IMMUNIZATION AGAINST DIPHTHERIA WITH ALUM-PRECIPTATED TOXOID

EFFICIENCY, DURATION, AND GRADE OF IMMUNITY

BY

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I have reported previously the results of Schick tests on 162 children about two months after 0.4 c.cm. of alum-precipitated toxoid injected three to four weeks after an initial dose of 0.1 or 0.2 c.cm. (Chesney, 1936). Only one child was positive, giving a conversion rate of virtually 100 per cent. Using a similar two-dose method Parish (1936), in 164 children, obtained equally satisfactory results.

Efficiency

The majority of children immunized in Poole (population 67,000) have belonged to the middle and lower classes. A severe epidemic of diphtheria occurred in 1929-30, but the attack rate has now dropped to a low level in comparison with the figures for London and for England and Wales.

Diphtheria Attack Rate per 1,000 Population

	1929	1930	1931	1932	1933	1934	1935	1936
Poole	4.25	3.25	1.51	0.94	0.19	0.14	0.27	0.29
London	2.68	3.03	1.95	1.88	2.25	2.81	2.25	—
England and Wales ...	1.59	1.84	1.26	1.08	1.18	1.70	1.60	—

The processes of natural immunization have lately been minimal. During the last three years nose and throat swabs from 500 children, who had incidentally some local abnormality, did not reveal a single positive culture. The Schick-positive rate on primary tests, mostly of children over 10 years of age, has been high; from 1930 to 1936 it was 75.8 per cent. of 1,125 children, and in 1936 78.6 per cent. of 210 children. At present the rate for all children under 10 years is probably 80 per cent. or higher.

Since my former report in February, 1936, a further 1,038 children have been immunized, making a total of 1,200 children immunized with the two-small-dose method. Of these, 1,078 have been Schick-tested two months after the second dose, and only two children have shown a Schick-positive reaction. The efficiency of immunization is therefore approximately 100 per cent.

Duration of Immunity

One hundred and twelve children who had been immunized with two small doses of A.P.T. and found Schick-negative when tested two months later were again tested eighteen months or more after the previous test; all were still negative. This result is the more significant, for in 80 per cent. of these children the "fourfold" Schick toxin test was used (see later).

Grade of Immunity Reached

I was interested to inquire whether the method of immunization in use converted children previously Schick-positive to the "just-negative" condition or to a higher level. I therefore used "fourfold" Schick toxin (kindly placed at my disposal by the Wellcome Physiological Research Laboratories). Glenny and Waddington (1929) showed that "multiple Schick dilutions" could be used

to test for a higher grade of immunity than the standard dilution. A child who is negative to the "fourfold" dilution has a higher level of antitoxin per c.cm. than one who is just negative to the standard but positive to the "fourfold" dilution. Five hundred and sixty-four children were tested with the "fourfold," and 514 with the standard dilution. Only two positive reactors were found in the whole group, and both were positive in the ordinary Schick test. The blood of one of them was tested by the kindness of the staff of the Wellcome Physiological Research Laboratories, and 1/50 of a unit of antitoxin per c.cm. was found.

I have also reported the results of Schick-testing 127 children who had been immunized with formol toxoid; of ninety-four tested with the "fourfold" Schick dilution 87.3 per cent. were negative and 12.7 per cent. were positive, whereas of thirty-three children tested with the standard Schick dilution 97 per cent. were negative and 3 per cent. were positive. In forty-five cases the two tests were used simultaneously, and forty children were negative to both strengths, four were negative to the standard and positive to the "fourfold," and one was positive to both standard and "fourfold" (Chesney, 1935).

With A.P.T. the Schick-negative rate was consistently high with both the standard Schick toxin test and the "fourfold," and the results suggest that A.P.T. gives a higher level of immunity than formol toxoid.

Reactions of Immunizing Injections

No material difficulties have been encountered in the work. Following the initial "detector" dose of 0.1 c.cm., 3 per cent. of the children showed mild local reaction; only 0.1 c.cm. or 0.2 c.cm. was therefore injected into those subjects as the second dose. By this procedure severe local reactions were avoided. In four children who gave a history of a blow on the arm during vigorous games a slight swelling formed eight to twelve days after the second dose, from which a small amount of sterile discharge was easily evacuated. Subsequently the lesions healed rapidly.

Conclusion

Alum-precipitated toxoid used in two doses of 0.2 c.cm. and 0.4 c.cm. at an interval of four weeks gives a high level of Schick immunity. The initial small dose, acting as a detector of hypersensitive persons, eliminates reaction difficulties. The high Schick-negative rate obtained obviates the necessity for routine Schick-testing after immunization.

Summary

1. Of 1,200 children immunized with A.P.T.—0.1 or 0.2 c.cm. followed by 0.4 c.cm. four weeks later—1,078 were available for retest two months later. In only two children was the Schick test positive. The immunizing efficiency of the prophylactic, therefore, approached 100 per cent.

2. The grade of immunity reached was high, for over 99 per cent. of the children tested with the "fourfold" Schick dilution were negative to this test.

3. One hundred and twelve children who had been negative two months after immunization were retested eighteen months later; all were negative.

4. Reactions immediately after injection caused no material trouble and no interference with work. Small local lesions formed eight to twelve days after injection in four children who had received knocks on the arm in vigorous play; the slight discharge was sterile and disappeared rapidly.

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TREATMENT OF HAY FEVER BY INTRANASAL ZINC IONIZATION

PRELIMINARY REPORT OF 243 CASES

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In 1936 the opportunity occurred at St. George's Hospital of treating a number of cases of vasomotor rhinorrhoea by intranasal zinc ionization. Owing to the number of applications for treatment received (over 2,000) it was realized that the normal staff of the physiotherapy department would be unable to deal with more than a small fraction of these cases. Four special hay fever clinics were therefore set up and the services of five extra assistants accepted in order that a rapid statistical study of the method might be made. We desire to record our thanks to these voluntary workers for their invaluable assistance and to the Medical Committee for permission to establish the clinics.

During the period under survey 243 cases were treated; these were of both sexes, and the ages ranged from 5 to 77 years. A special analysis of 100 cases showed that 88 per cent. were of the seasonal type; 12 per cent. were of the non-seasonal variety and presented symptoms of varying severity throughout the twelve months. In only one case of seasonal vasomotor rhinorrhoea was there failure to give a considerable measure of relief; the only complete failures met with were in non-seasonal cases of long standing.

It should be emphasized that the figures in this paper and the conclusions drawn apply to the 1936 season after treatment earlier in the year. By "complete relief of all symptoms" is not meant "cure" of the disease, and in fact arrangements have been made for the cases already treated to have at least two applications in 1937.

In the present series the patient was first examined for infection of the paranasal sinuses, septic tonsils, dental sepsis, or gross structural abnormality of the upper respiratory passages. Intranasal ionization was not given until these, if present, had been dealt with. The routine practice was to give three treatments at intervals of one week; a few cases required as many as five applications; some were completely free after one. As a general rule the treatment was not given unless there was a chance of shortening the subject's season by at least four weeks.

In no case in the series was any anxiety caused by the primary or secondary reaction. There were no complications such as acute sinusitis, anosmia, otitis media, or extensive sloughing of the nasal mucosa. One case of mild cocaine idiosyncrasy was encountered.

No other treatment for the condition was given except that in a few cases where the secondary reaction was more

marked than usual ephedrine, 1/2 grain, and "sedobrol," 2 tablets, were ordered that night. No sprays, douches, or local applications were prescribed, and the patient was asked to omit these if already in use.

It should be stated that the great majority of cases had had other treatment in previous years without relief, and from the fact that the average duration of symptoms was eleven years it will be realized that the condition was in most instances well established. Previous treatment took the form of desensitizing injections, injections of peptone, local applications, dietetic restrictions, and operations such as submucous resection, ethmoidectomy, antrostomy, etc. In many instances the patient had had more than one of the above methods applied without improvement.

Details of the technique employed are not included here as they have already been published.¹

The following table shows the results obtained:

Complete relief of all symptoms	...	57.6%	} 93.6%
Considerable relief	...	36.0%	
Some improvement	...	5.0%	
No improvement	...	1.4%	

Conclusions

1. The technique employed is safe, and complications are not met with.

2. The method gives a satisfactory result in the great majority of cases of seasonal vasomotor rhinorrhoea, and in many cases of the non-seasonal type.

3. The treatment frequently gives relief when other methods have failed.

It is hoped in due course to publish a "follow-up" of these cases, and to record any remote after-effects.

REFERENCE

¹ *Practitioner*, May, 1936.

Clinical Memoranda

Thrombosis of Subclavian Vein Complicating Hyperthyroidism

The following case is of interest since venous thrombosis is a rare complication of thyrotoxicosis.

A single woman, aged 47, who was employed as a sewing machine operative, first consulted her doctor on May 30, 1936. She had been at work until a few days before this, but stated that for twelve months she had suffered from attacks of palpitation and dyspnoea on exertion. She had lost weight and more recently had sweated excessively. She admitted that she was unduly nervous, and that her limbs trembled. When seen by her doctor the pulse rate was irregular—200 per minute—and the thyroid was slightly enlarged. There was no definite exophthalmos. She was kept in bed on bromide and digitalis therapy for three weeks. The rate fell to 180 but was still irregular. On June 23 she was admitted to St. James's Hospital, Leeds.

She was grossly thyrotoxic. The pulse was 144 and irregular (fibrillating), the temperature was 97° F., and the respiration ranged between 24 and 36. The veins of the neck were over-filled. The apex beat was just inside the mid-clavicular line, though the heart was overacting grossly. The liver was palpable. There were moist sounds over the right lower lobe. The thyroid was soft and slightly enlarged. There was a fine tremor of the hands, and a trace of albumin was found in the urine.

On the morning of June 30, seven days after her admission to hospital, she awoke to find the whole of her right arm swollen and blue. She complained of aching pains along the inner side of the arm and forearm. Although the patient was