

become taciturn, moody, and fitful in temper. Take, for example, a latent sinus case in a girl of 18 or 20; the parents may say that she gets moods and is difficult, but is all right when she takes an interest in things and thinks less of herself. The explanation is that when toxic absorption is marked she cannot interest herself, and cannot be bright and happy and full of life. All sinus infections are prone to be more active at the time of menstruation, which fact accounts for increased symptoms corresponding to the period in such cases. If the poisoning be continuous the patient is permanently altered in character, and in her outlook on life; she becomes a neurasthenic. Again, a business man who has been quick, mentally alert, and able to initiate and control a large business under similar conditions becomes neurasthenic, loses his initiative, feels he has to let things slide, worries over trifles, and becomes depressed.

Quite a large proportion of neurasthenic patients are puzzling unless one seeks and finds some definite cause of toxic absorption accounting for altered character and mentality. Such neurasthenic phenomena may be due to mental strain—e.g., at the front, in business, or from home anxieties—but I believe that many of these would not succumb were it not that toxic absorption rendered them susceptible to adverse environment. We all realise that the gastro-intestinal tract, pyorrhoea, or a weak heart action—e.g., that following diphtheria—may be the source of trouble. While not failing to look for such possible causes, let us remember that in the nasal sinuses, once persistent infection is established, the pyogenic organisms find a happy home and breeding ground; these infected sinuses become perfect physiological culture-tubes, maintained at blood heat with a never-failing pabulum.

Nor do the mental aberrations stop at neurasthenic symptoms, and slight alterations in character and mental alacrity. The depression that is so constant a manifestation of sinus infection may be so dominating as to cause melancholia and suicidal impulses, or mental delusions. The subjective foul odour that is a common symptom of antral and other sinus suppurations is an annoyance to the sane, but is probably one of the causes of olfactory illusion that the alienist accepts as a symptom of insanity.

CONCLUSION.

How are we to diagnose and at least be led to suspect nasal infection as the cause of such symptoms? The existence of a persistent or recurrent purulent catarrh may be obvious or elicited by inquiry, but the non-purulent discharge is apt to be ignored by the patient, and must be sought for. The neurasthenic symptoms are usually worse in the morning on waking, or for the first hour of two after rising; they are often periodic, and better in warm dry weather, worse in cold and damp, and always aggravated by intercurrent colds. But the history of the case may reveal many facts which point to a source of recurrent infection; headache or heaviness, recurring sore-throats, muscular rheumatism, rheumatoid arthritis, gastro-intestinal catarrh, appendicitis, are so frequently associated with a chronic sinus infection that their interdependence is sometimes hardly open to doubt. Although these incidents in the patient's life may have occurred long previously, one must remember that a sinus infection may be of some years' standing, and a constant source of ill-health, without seriously arresting the patient's notice. Often enough the existence of a latent nasal catarrh can only be determined by direct inspection of the nasal passages anteriorly and posteriorly, and perhaps only by passing a fine cannula into the sinuses, and washing out or sucking the contents back into a sterile syringe, and submitting them to bacteriological examination and culture. In many cases the health or happiness of the individual is at stake, and in the absence of other causes no stone should be left unturned to determine the existence or otherwise of a sinus infection.

THE SCHICK TEST

FOR THE DETERMINATION OF SUSCEPTIBILITY TO DIPHTHERIA: A RECORD OF 1200 CASES.¹

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A STUDY of the tables and charts contained in the Metropolitan Asylums Board Report for 1919-20 would seem to indicate that there has been no decline in the incidence of diphtheria in London during the past 30 years. Reference to the annual report of the Chief Medical Officer to the Ministry of Health, 1919-20, p. 29, shows that the case rate for diphtheria per 1000 population, England and Wales, has remained stationary during the past decade. At present, however, there are indications that it may be possible to establish a system of active immunisation against diphtheria which, in time, will result in its final disappearance. Park and Zingher,³ of the city of New York Health Department, as the result of experiments extending over several years, conclude that immunity to diphtheria, possibly life-long, can be obtained by injecting subjects with small doses of diphtheria toxin-antitoxin mixture. From the researches of Schick¹ and others it has been known for some time that certain individuals possess natural immunity to diphtheria by virtue of an antitoxin circulating in their blood serum. To attempt to immunise the entire population by toxin-antitoxin injections obviously is impossible. But if some method could be found which would enable one to distinguish the naturally immune from the non-immune, so that only the latter group need be immunised; further, if it could be shown that more than half the population do possess natural immunity, and that the majority of the non-immune were children, who could be conveniently immunised in batches—then a distinct advance would have been made towards the realisation of immunisation upon a large scale. Such a method or test, a necessary step in the control of diphtheria, has been devised by Schick. He has found that the intracutaneous injection of a minute dose of diphtheria toxin is followed by a skin reaction if the person be not immune to diphtheria. If such person be immune, then there is no skin reaction; the antitoxin circulating in the blood serum of persons naturally immune neutralises the toxin injected into the skin, and nothing happens. If there is no antitoxin in the blood-serum the unneutralised toxin exerts an irritant action on the skin, producing the clinical sign known as the positive Schick reaction. This test is safe, for in my series of 1200 cases there was no single instance of sepsis, or untoward after-effect of any description; it is easy to perform; only a little practice being required to enable one to make intracutaneous injections with ease and facility. That the test is reliable I hope to demonstrate in the course of the paper. Results obtained in different series of tests will be found in papers indicated in the bibliography.

Method of Test and of Recording Results.

The toxin solution for the test was obtained from the Burroughs Wellcome Research Laboratories, London. It is sent out in sealed phials, each containing 1 c.cm. of diluted toxin. The dilution is 1 in 500 in 0.7 per cent. saline containing 0.5 per cent. phenol. It is made up fresh each week and tested each week on the skins of guinea-pigs. It is a ripened toxin, and standardised so that its minimum lethal dose (M.L.D.) is accurately known. The M.L.D. is that amount of toxin which, in four days, will kill a guinea-pig of 250 g. weight. The dilution is such that 0.2 c.cm. contains exactly one-fiftieth part of an M.L.D., and this is the amount used for one injection. The control injection was put up in similar sealed phials, marked to distinguish it from the toxin. The control is toxin heated to 75°C. for

¹ Abstract of a thesis submitted in May, 1921, for the degree of Doctor of Medicine at the Victoria University of Manchester.

10 minutes in order to destroy the active toxin, but not the protein constituents of the solution. The syringe used was all glass, 1 c.cm. in capacity, graduated into tenths. The needle was Burroughs Wellcome No. 1 dental needle, about 0.5 of a millimetre in diameter.

Technique.—In every case the injection was made into the right forearm, and a control injection into the left forearm. The skin of the anterior aspect of the forearm just below the elbow-joint was cleaned with ether. The needle and syringe having been boiled, the neck of the phial was broken off and the contents drawn up into the syringe. In order to make the skin taut, and thus facilitate intra- instead of sub-cutaneous injection, the arm was grasped from behind by the left hand, the thumb and fingers pulling backwards, thus putting the skin on the stretch. The needle, bevelled surface uppermost, was then thrust into the skin, until $\frac{1}{4}$ to $\frac{1}{2}$ of an inch had passed in, care being taken so to guide it that the whole of the portion within the skin showed through the superficial epidermis as a blue line. The needle being in position within the skin, bevel uppermost, the left hand was brought round to steady the head of the needle, whilst with the right hand the piston was pressed home until just 0.2 c.cm. of toxin solution had been injected. The needle was then withdrawn, and the puncture immediately sealed with collodion and gauze. There was always a feeling of resistance when pressing down the piston, most pronounced in infants, possibly because of the more closely-set texture of their skin. When there were several tests to do in the same ward, the needle at this stage was disengaged from the nozzle of the syringe, placed in methylated spirit, a fresh sterile needle placed on the syringe, and the next 0.2 c.cm. injected into the next patient. This process was repeated until all the right arms of all the cases had been injected. Usually a dozen needles were in use, being transferred to methylated spirit, then syringed through with sterile water, ready to be used again. The left arms were then injected intracutaneously in the same manner with the heated toxin, or control solution. A different sterilised syringe was used, the needles boiled up again, and fresh methylated spirit and sterile water used, so that there was no possibility of any mixture, even in enormous dilution, of toxin solution with control solution.

When the injection was made, there immediately appeared a raised white urticarial area or wheal, one to two centimetres in diameter. In this the openings of the glands showed very distinctly. There is a momentary sensation of pain as the point of the needle enters the skin, and a slight burning sensation when the solution is injected. For some reason which I have not been able definitely to determine, the burning sensation was nearly always more pronounced in the case of the control injection into the left arm. This was so in my own case: some volunteered this information, and others gave it when asked which was the more painful injection. But, generally speaking, the injection is practically painless. Children up to the age of 9 or 10 often cried, but this was due to fear aroused by the sight of the needle more than to actual pain. Infants a few days old often evinced no displeasure. There was no sign of sepsis in any one of the 2400 injections. An important point is to make sure that there is no leakage, either below into the subcutaneous tissue, or externally on to the surface of the skin. This happened a few times, especially during the first injections, and in every case a fresh injection was made well away from the previous attempt. If the puncture is sealed with collodion and gauze this should be removed in two or three hours, otherwise a meshwork imprint is left on the skin, and this tends to obscure any reaction which may follow, especially if it be faint.

Record.—In every case the date of the test was marked on the patient's chart, and also the dates for taking readings at intervals of 24 hours, 72 hours, and 10 days. At each of these periods an inspection of each arm was made, and results noted on the back of the chart. In addition, special records were kept.

Readings.—I made an inspection of both arms of each case 24 hours, 72 hours, and 10 days after the test was made. Many cases were seen more frequently, a good number of especially interesting or anomalous cases every day for ten days, and again at varying intervals up to one month. In the vast majority the result of the test was evident when the 72 hours reading was taken, but in no case was the final result entered until after the ten days reading. Two patients left hospital before readings were completed, but came up on the tenth day for me to inspect their arms. The only exception to the above routine was made in the case of patients who died before the tenth day after the test. In all, eight patients died out of the number tested—four within three days of making the test, and these are not included in the series. Four died from three to eight days after the test; all were negative up to the time of death, and are included in the series.

The Positive Reaction.

At the site of injection the toxin arm presents the following appearance. In 24 hours there is an area 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 mm., usually 15 to 25. Usually there is no pain, itching, or any feeling of discomfort. The reaction is at its height from 48 to 72 hours after the test. At this stage all the above features are unmistakably present. About the end of the first 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. In one of my cases (No. 628) the skin was detached in one piece the size of a sixpenny coin (20 mm. in diameter). Very occasionally scaling occurs as early as the third day, or may be delayed until the end of the second week. After the scaling is completed the brown pigmentation gradually disappears.

Variations in the Positive Reaction.

The foregoing is a description of the course and stages of a typical positive reaction. The following is an account of the main variations of the positive reaction observed in 1091 cases. In discussing the variations of the positive reaction, and in stating the respective percentage numbers, 109 cases which previously had diphtheria antitoxin are not taken into account. One effect of the previous administration of antitoxin is to abolish the positive reaction, hence a percentage based on a total which included the antitoxin cases would be misleading.

1. *Delayed Reactions.*—Schick¹ states that with occasional solutions of toxin, 48 hours have to elapse before a definite reaction occurs. In the present series, such cases numbered 154, or 14.1 per cent. They occurred in normal cases, and in every disease except puerperal fever, and with every batch of toxin; 147 were delayed one day, 6 delayed four days, and in one case (No. 230) five days elapsed before a positive reaction appeared. It afterwards went through the characteristic changes, the whole sequence being delayed five days. No feature about the case suggested any explanation of the anomaly. A consideration of the above group emphasises the necessity of waiting till all the readings have been taken before arriving at a definite conclusion as to the result of the test.

2. *Abnormal Pigmentation.*—In ten, or 0.9 per cent. of cases, a very marked purplish-red or dark plum colour developed. This abnormal pigmentation was not fully evident until the tenth day, except in one case when it appeared on the third day. Here the reaction was very intense, and accompanied by vesiculation. Four reactions were delayed one day in all cases of scarlet fever.

3. *Massive Scaling.*—This occurred in two cases. Both were children (females) with scarlet fever.

Different batches of toxin were used. In the more remarkable case the epidermis peeled off in one piece measuring 20 mm. in diameter.

4. *Vesiculation*.—This occurred in three cases on the third day. All were children, and cases of scarlet fever.

TABLE I.—Results for 1091 Cases.

The table shows the age-distribution of the positive reactions in 1091 cases—viz., scarlet fever, 650; typhoid fever, 13; puerperal fever, 28; erysipelas, 19; normal, 381.

Age in years.	Total	Pos.	Neg.	% Pos.	Age in years.	Total	Pos.	Neg.	% Pos.
0-1	20	6	14	30.0	6-8	134	75	59	55.9
1-2	10	6	4	60.0	8-10	112	51	61	45.5
2-3	33	19	14	57.5	10-15	228	99	129	43.4
3-4	40	26	14	65.0	15-20	86	21	65	24.4
4-5	36	22	14	61.6	20 and over	335	136	199	40.6
5-6	57	31	26	54.3					
					Total	1091	492	599	45.09

Table I. shows the age-distribution of the positive reactions for 1091 cases. It will be seen that the greatest percentage of positive reactions occurs between the ages of 3 and 4 years—i.e., in the fourth year of life; that the second, third, fourth, and fifth years of life stand out from the other years; that the first year and the tenth year and over are below the average. The above figures afford important evidence of the reliability of the Schick test, for the age-groups which give the greatest number of positive reactions exactly coincide with the age-period when the incidence of clinical diphtheria is most marked. Ker¹⁷ states that the disease is most frequent during the period from 2 to 5 years. In London, during 1919, the greatest number of diphtheria notifications were of children between the ages of 4 and 5 years.¹⁸ In the annual report on the health of the City of Manchester for 1919,¹⁹ a table is given which shows that the number of attacks is highest at the ages 3 to 5. Zingher¹⁴ gives a table, which I reproduce, showing the age-incidence of 2711 cases of diphtheria admitted to Baginsky's Children's Hospital in Berlin between 1890-1897. (Table II.)

TABLE II.—Age-Incidence of 2711 Cases of Diphtheria admitted to Baginsky's Children's Hospital, Berlin, 1890-1897.

Age.	No. of cases.	Per cent. of total of cases.	No. of deaths.	Death-rate	
				per 100 admissions.	at each age-period.
0-6 mths. . .	15	0.55	4	0.15	26.6
6-12 " . .	69	2.50	36	1.32	52.2
1-2 years . .	227	8.30	110	4.06	48.4
2-3 " . .	317	11.60	119	4.30	37.5
3-4 " . .	354	13.05	121	4.40	34.2
4-5 " . .	337	12.40	84	3.09	24.9
5-6 " . .	264	9.70	61	2.25	23.1
6-7 " . .	280	10.30	61	2.25	21.8
7-8 " . .	209	7.70	26	0.95	12.4
8-9 " . .	175	6.40	23	0.84	13.1
9-10 " . .	146	5.30	19	0.70	13.0
10-11 " . .	101	3.70	9	0.33	8.9
11-12 " . .	80	2.90	8	0.29	10.0
12-13 " . .	65	2.40	7	0.25	10.8
13-14 " . .	72	2.65	6	0.22	8.3
Total . .	2711	—	694	—	Av. 25.6

It will be seen that the greatest number of cases occurred from 2 to 5 years. I submit that the close agreement between the results of over 1000 tests and the statistics relating to the age-incidence of diphtheria sufficiently demonstrates the reliability of the Schick test.

The Pseudo-Reaction.

Schick¹ described an inflammatory reaction not due to diphtheria toxin and differing from the reaction caused by it. He ascribed it to a hypersensibility of the person in question to protein substances in the solution of diphtheria toxin. Zingher¹³ states: "The

pseudo-reaction depends on a hypersusceptibility of the tissue cells of individuals to the autolysed protein of the diphtheria bacillus which is present in the toxin broth used for the test. The reaction is, therefore, of the nature of a local anaphylactic response." The pseudo-reaction is clinically differentiated from the positive reaction by the following features: it reaches a maximum in 20 or 30 hours; it begins to fade before 48 hours; it may occasionally leave faint pigmentation and occasionally scales; its colour is a more vivid red; the skin is more infiltrated; there is often a well-marked pink zone round it. To sum up, it is a transient inflammatory reaction as compared with a persistent specific reaction. It occurs comparatively frequently in adults, more rarely in children. It may be combined with a positive reaction.

In every case in this series a control injection of heated toxin was made into the left arm. Heating the toxin to 75° C. for 10 minutes destroys the toxin content, but leaves unaffected the protein content. Hence in every case the right arm was injected with toxin plus protein, the left arm with protein only. Any reaction in the left, or control, arm must be due to protein only; a reaction in the right arm may be due to toxin or protein alone or to toxin plus protein. Hence a reaction in both arms indicated a pseudo-reaction. In order to see whether this was combined with a positive reaction it was necessary to wait one or two days. In the case of a pseudo-reaction only the reaction would fade equally from both arms. In the case of a combined positive and pseudo-reaction the left or control arm would clear up quickly, while the right or toxin arm would pass through the characteristic stages of the positive reaction. (It is possible after some experience with the test to differentiate the two reactions without using a control, but it is always safer to use one.) With a negative reaction nothing is visible after 24 hours, except perhaps an ill-defined red line marking the needle track.

Variations in the Pseudo-Reaction.

1. *Persistent Pseudo-reactions*.—One of the distinguishing features about the pseudo-reaction is its rapid disappearance in three or four days. Out of a total of 222 pseudo-reactions (including the diphtheria cases) 10, or 4.5 per cent., persisted for longer than a week; the 263 batch of toxin was used in each case and all results were negative. (Table III.)

TABLE III.

No.	Sex.	Age.	Disease.	No.	Sex.	Age.	Disease.
241	F	10	Scarlet fever.	301	M	22	Typhoid.
260	F	30		303	M	16	Nil.
270	F	31		304	M	40	Typhoid.
293	F	22	Puerperal fever.	305	M	55	Nil.
296	F	21	Typhoid.	310	F	17	Erysipelas.

Laboratory tests with batch 263 did not reveal any difference between this and the other 14 batches used.

2. *Scaling Pseudo-reactions*.—Out of 222 pseudo-reactions, 15, or 6.7 per cent., showed definite scaling. This anomaly might easily lead to confusion between a pseudo-reaction and a true reaction if toxin only and not control also were used in the test.

The following comparison is intended to show the differences between the true and the pseudo-reaction.

True (or Positive) Reaction.

1. Colour: medium to dark red.
2. Size: usually 15-25 mm. in diameter.
3. Areola: seldom present.
4. Infiltration: slight.
5. Height of reaction: third day.
6. Fades slowly, with pigmentation and scaling at tenth day.

Pseudo-reaction.

1. Colour: brighter red.
2. Size: usually more than 25 mm. in diameter.
3. Areola: often marked.
4. Infiltration: more marked.
5. Height of reaction: 20 to 30 hours.
6. Fades quickly; rarely pigmentation or scaling; usually little or no trace after three or four days.

Effect of Age and Disease on the Pseudo-Reaction.

Table IV. shows all the cases except diphtheria, arranged to show the influence of age and disease on the pseudo-reaction.

TABLE IV.

Scarlet fever.				Normal.			Erysipelas, puerperal and typhoid fevers.		
Age in years.	Total No.	Ps.	% Ps.	No.	Ps.	% Ps.	No.	Ps.	% Ps.
0-1 ..	2	0	0.0	18	2	11.1	—	—	—
1-2 ..	6	0	0.0	4	0	0.0	—	—	—
2-3 ..	28	2	7.1	5	1	20.0	—	—	—
3-4 ..	40	2	5.0	—	—	—	—	—	—
4-5 ..	30	5	16.6	6	0	0.0	—	—	—
5-6 ..	54	5	9.2	3	0	0.0	—	—	—
6-8 ..	123	15	12.1	11	0	0.0	—	—	—
8-10 ..	98	9	9.1	14	0	0.0	—	—	—
10-15 ..	152	13	8.5	75	5	6.6	1	0	0.0
15-20 ..	47	3	6.3	30	4	13.3	9	1	11.1
20 and over	70	7	10.0	215	56	26.0	50	9	18.0
Total	650	61	9.38	381	68	17.84	60	10	16.66

Ps. = Pseudo.

As regards age, the result is as follows:—

	Cases.	Pseudo.	% Pseudo.
Total below 15 years ..	670	59	8.8
Total 15 years and over ..	421	80	19.0
Totals ..	1091	139	12.7

It will be seen that the percentage of pseudo-reactions above the age of 15 years is more than twice that under 15 years.

The following is the summary with regard to health and disease:—

	Cases.	Pseudo.	% Pseudo.
Normal ..	381	68	17.8
All diseases ..	710	71	10.0
Totals ..	1091	139	12.7

The pseudo-reaction occurs nearly twice as often among normal cases as among those with enteric fever, erysipelas, puerperal fever, and scarlet fever taken as a whole.

Scarlet Fever Cases.

Among 650 scarlet fever cases, the positive percentage curve closely followed that for the 1091 combined cases, but the total percentage was slightly higher—viz., 47.38 as against 45.09. The cases are sufficiently numerous to warrant the suggestion that scarlet fever tends, very slightly, to increase susceptibility to diphtheria. The "pseudo" rate was 9.38 per cent. Eleven cases had doses of antistreptococcic serum, varying from 40 to 280 c.cm., before the test was made. Of the 11, only one was positive, giving a percentage rate of 9.09, or less than one-fifth that of the total scarlet rate. The numbers are too few to warrant one making any definite statement, but there is a suggestion that the previous administration of antistreptococcic serum tends to inhibit the development of a positive Schick reaction. Three cases out of the eleven, or 27.27 per cent. gave a pseudo-reaction, and this is three times the total scarlet fever pseudo percentage rate. Later it will be pointed out that the previous administration of anti-diphtheritic serum greatly increases the percentage of pseudo-reaction in the Schick test, and should further experiments establish the same conclusion in the case of anti-streptococcic serum, it would be reasonable to assume that in both cases the phenomenon is in the nature of a local anaphylactic response, to a foreign protein, of tissue cells previously super-sensitised likewise by a foreign protein.

Effect of Toxæmia on the Schick Test.

Twenty-one of the 650 cases, or 3.2 per cent., were examples of "scarlatina anginosa," and markedly toxic. Four were positive, giving a percentage of 19.0, as compared with the total scarlet fever average of 47.38. Among these 21 cases, therefore, there is a marked depression of the positive percentage rate, and this agrees with the statement of Schick¹ that toxic individuals tend to give a negative reaction. Four cases, or 19.0 per cent., gave a pseudo-reaction, and three of them had anti-streptococcic serum.

Typhoid Fever, Puerperal Fever, and Erysipelas.

The following numbers were tested:—

	Cases.	% Pos.	% Pseudo.
Typhoid ..	13	15.38	30.76
Puerperal fever ..	28	17.85	3.57
Erysipelas ..	19	26.31	26.31

An analysis discloses certain suggestive features.

Typhoid Fever.—The outstanding feature is the high percentage of pseudo-reactions. Four cases out of 13, or 30.7 per cent., gave a pseudo-reaction. Further research will show whether this is a coincidence or a permanent feature. There were no combined reactions.

Puerperal Fever.—Of 28 cases, only one, or 3.5 per cent., gave a pseudo-reaction. Further, of 17 cases which had antistreptococcic serum, not one gave a pseudo-reaction. This is the reverse of the tendency exhibited by the scarlet fever cases which had antistreptococcic serum. A possible explanation lies in the fact that most of these cases had suffered from uterine hæmorrhage, often severe, for several days before admission, and at the time the test was performed were in an anæmic, asthenic condition. Their tissue cells, therefore, were to some extent devitalised and not so liable to react to the injection of a foreign protein substance.

Erysipelas.—These cases show an identical positive rate and pseudo rate. Taking the positive percentages, that of erysipelas considerably exceeds the other two diseases. So far as the numbers go, then, there is an indication of a high pseudo-reaction rate among cases of enteric fever and erysipelas, and a low rate with cases of puerperal fever.

Normal Cases.

It was extremely difficult to obtain normal children below the age of 10 years upon whom to perform the test. For infants I had to depend upon the babies who were admitted along with mothers suffering from puerperal fever. A few normal children from 6 months to 2 years were found among child welfare cases in the hospital creche; to these were added several instances of healthy children admitted to hospital as cases of scarlet fever or diphtheria. Permission, unfortunately, could not be obtained to do the test in schools where there is plenty of material. Among 381 normal cases, the total positive percentage rate was 45.14, and the pseudo rate 18.37. The greatest number of positives was found between the ages 1-10 years, and the greatest number of pseudo reactions at 20 years and over.

Influence of Vaccines on the Test.

Nineteen of the cases had been vaccinated (Table V.).

TABLE V.

Case No.	Sex.	Age.	Vac-cine.	Result.	Case No.	Sex.	Age.	Vac-cine.	Result.
216	M	32	Ty.	P. († ps. 24 hrs.)	631	F	21	Ty.	N.
316	F	20	"	N. ps.	699	F	24	"	P.
380	F	26	"	P. († ps. 24 hrs.)	700	F	20	"	N. ps.
					704	F	25	"	P. ps.
422	F	20	"	N. ps.	771	F	22	"	N. ps.
458	F	21	"	N. ps.	780	F	27	"	P.
460	F	21	"	N. ps.	782	F	23	"	P.
462	M	26	Dy.	P. ps.	783	F	21	"	N.
467	F	23	Ty.	N. ps.	786	F	24	"	P.
619	F	24	"	N.	814	F	20	"	N.

Ty. = typhoid. Dy. = dysentery. P. = Positive.
N. = negative. ps. = pseudo.

The positive percentage rate is 42.1, and the pseudo-reaction percentage rate is 47.3. Compared with the combined normal and disease ratio, there is nearly a five-fold increase in the pseudo-reaction percentage. This very strongly suggests that the effect of vaccines on the test is to raise markedly the pseudo-reaction percentage. Again, this effect is probably due to super-sensitisation by foreign protein.

The Test in Infancy.

Sixteen children under 6 months gave the result:—

Total.	Pos.	Neg.	% pos.	Pseudo.
0-6 mths. 16 ..	3 ..	13 ..	18.7 ..	2 12.5

Among 14 cases under 5 months, there was only one, or 7.1 per cent., positive. The mother of this case was also positive. Thus infancy diminishes both the positive and the pseudo-reaction percentages.

The Test and Diphtheria Antitoxic Serum.

One hundred and nine cases had injections of diphtheria antitoxic serum before the test, viz:—

Diphtheria	85
Scarlet fever, and diphtheria plus scarlet fever	18
Normal	6

These cases showed a very high percentage of pseudo-reactions: 83 out of 109 cases, or 76.14 per cent., gave the reaction. The protein in the serum solution had apparently sensitised the individuals, and rendered them hyper-susceptible to the protein in the toxin solution. The first positive reaction, indicating loss of immunity, occurred in the third week. No final conclusion can be drawn from the number tested, but there is an indication that, by means of the Schick test, it would be possible to demonstrate that the larger the quantity of antitoxin given, the longer would be the duration of immunity (Table VI.).

Effect of Diphtheria Antitoxin given after the Test.—Diphtheria antitoxin was given subsequent to the performance of the test in one instance. This patient received 8000 units 24 hours after the test. No impression was made on the definite positive reaction which had by that time developed.

For some months past I have been immunising the nursing staff of the Monsall Hospital with toxin-antitoxin mixture, and I hope to submit a paper on the subject when a sufficient number of cases has been collected.

For permission to publish the results, I am indebted to Dr. James Niven, medical officer of health for Manchester, at whose instigation the work was undertaken; my thanks are also due to Dr. William Park, of the New York Health Department; to Dr. R. A. O'Brien, of the Wellcome Research Laboratories; to Dr. C. B. Ker, of the City Fever Hospital, Edinburgh, for letters of advice and help; and to the committee of the Manchester and Salford Boys' and Girls' Refuges, for permission to perform the test upon members of their orphanage.

TABLE VI.

Cases which had diphtheria antitoxin arranged to show duration of immunity. The first column shows the interval of time in weeks between the administration of diphtheria antitoxin and the test with toxin.

Thousand units.	2		4		8		10		12		16		18		20		Over 20		Total	% pos.
No. of cases.	3		3		48		5		18		22		2		3		5		109	
Interval in weeks.	P.	N.	P.	N.	P.	N.	P.	N.	P.	N.	P.	N.	P.	N.	P.	N.	P.	N.		
1	—	—	—	—	—	7	—	1	—	5	—	5	—	—	—	1	—	—	19	0
2	—	1	—	2	—	12	—	—	—	1	—	2	—	—	—	—	—	—	18	0
3	—	1	—	—	1	7*	—	—	—	1	—	4	—	1	—	—	1	—	16	6
4	—	—	—	—	—	1	—	1	—	3	—	4	—	—	—	—	1	—	10	0
5	—	—	—	—	—	4*	—	2	—	1	—	2*	—	—	1	—	—	—	10	0
6	—	—	—	—	—	2*	—	—	—	1*	—	1	—	1	—	—	2	—	7	0
7	—	—	—	—	1	2	—	—	—	1	—	1	—	—	1	—	—	—	6	16
8	—	—	—	—	—	—	—	—	—	2	—	1	—	—	—	—	—	—	6	0
9	1	—	—	—	—	2	—	—	—	2	—	1	—	—	—	—	—	—	6	16
10	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	2	100
11 and over	—	—	1	—	5	1	—	1	—	1	—	—	—	—	—	—	1	—	9	66
Per cent. pos.	33		33		14		0		0		4		0		0		20			

P=positive reaction. N=negative reaction. *=1 case doubtful.

Effect of Consanguinity on the Test.—Excluding the diphtheria cases, 84 family groups were tested, as follows:—

Two in a family .. 74 groups.	Five in a family 1 group.
Three „ „ 8 „	Eight „ „ 1 „

The results were:—

Total.	Pseudo.
Like .. 60 = 71.4 %	Like .. 4 = 28.5 %
Unlike .. 24 = 28.5 %	Unlike .. 10 = 71.4 %

(A like pseudo-reaction means that all the members of the family gave a pseudo-reaction, irrespective of their agreement or otherwise in the positive test. Conversely, they might all have given the same positive test, but one has given a pseudo-reaction, and the others not, in which case they are classed as "unlike" for the pseudo-reaction section.) From this one may deduce that members of the same family tend to give the same positive or negative reaction, but do not agree in their pseudo-reactions. Zingher¹⁶ came to the same conclusion after an analysis of 93 groups.

Cases Re-tested.—Fourteen cases out of the total of 1200 were re-tested at intervals varying from 3 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.

Duration of Potency of Toxin.—With five of the cases re-tested a batch of toxin was used which had been kept on ice for five months. The results agreed with those obtained by the fresh toxin, except that in one or two cases the positive reactions were very slightly fainter, and the pigmentation did not last quite so long. A possible explanation of this is that the minute amount of toxin in the test dose is enough to produce a slight increase in the patients' immunity, and cause the just perceptible decrease in intensity of the second series of reactions.

Bibliography.

1. Schick, B.: Die Diphtherietoxin-Hautreaktion des Menschen als Vorprobe der Prophylaktischen Diphtherieheilserum-injektion, München. med. Wehnschr., 1913, ix., 2608.
2. Park, William H., Zingher, Abraham, and Serota, Harry M.: The Schick Reaction and Its Practical Applications, Arch. Pediat., 1914, xxxi., 481.
3. Park, W. H., and Zingher, A.: Active Immunisation in Diphtheria, Jour. Am. Med. Assn., 1914, lxiii., 859.
4. Bundesen, Herman N.: Schick Reaction, Jour. Am. Med. Assn., 1915, lxiv., 1203.
5. Moody, Ellsworth E.: The Intradermic Diphtheria Toxin Test, Jour. Am. Med. Assn., 1915, lxiv., 1206.
6. Kolmer, John A., and Moshage, Emily L.: The Schick Toxin Reaction for Immunity in Diphtheria, Am. Jour. Dis. Child., 1915, ix., No. 3.
7. Kolmer, J. A., and Moshage, E. L.: A Note on the Occurrence of Pseudo-reactions on the Skin, Jour. Am. Med. Assn., 1915, lxv., 144.
8. Weaver, G. H., and Maher, L. K.: The Diagnostic Value of Intracutaneous Injection of Diphtheria Toxin (Schick Reaction), Jour. Infect. Dis., 1915, xvi., No. 2.
9. Linenthal, H., and Rubin, S. H.: The Use of the Schick Test in a Children's Institution, Boston Med. and Sur. Jour., 1915, clxxiii., No. 12.
10. Levinson, A., and Blatt, M. L.: Studies in the Schick Diphtheria Reaction, Arch. Diag., 1915, viii., No. 3.
11. Neff, Frank C.: The Recent Methods of Treating Diphtheria, Jour. Am. Med. Assn., 1915, lxv., 585.
12. Moffatt, R. D., and Conrad, Arthur C.: Observation on the Intracutaneous Reaction of Schick in 455 Infants and Children, Journal of the American Medical Association, 1915, xv., 1010.
13. Zingher, A.: Further Studies with the Schick Test, Arch. Int. Med., 1917, xx., 392.
14. Zingher, A.: Active Immunisation of Infants against Diphtheria, Am. Jour. Dis. Child., 1918, xvi., 83.
15. Leete, H. Mason: The Schick Reaction for the Determination of Susceptibility to Diphtheria, THE LANCET, 1920, i., 192.
16. Zingher, A.: The Accuracy of the Schick Reaction, Jour. Am. Med. Assn., 1920, lxxv., 1333.
17. Ker, Claude Buchanan: Infectious Diseases, A Practical Text-book, Second Edition, 1920, 373.
18. Annual Report, 1919-20, Metropolitan Asylums Board, 87.
19. Niven, James: Report on the Health of the City of Manchester, 1919, 96.