earlier appearance, its less sharply circumscribed form, greater infiltration, and the fact that it disappears in twenty-four hours or two days at the latest. The spot is less pigmented later, and superficial scaling is not noted. The directions for making the test are as follows:

An accurate syringe with a sharp but short-pointed, fine needle is necessary. The usual 1 c.c. record tuberculin syringe with a fine platinum iridium needle serves well.

1. Schick: Spezifische Therapie der Diphtherie, *Centralbl. f. Bacteriol.*, 1913, lvii, Part 1; Ref., *Beiheft*, p. 16; Die Diphtherietoxin-Hautreaktion des Menschen als Vorprobe der Prophylaktischen Diphtherieheilserum-injektion, München. med. Wchnschr., 1913, ix, 2608.

2. Park, W. H., and Zingher, Abraham: Practical Applications Obtained from the Schick Reaction, *Proc. New York Path. Soc.*, October, 1914. Park, W. H.; Zingher, Abraham, and Serota, H. M.: The Schick Reaction and its Practical Applications, *Arch. Pediat.*, July, 1914.

A standard diphtheria toxin is diluted at first 1:10, in 0.5 per cent. phenol (carbolic acid); this dilution will keep in the ice box for at least two weeks. Park advises care in securing a proved quality of toxin. The diphtheria toxins provided for this purpose by the commercial houses have not proved reliable. For use, further dilutions are now made in normal saline, of such strength that 0.1 c.c., or as stated above, 0.2 c.c., contains $\frac{1}{50}$ minimum lethal dose for the guinea pig. This amount is injected intracutaneously on the flexor surface of the arm or forearm.

The intensity of the reaction varies in different individuals, but a well-marked redness indicates an almost complete absence of antitoxin. Faint reactions point to the presence of a very small amount of antitoxin, not sufficient to protect against diphtheria. To prevent the appearance of the reaction, according to Schick, at least $\frac{1}{50}$ unit of antitoxin per cubic centimeter of blood is required. This amount he considers sufficient to protect against diphtheria. According to von Behring, even as little as $\frac{1}{100}$ unit of antitoxin will protect against the disease in uncomplicated cases.

The following tests were made in Lincoln Hospital, New York, and were begun because of a troublesome outbreak of diphtheria among the nurses in December, 1914, which continued to crop out at intervals through the following January; 0.2 c.c. were used for each injection.

The nurses were colored women ranging from 25 to 35 years of age.

Seven had no history of diphtheria, or of having had antitoxin. Three gave Schick positive; four, Schick negative.

Five cases had clinical diphtheria within six weeks of the test; all gave a negative Schick.

Eleven cases were isolated because the Klebs-Loeffler bacilli were found in the throat. They all gave a negative Schick and did not develop clinical diphtheria. They were given local treatment for the throat, and repeated cultures were made. Two gave a positive culture once. Two gave a positive culture twice, and the other seven gave more than two positive cultures.

Twelve cases had no diphtheria, but had immunizing doses of antitoxin within six weeks of the test. Ten were Schick negative; two were Schick positive.

Three cases had diphtheria from eight to ten years previously. Two were Schick positive and one was Schick negative.

Eighteen children ranging in age from 3 weeks to 5 years were also tested. These patients were in the hospital for a variety of causes: feeding, intestinal troubles, hernia, pneumonia, fractures, etc.

In nine children under 14 months, three were Schick negative and six Schick positive. In nine children from 14 months to 5 years, two were Schick negative and seven Schick positive.

None of the children had had diphtheria or antitoxin.

Twenty-six patients, adults, were also tested. Eighteen gave a positive Schick and eight a negative Schick. One of the negative cases had received antitoxin a month previous. So far as these tests were carried, they confirm the findings of Schick, Park and others.

CONCLUSIONS

1. The most susceptible age is between 1 and 5 years.

2. Immunity obtained by having the disease or by the use of immunizing doses of antitoxin lasts from a month to several years, varying greatly in different individuals and being very brief in children.

3. The Schick test is a helpful agent in testing the efficiency of immunization by antitoxin as well as the natural immunity existing in many persons.

4. It has helped to place on more certain grounds the assurance that bad cases of diphtheria should receive early and large doses of antitoxin by intravenous injections. Antitoxin is ten times as effective when so used, as compared with the ordinary method of administration.

5. Park has obtained results in families showing a striking similarity in reactions to the test. If the youngest child of a family has a negative reaction, all the older children are likely to be negative, and if the older children are positive, the younger ones are also. When variations are found, the younger children show the positive reaction.

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THE INTRADERMIC DIPHTHERIA TOXIN TEST *

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It has been known for some time that a certain percentage of persons have antitoxin to diphtheria in their blood, and that only those individuals whose natural immunity is low, or who have no natural immunity whatever, are susceptible to the disease. Römer designed a biologic test for estimating the quantity of antitoxin in the blood, but it was too tedious and cumbersome to be of practical use. In 1909, Schick conceived the idea of using diphtheria toxin in the manner employed by von Pirquet for the use of tuberculin in the diagnosis of infection with the tubercle bacillus in children, and he found, by running controls by the Römer method, that individuals who reacted to the toxin were susceptible to diphtheria while those giving negative tests were immune. Somewhat later, in order to control the amount of toxin absorbed, he began using intracutaneous injections and found that a negative reaction to $\frac{1}{50}$ the minimum lethal dose for a 250 gm. guinea pig indicated that the individual had at least 0.031 units of antitoxin per cubic centimeter of blood, which quantity he believes to be sufficient to protect against the development of clinical diphtheria. Von Behring believes that even $\frac{1}{100}$ unit of antitoxin per cubic centimeter of blood will protect against the development of the disease, and Park reports the suppression of the Schick test in a 3 year old child weighing 35 pounds, twenty-four hours after the injection of ten units of antitoxin.

Schick, in his work, used 0.1 c.c. of toxin dilution which contains exactly $\frac{1}{50}$ the minimum lethal dose, and Park preferred to use 0.2 c.c. We, however, have been using a dilution in which 0.05 c.c. contains $\frac{1}{50}$ the minimum lethal dose, as the results seem to be quite as constant and the discomfort accompanying the injection of the smaller quantity is less.

The positive reaction which indicates the absence of antitoxin in the blood appears in twenty-four hours as a circumscribed hyperemic, indurated area, usually becomes most marked in forty-eight hours, persists for from a week to ten days and heals by central brownish pigmentation and scaling which clears up in

* From the Department of Pediatrics of the Washington University Medical School and St. Louis Children's Hospital. Read before the St. Louis Medical Society, Jan. 23, 1915.