are just and reasonable. The Society claim that their members are doing specialised work, that many of them require in addition to the ordinary qualifications of a doctor a registrable qualification in public health, and they ask that they be paid on the basis of the earnings of efficient medical practitioners working whole-time in other salaried services or private practice. The request is moderate, and if a claim so just is withstood, then the Public Health Medical Service regarded as a career must be considered as closed, for first-rate men will not enter or remain. In these circumstances the Service is bound to deteriorate, and the development of preventive medicine and the discovery and institution of measures for the improvement of the public health will be long delayed.

THE SCHICK TEST AND DIPHTHERIA TOXIN-ANTITOXIN IMMUNISATION.

BY

T. E. DICKINSON, M.D., D.P.H.

In addressing a meeting of medical officers of health, it would be superfluous for me to stress the formidable role of diphtheria, either as an administrative problem or as a clinical entity. In spite of the time, money, and energy spent upon prevalent methods of control, the incidence and mortality of diphtheria have not declined during the past decade; rather, on the other hand, they have increased. This condition of affairs renders the Schick test for the determination of susceptibility to diphtheria a subject of more than academic interest, and it is the purpose of this paper to outline, briefly, my personal experience with the test, and to hazard certain suggestions as to the manner in which it might be employed most profitably in the public health services.

The utility of the test depends upon the fact that persons, whose blood serum contains no diphtheria anti-toxin, react in a specific manner when diphtheria toxin is injected into their skins. The intracutaneous exhibition of 1/50 M.L.D. of toxin produces, in the non-immune, a skin reaction having the following characteristics:—After 24 hours the area at the site of inoculation becomes very slightly raised and infiltrated. In colour, it varies from a deep pink to a dark dusky crimson. In shape, it is round or oval. The edge is distinctly, but not very sharply, defined. The surrounding skin is usually normal; rarely there is a faint

pink enclosing zone, which fades in the course of 24 or 48 hours. The diameter of the area varies from 10 to 30 millimetres, usually 15 to 25. There is no pain, itching, nor any feeling of discomfort. The reaction is at its height from 48 to 72 hours after the injection. At the end of a week the skin shows brown pigmentation and scaling. The scaling assumes all degrees of intensity, from a very fine powdery desquamation marking out the folds of the skin, to massive exfoliation. Very occasionally scaling occurs as early as the third day, or may be delayed until the end of the second week. The pigmentation gradually disappears in the course of weeks or months.

The above phenomena constitute the positive Schick reaction. There is another reaction, not specific, which sometimes occurs, especially in adults. It is due, not to toxin, but to protein substances in the toxin broth used for the test, and it may be regarded as being due to a hypersensibility of the person in question to foreign protein. This, the pseudo-reaction, when compared with the positive reaction, presents certain distinguishing features: it reaches a maximum in 20 or 30 hours; it begins to fade before 48 hours; it rarely leaves pigmentation or scaling; the colour is a more vivid red; the skin is more infiltrated; there is often a well-marked pink zone round it. In other words, it is a transient inflammatory reaction, as opposed to a persistent specific reaction. It occurs comparatively frequently in adults, more rarely in children. It may be combined with a positive reaction. With a negative reaction, nothing is visible after 24 hours, except, perhaps, an ill-defined red line marking the needle track.

In the early part of 1921, at the suggestion of Dr. Niven, Medical Officer of Health for Manchester, I performed the Schick test upon 1,200 persons, normal and diseased. A detailed account of the technique and an analysis of the results obtained will be found elsewhere; this afternoon I can only mention the more salient features.

To perform the test, one requires a ripened, standardised toxin, a sterile diluting medium, a graduated all-glass 1 c.c. syringe, and a very fine needle. The toxin is diluted with phenol-saline so that 0.2 c.c. of the mixture contains exactly 1/50 M.L.D. This quantity is injected into the skin on the flexor aspect of the forearm. The other arm receives a control injection of heated toxin. (Heating to 75 degrees C. for

ten minutes destroys the toxin content of the solution, but does not affect protein.) Hence a reaction on both arms would denote pseudo; the final result would be positive or negative, according to whether the toxin arm reaction persisted or not. Readings are made at intervals of 24 hours, 72 hours, and ten days.

Among 1,091 cases, normal and diseased, children between the ages of two and five years gave the greatest percentage of positive reactions, the figure reaching 65 in the 3-4 years group. This period of life, 2-5 years, is that in which the incidence of clinical diphtheria is most marked. The agreement between clinical experience and experimental test is significant, and is strong presumptive evidence of the reliability of the Schick test.

Among 650 scarlet fever cases the test gave a slightly higher percentage than 381 normal cases. This again demonstrates the accuracy of the test, for it is a well-known clinical fact that persons suffering from scarlet fever are more susceptible to diphtheria than are normal people. The pseudo-reactions varied directly with age and normality, occurring more than twice as often above fifteen years, and nearly twice as often in healthy people.

Injections of diphtheria anti-toxic serum were given in 109 cases, ranging from 2,000 to over 20,000 units, before the test. Eighty-three out of the 109, or 76 per cent., gave a pseudo-reaction. It would appear that the protein in the serum solution had sensitised the individuals, and rendered them hyper-susceptible to the protein in the toxin solution.

A table was arranged to show the quantity of anti-toxin given to each of the 109 cases, and the time elapsing before the test was performed. The first positive reaction, indicating loss of passive immunity, occurred in the third week. Once more there is agreement with clinical experience. Further, the positive reactions gravitated to that quarter of the table where the factors of small dose and long period acted in unison. No final conclusion can be drawn from the numbers tested, but there is indication that, by means of the Schick test, it would be possible to demonstrate that the larger the quantity of anti-toxin given, the longer would be the duration of passive immunity.

Eighty-four family groups were tested, and it was found that like positive or negative results occurred in 60 groups, or 71 per cent.; but that with pseudo-reactions the reverse was

the case. Fourteen persons out of the total of 1,200 were retested at intervals varying from three to 75 days. Some were borderline cases, and in nearly every instance the different readings for the first test agreed with the corresponding readings for the subsequent test. The final results were always the same. Among fourteen infants under three months, there was only one positive reaction. The mother of this case was positive also.

The above results may be interesting from a purely scientific point of view, but it is when considered in relation to toxin-anti-toxin active immunisation against diphtheria that the Schick test becomes of practical importance. As a result of experiments extending over several years, Drs. Park and Zinger, of the City of New York Health Department, have come to the conclusion that immunity to diphtheria, possibly life-long, can be obtained by the injection of a mixture of toxin and anti-toxin. As a preliminary to such immunisation, it is very desirable to possess a means of distinguishing the naturally immune from the non-immune. To attempt to immunise the whole of the population by means of toxin-anti-toxin injections would, obviously, be impossible. But if some method—safe, reliable, and easy to perform—were discovered which would enable one to distinguish the immune from the susceptible, so that only the latter need be protected; and, further, if it could be shown that the majority of the non-immune were children, who could be immunised conveniently in batches in schools and elsewhere; then a distinct advance would have been made towards the realisation of immunisation upon a large scale. Such a method we do possess in the Schick test. I have pointed out that the majority of non-immunes are, in fact, children; that the test is reliable, I have tried to make clear; that it is safe is shown by the fact that in the whole of my series there was no case of sepsis nor any untoward after-effect; that it is easy to perform; I hope to demonstrate at the close of the meeting.

Since the original papers of Schick and V. Behring in 1913, a great amount of work has been carried out in New York, where tens of thousands of children have been tested and immunised. A detailed account of the methods and results of Park, Zinger, and other workers will be found in the Archives of Pediatrics, vol. 38, No. 6 (June, 1921), and also in the Collected Studies of the New York

Bureau of Laboratories, vol. 9 (1916-1919). Here I will epitomise some of the more important conclusions.

1. All children from six months to five years should be injected with toxin-anti-toxin, without a preliminary Schick test, as most of the children in this age-group give a positive reaction. No child should be pronounced immune until, when tested some months later, it gives a negative Schick reaction.

2. Children under six months should not be injected with toxin-anti-toxin, as they are generally immune (85-90 per cent.).

3. Children above five years should be Schick tested, and the positive reactors immunised.

4. A control of heated toxin should always be used along with the Schick test, in order to facilitate the recognition of pseudo-reactions.

5. In 90 per cent. of the cases injected, toxin-anti-toxin confers immunity to diphtheria for five years at least, probably much longer—possibly for life.

In this country, for information regarding the test and immunisation, we are mainly indebted to Dr. R. A. O'Brien and his co-workers at the Wellcome Research Laboratories. In the "British Journal of Experimental Pathology" for February, 1922, there is a paper by Dr. Moncton Copeman, Dr. O'Brien and his colleagues, showing, among other things, immunisation results for 102 children. Eleven weeks after injection, 98 per cent. gave a negative Schick reaction, and were therefore immune.

With Dr. Moncton Copeman's report to the Ministry of Health, dealing with the test and immunisation, you are all doubtless familiar, and I shall not dilate upon it.

At the Monsall Fever Hospital I have started to immunise the Schick-positive members of the nursing staff. For a variety of reasons the work has progressed slowly, but by the end of the year I hope to have protected all those who are susceptible. Three injections were given at weekly intervals. The mixture consists of toxin which is just under-neutralised with anti-toxin. (Technically, each c.c. contains 3 L + doses of toxin and 3.5 units of anti-toxin. The L + dose is that amount of toxin which, when added to one unit of anti-toxin, will cause the death of a 250 gram guinea-pig, on the fourth day after injection.)

In all, twelve nurses have been inoculated, and ten, or 83 per cent., gave a negative Schick test from one and a half to three months after

injection. In two cases there were rather severe local and constitutional after-effects. Within 24 hours the temperature rose to 103 degrees F., there was headache, vomiting, prostration, and the arm became very inflamed and swollen. These signs and symptoms subsided in two days. I discovered that both these nurses had given a combined positive-pseudo reaction with the Schick test. Thereafter, in every such case, I started with 1/10th of the dose, giving 0.1 c.c. for the first inoculation, increasing it to 0.2 for the second, and 0.5 c.c. for the third; there were no further reactions. With these doses, I believe, there is no danger of such distressing sequelæ. Children are far less liable to local and constitutional reactions. When they occur they are doubtless anaphylactic in nature, being due to foreign protein.

Reference to the last annual report of the chief medical officer of the Ministry of Health will show that both the incidence and mortality of diphtheria have increased during the past four years. In 1920 there were 5,641 deaths from the disease, the majority being young children. When we consider the amount of money spent upon notification, isolation, disinfection, anti-toxin, and upkeep of hospital accommodation, this can hardly be regarded as a satisfactory outcome, and we are bound to consider whether it would be practicable to employ toxin-anti-toxin immunisation for the control of diphtheria. According to American observers, it is possible to confer immunity for at least five years. Even if no more could be accomplished, this in itself would suffice to protect children during that period—1-6 years—when the disease is most prevalent and deadly. But there is reason to believe that immunity, once conferred, will last much longer—possibly for life.

There would seem to be no insuperable difficulty about performing toxin-anti-toxin immunisation on a large scale in this country. According to Sir George Newman, at least 1/6th of the total number of babies born come directly under medical control at the infant welfare centres. The medical personnel is already in existence, and the only thing further required is a supply of toxin-anti-toxin. Other young children could be reached in hospitals of all kinds, orphanages, homes, day nurseries, dispensaries, and finally in their own homes. Use could be made of the school medical service for older children. Here again the

personnel is in existence, the children are under control, and are so situated that the necessary inspections can be made at any time. Already a start has been made at certain hospitals, orphanages and schools, and, in a large measure, it depends upon the action of medical officers of health whether the work shall be greatly extended. Propaganda among the medical profession, municipal bodies, and the general public would be a necessary preliminary, but once medical officers themselves are convinced, the rest will follow.

It is possible that the Schick test may become of importance in the treatment of diphtheria "carriers." In his report to the Ministry of Health, Dr. Moncton Copeman says that the diphtheria bacilli in a majority of otherwise healthy carriers are non-virulent: Dr. O'Brien has recently stated ("Lancet," 1922, I, 227), it is probable that all true carriers of virulent bacilli give a negative Schick response, and that if positive they are incubating the disease. Should these statements be confirmed, the carrier problem will be simplified. Healthy carriers who gave the positive reaction would only need to be isolated for a few days, to make sure they were not incubating diphtheria, and then released on the assumption that they were non-virulent.

As regards expense, 1,000 Schick and control tests can be made at a cost of £20. To immunise 1,000 people would entail an outlay of £300.

In conclusion, the Schick test and toxin-anti-toxin immunisation against diphtheria are still in the experimental stage in this country, and one must not be too sanguine. Yet there are valid reasons for believing that we may be in possession of a method which will not only effectively control the disease, but in the course of time stamp it out. If, as the result of the efforts of the medical officers of the present day, future generations regard diphtheria as we do smallpox, then to those medical officers will belong no small share of the credit for one of the most signal achievements of preventive medicine.

WILLS proved during the past month include those of Dr. James Lawrence, formerly medical officer of health for Darlington (£11,800) and Dr. G. S. Elliston, C.B., formerly medical officer of health for Ipswich (£15,932).

THE PRESENT POSITION OF THE ISOLATION HOSPITAL IN PREVENTIVE MEDICINE.*

BY

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(1) When the policy of isolation in special hospitals was generally adopted between 1880-1890 the so-called major epidemic diseases, smallpox, scarlet fever, diphtheria, enteric fever, and typhus fever both as regards incidence and death rate were a most serious menace, and even in retrospect the policy of setting up isolation hospitals must be justified.

(2) The position to-day is vastly different in certain of these diseases.

(a) *Scarlet Fever.*

The total death rate is 1/20th of what it was in the decade 1870-1880.

The incidence is still high.

The case mortality is only about 1 per cent.

(b) *Enteric Fever.*

The mortality is now only 1/20th of that of 1870-1880.

The severity of the disease, both as regards incidence and death rate is rapidly decreasing.

(c) *Diphtheria.*

The total mortality is as great now as it was between 1870-1880, although the severity of the disease is generally diminished.

(d) *Typhus Fever.*

Has practically disappeared.

(e) *Smallpox.*

In spite of spasmodic outbreaks, only a very few deaths in the past few years, as compared with 5,762 annually between 1871-1880.

(3) In estimating the factors responsible for the reduction of infectious disease incidence and mortality, due weight must be given to the widespread improvements in general hygiene during the past 40 years.

(4) Parson's Report (L.G.B., 1911) gave a modified blessing to isolation policy as practised at present—admitted faults, *e.g.*, cross-infection, overcrowding of wards in epidemics; but claimed some of the credit in the reduction of the mortality of scarlet fever, and advocated up-to-date provision where required, especially of the isolation pavilion or the cubicle system.

(5) From an early period in the history of isolation hospitals there have been active critics of the value of isolation especially as regards scarlet fever; for example—inquiries have proved that the case incidence in non-isolation areas of exactly similar type over a prolonged period has been less than that of areas in the same district which

* Summary of Paper read at the Northern Branch.