

ELEVEN YEARS EXPERIENCE WITH TOXIN- ANTITOXIN

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(Introduced by B. K. Richardson)

It is our purpose in this article to report the practical clinical results of our attempt to prevent the incidence of diphtheria over a period of half a decade. The theories of purely scientific interest developed in the research laboratory of yesterday have been subjected to the test of actual clinical experience. Gradually have the uncertainties so long dominating and obscuring an intelligent comprehension of the subject been cleared away; mistakes explained; and hypotheses established as proven facts. The older textbooks told us how to treat many diseases; the modern textbooks tell us how to prevent these diseases.

An institution offers an exceptional field for the practice of preventive medicine. An opportunity is presented to study large groups of children of all ages over a prolonged period of time, to examine the children at periodical intervals, and to keep a detailed health record and history through constant medical supervision. The practical clinical results of immunization against diphtheria are of considerable statistical value since the children are housed in large groups, contacts and exposures to contagious diseases being more pronounced than in the small family group. Moreover, some institutions are the mecca for thousands of visitors annually, and cases of contagious diseases developing among institutional children can be traced to visitors who have, perhaps innocently, transmitted the disease.

Mooseheart is one of the large homes and schools for children. For several years prior to 1919, diphtheria had been almost constantly present, at times epidemic in form. All the accepted scientific methods of the time were employed to prevent the spread of the disease. When a case of diphtheria developed in one of the cottages, the case was removed and isolated, the children in the hall quarantined and given prophylactic doses of antitoxin. Another case would develop in one of the other cottages and the same program of attempted prevention would be repeated. A varying number of cottages were constantly under quarantine,

with all the difficulties and troubles which a quarantine incurred. There seemed no solution for the problem.

During 1919, eleven years ago, the entire student body, consisting at that time of approximately 600 children, were immunized with three doses of toxin-antitoxin. Since that time, every child has been immunized immediately after admission to Mooseheart without Schicking. During the past eleven years, the institution has grown numerically to 1,300 children, exclusive of a large number of students who have annually left Mooseheart following graduation or demission.

More than 2,400 children have been immunized and there has been but one case of diphtheria among the immunized children. On January 19, 1927, a four and one-half year old boy, who had been immunized three years previously, died of laryngeal diphtheria. A careful examination of the student body after this case developed failed to disclose another case of clinical diphtheria. Then 140 throat cultures were taken from those who had been in close contact with this active case, and two small boys, living in the same cottage, were found to be diphtheria carriers with no active symptoms of the disease. A few days of isolation and treatment were sufficient to produce two negative cultures.

Four other cases of diphtheria among non-immunized persons have developed sporadically at different times during the past eleven years. In 1920, a small boy, whom we overlooked when immunizing the student body, developed the disease. During the same year, another boy with large tonsils contracted the disease a few days after he was immunized and before sufficient time had elapsed for immunity to be established. During February, 1923, two non-immunized adults, employed in cottages containing about 30 children each, developed diphtheria at different times. They were isolated, but the cottages were not quarantined and no prophylactic measures were employed for the boys directly exposed.

This clinical experience at Mooseheart during the past eleven years with five known cases of diphtheria which developed at different times, coming in direct contact with an innumerable number of immunized children without a single case of the disease developing, demonstrates the unquestionable value and efficiency of immunization as a preventive of diphtheria. We are furthermore confronted by the constant menace of the diphtheria carrier, that unknown, unsuspected person, who is frequently the cause of sporadic cases of diphtheria.

SCHICK TESTS

Schick tests have been given at Mooseheart on three different occasions. Immediately prior to the general immunization in 1919,

the entire student body, consisting of 639 children, was Schicked. The result of this test was: negative, 371, or 58 per cent; and positive, 268, or 42 per cent; the later being divided as follows: 1 plus, 129, or 20.18 per cent; 2 plus, 59, or 9.23 per cent; 3 plus, 48, or 7.51 percent; and 4 plus, 32, or 5 per cent. The positive Schicks included several students who were known to have had diphtheria. However, the results of this test were totally disregarded and all the students given three doses of toxin-antitoxin. The Schick test was not given after immunization.

After the death of the Mooseheart boy from diphtheria in January, 1927, the entire institution was again Schicked. The total number tested was 1,234, of which 504, or 40.84 per cent, were negative; and 730, or 59.16 per cent, were positive; the later divided into groups as follows: I plus, 333, or 26.99 per cent; 2 plus, 395, or 32.01 per cent; and 3 plus, 2 or 0.16 per cent. The result of this test was astonishing when the entire student body was considered immune, all of them having been immunized from one to eight years previously. Questioning this result as conclusive, some of the Schick material was submitted to the State Department of Health for testing, and the report was received that the test solution was considerably stronger than the requirements of the standard solution.

However, the 2 and 3 plus positive Schicks, 397 in all, were immunized, the I plus positive being considered negative. For this immunization, the State Department supplied us with the Canadian product, toxoid, two doses of 1 c. c. each to be given one month apart. Unfortunately a sufficient amount of toxoid was not furnished and we were required to supplement with 1/10 L plus toxin-antitoxin, 230 students receiving two doses of toxoid and 167 receiving one dose of toxoid and two doses of toxin-antitoxin.

Five months later, this reimmunized group of 397 students was again Schicked. All were negative except three who had received one dose of toxoid and two doses of toxin-antitoxin. These three were later given three doses of toxin-antitoxin without subsequent Schicking.

While the results of the Schick tests can not be considered reliable, we made some general deductions, without reducing the tabulations to a percentage basis, as follows:

1. The ratio of the positives to the negatives, immunized during the various years, was practically the same. In other words, the same ratio prevailed for those immunized during 1919, 1922, 1925, and every other year, and approximated the percentage in the general result.
2. The ratio of positives to the negative immunized with 3 L plus and 1/10 L plus toxin-antitoxin was practically the same. The 3 L plus

toxin-antitoxin was used exclusively prior to 1924, and the 1/10 L plus subsequently.

3. The age of the child when immunized has no effect upon the susceptibility.

IMMUNIZATIONS AND REACTIONS

Prior to 1924, 3 L plus toxin-antitoxin was used exclusively. This produced a marked local reaction in practically all cases, while a large percentage had a varying degree of constitutional symptoms, manifested by headache, nausea, some urticaria, and a temperature which rendered some of them bedfast from one to three days.

Since 1924, 1/10 L plus toxin-antitoxin has been used, with a decided reduction in both local and general symptoms. The Canadian product, administered in the immunization of 1927, produced a local and general reaction more severe in most cases than the 3 L plus toxin-antitoxin. This marked reaction can be avoided, however, if the children are first tested for toxoid reactors, and toxin-antitoxin administered to those who react instead of toxoid. However, no unfavorable complications developed from any of the immunizations.

During the past one and one-half years, the 1/10 L plus toxin-antitoxin has been supplied with goat serum as the medium, and the local and general reactions have been negligible. Horse serum was previously employed exclusively, and we are of the opinion that a greater part of the severe local and general reactions were due to horse serum hypersensitiveness.

CONCLUSIONS

From these eleven years experience with toxin-antitoxin at Mooseheart, we have drawn the following conclusions:

1. From a clinical standpoint, the administration of toxin-antitoxin has immunized our children against diphtheria when all other methods of preventing the disease had failed. Toxin-antitoxin does immunize, as evidenced by the direct exposure of our children to active cases of diphtheria without contracting the disease.

2. The Schick test, as ordinarily done with commercial material, is not an infallible test for susceptibility to diphtheria; for on the one hand the instability of the preparation results in deterioration and negative reactions in those actually susceptible, and on the other hand the lack of proper standardization in some instances may result in the use of material so strong as to give positive reactions in those actually immune.

3. A media skin-test control should always be given in conjunction with the Schick test. Our experience has shown that our students react to a serum or protein injection. A Schick may easily be considered positive when, in the absence of a control, it is in reality nothing more than a reaction to the medium.

4. Immunization with toxin-antitoxin should be done on every child without preliminary Schicking.

5. Schicking may be done six months after immunization. However, Mooseheart experience with large groups has shown that one series of toxin-antitoxin administration has been sufficient to practically eliminate diphtheria from the institution. Furthermore, statistics show that eighty-five per cent of the children in public schools are rendered immune with one series of toxin-antitoxin administration.