SCHICK IMMUNITY AFTER ACTIVE IMMUNIZATION COMPARED WITH THAT FOLLOW- ING DIPHTHERIA

BY

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The Schick-negative rate has been used extensively as an index of the relative value of the various methods of immunization in common use. It occurred to me that it might be instructive to compare the Schick-negative rate after immunization with that following an attack of diphtheria. Accordingly, I proceeded to Schick-test two comparable groups of school children. One group (hereafter called the immunization group) was composed of children who had been immunized some time between 1930 and 1935. The other group (the diphtheria group) was composed of children who had had an attack of diphtheria, also between 1930 and 1935. All the children tested were Blackburn elementary school children and all had lived in the borough for at least three years, and the vast majority for much longer periods, so that it is reasonable to assume that these children throughout most of their lives had been equally exposed to infection with the diphtheria bacillus. The two groups were comparable in regard to age and sex.

The Investigation

Burroughs Wellcome's Schick material was used throughout, a control being done in each case, and the Schick-testing and reading were all carried out by me. The result was read exactly seventy-two hours after the test, and again at intervals of twenty-four hours until a definite conclusion could be arrived at.

Previous records of immunization were available for every one of the children in that group, and showed that in 1930 and early in 1931 the immunizing agent used was T.A.M. in three weekly doses of 1 c.cm., whereas throughout the remaining period under review the children received three weekly doses of 1 c.cm. T.A.F. All the children immunized before 1934 had received a post-Schick test three to six months after the last injection, and in all the children concerned this had been recorded as negative. Similarly, the hospital case sheets were available for the majority of the diphtheria group and gave clear proof of infection. Where the case sheet was not available the child was only accepted as having had diphtheria if the length of stay in a diphtheria ward had been at least one month. The latter assumption is open to criticism, but I consider the time period a reasonably adequate safeguard. The results of the investigation are given in Table I.

TABLE I

	Immunization Group			Diphtheria Group		
	Schick-tested	Neg.	Pos.	Schick-tested	Neg.	Pos.
1930	17	17	0	14	7	7
1931	24	22	2	6	5	1
1932	16	13	3	9	7	2
1933	23	22	1	13	10	3
1934	14	12	2	22	17	5
1935	16	16	0	28	22	6
Totals ..	110	102	8 (7%)	92	68	24 (25%)

The high figure of Schick-positive children in the diphtheria group is all the more remarkable as fifteen of the children had also been immunized, thirteen of these now being Schick-negative and two still Schick-positive.

Several other workers have Schick-tested individuals after diphtheria, and the results of a perusal of recent literature are shown in Table II. My own figures are included for easy comparison.

TABLE II

Investigator	No. of Individuals Schick-tested	Interval after Diphtheria	Percentage Positive
Dudley (1923)	50	3-6 months	16
Ker and McGarrity (Joe, 1938), 1924	157	Individuals with a previous history of diphtheria	46.4
Benson (Joe, 1938), 1924	245	" "	48
Joe (1938), 1931 ..	68	4-8 weeks	11.7
Dwyer (1938) ..	12	5-6 "	25
Pygott (1938) ..	87	6-24 "	10
Pulley and Fleisher (1938)	96	Students aged 22 to 27 with a previous history of diphtheria	27
Warin	92	3-8 years	(19% also immunized) 25

Discussion

My results show a Schick relapse rate which is three times greater in children who have had an attack of diphtheria than in children who have been actively immunized against diphtheria, and in all the other results quoted there is an unexpectedly high Schick relapse rate. Does this mean that immunization against diphtheria gives better protection than an attack of the natural disease? Definitely this is not a safe deduction to make, because the Schick test is not an entirely reliable method of testing a person's susceptibility to diphtheria. It is now realized that it is the capacity of the tissues of the body to produce antitoxin in response to a suitable antigenic stimulus which is the true measure of protection, and not the amount of circulating antitoxin in the blood. For instance, a person with little or no circulating antitoxin, and therefore probably Schick-positive, may by reason of a maximum tissue response to a minimum stimulus be far better protected than a Schick-negative individual whose tissues cannot make such an adequate response. Allowing for the limitations of the Schick test, however, one may draw the conclusion that in this series immunization produced at least as good an immunity as that resulting from an attack of diphtheria.

Is a possible explanation of this high Schick-positive rate following diphtheria to be found in the statement, now generally accepted, that a large dose of a powerful antigen produces results inferior to those obtained from two or more smaller doses given at appropriate intervals? For instance, it has been definitely shown that two small well-spaced doses of A.P.T. give better protection than one large dose. The child who has had diphtheria may be in the same position as regards immunity as a child who has received only one dose of A.P.T. In other words, if the attack of diphtheria is the primary stimulus it will in all probability leave the child only partially protected, although of course in a diphtheria ward the patient has ample opportunity to receive, and probably in many cases does receive, an adequate secondary stimulus. On the other hand, if the attack of diphtheria occurs in a child who has previously received a primary stimulus, either naturally or artificially by immunization, then generally the attack will tend to be mild and the immunizing process will be completed. This theory could only

account for a proportion of the Schick-positive results and could not explain the persistent Schick-positive state of those individuals who had both passed through an attack of diphtheria and been immunized.

The Schick level after diphtheria should have some relation to the frequency of relapses and secondary attacks, but it is difficult to come to any definite conclusion about this point. Goodall and Washbourn (1928) say that a marked relapse occurs in about 1 per cent. of cases, and they mention that relapses and secondary attacks are not very rare and probably one attack confers little, if any, lasting protection. Ker (1939) states that secondary attacks are quite common, while serious relapses are unusual. These authors agree that a slight recrudescence with or without patching of the sore throat occurs more frequently. It is quite likely that relapses and secondary attacks of diphtheria are more numerous than is generally realized, most of them being labelled as ordinary "sore throats." These are merely a completion of the process of immunization and are usually without danger to the individuals concerned.

Summary

An investigation is described which showed that a representative group of elementary-school children had gained a better Schick immunity following immunization than that obtained by a comparable group who had passed through an attack of diphtheria.

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Clinical Memoranda

Ruptured Ectopic Gestation

The circumstances of the two following cases of ruptured ectopic gestation are perhaps worthy of record as illustrating risks that have to be taken in a scattered community and results that with good fortune may be achieved.

CASE I

A married woman aged 35, a 5-para, was resident at a small station, 120 miles away by rail from this centre, where there is a medical practitioner but no hospital facilities. On October 2, 1939, she complained of some abdominal discomfort and saw her doctor. There were no localizing or distinguishing signs of any kind and her bowels were rather relaxed. She was watched on the 3rd and appeared much better, being up and about attending to her normal household duties. On the evening of the 4th she was found by her doctor alone in her house in a complete state of collapse, pulseless, pale, and complaining of severe abdominal pain referred to the left shoulder. There was no question of the diagnosis of ruptured ectopic, but the problem was how to deal with the patient.

The medical practitioner decided to give her morphine and transfer her in her bed by train to hospital—a six-hours journey. On arrival in hospital she was, under the circum-

stances, in good condition: not badly shocked, temperature 102° F., pulse 90, abdominal pain less marked (still referred to left shoulder), urine acid and loaded with pus cells, blood slides negative for malaria. After a short period of observation an operation was performed and her abdomen opened by a left paramedian incision. A considerable mass of blood clot was found in the abdomen and pelvis, and the left tube and ovary were thoroughly disorganized. These were removed and the patient made a successful recovery.

CASE II

On November 2, 1939, I was rung up by the sister in charge at a large sawmills camp 100 miles away in the bush. She was very worried about the state of Mrs. A., who had just called her in.

From the sister's description of the case I was able to diagnose a ruptured ectopic and made arrangements for the patient's removal to hospital. This consisted in having her brought in by aeroplane, and the nearest available aeroplane was 300 miles away. She therefore could not be moved before dark that day.

Her history was as follows. She was 28 years old and three years previously had had an abortion at three months. Periods had been regular, and she had just missed a period and hoped she was pregnant.

On October 28, 1939, she was out for a motor drive, had some abdominal pain and slight vaginal haemorrhage, and thought that she was going to start another period. During the next few days the abdominal pain and discomfort and vaginal haemorrhage were intermittent, and she rested or got up as she felt inclined. On November 1 she felt very much better and was up and about, but on the 2nd she had severe abdominal pain, greater vaginal haemorrhage, and called in the sister, who found her in a collapsed state and immediately reported by telephone.

Here again there were no hospital facilities on the spot, and the best line of treatment was to bring the patient 100 miles into hospital by aeroplane. While waiting for the aeroplane she was kept under morphine and given rectal saline, and the foot of the bed was raised, etc., to maintain circulation. On arrival in hospital she was in a completely collapsed condition; the pulse was very poor and 130; temperature 97.6° F.; pale, cold, and clammy; abdomen rigid and distended, with pain referred to both shoulders. She was given rectal saline and glucose and operated on immediately via a right paramedian incision. The abdominal cavity was full of blood and blood clots, and until this was taken away nothing could be distinguished. Over two pints of fluid blood was removed and strained for immediate transfusion. The left ovary was completely destroyed by a cyst (the size of an orange), into which free haemorrhage had taken place, and a portion of the left tube adjoining it. These were rapidly excised, the wound was closed, and two pints of citrated blood taken from the abdomen put back into the median basilic vein.

The patient made an uninterrupted recovery and was discharged from hospital in three weeks.

During the last two years I have given anaesthetics for two cases of ectopic gestation before rupture and have operated on two cases of ruptured ectopic gestation. In the whole area there are probably not more than 400 married women, which gives an abnormally high incidence for this unfortunate occurrence.

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The Ettore Marchiafava prize, founded by the University of Rome in October, 1938, for the best work on morbid anatomy or general pathology, has been awarded to Professor Mario Monacelli, director of the Dermatological Clinic of Messina University, and Professor Giulio Raffaele of the University of Rome.