AN OUTBREAK OF DIPHTHERIA IN A HIGHLY IMMUNIZED COMMUNITY

BY

JAMES FANNING, M.D., D.P.H.*Medical Officer of Health, Borough of Malden and Coombe and Urban District of Esher*

The outbreak described below is considered worthy of record because methods of immunization against diphtheria and of maintenance of the immunized state are still in the developmental stage, and anything which can throw light on the efficiency of our present methods is of value. One important point about which there still seems to be some disagreement is the value of the Schick test in the field as an indication of immunity. The amount of circulating antitoxin in the blood is considered to be a more accurate indication, but this investigation is impracticable for general application. The real measure of protection against diphtheria would probably be regarded as the rapidity and degree of response of the protective body mechanism to the toxins of the organism, it having already been sensitized by previous immunizing injections.

It is clear that immunization by generally accepted methods does not in every case necessarily protect from a sharp attack of diphtheria. It is also clear that diphtheria of at least moderate severity can occur in a Schick-negative person. In this event it could not be guaranteed that death would not occur if circumstances were unfavourable. The chief points brought out in the present outbreak are: (1) The possibility of an alarming outbreak of diphtheria in a highly immunized community (94% previously immunized; 80% Schick-negative). (2) The failure of previous immunization to protect against a severe attack in certain cases. (3) The occurrence of a high proportion of cases among Schick-negative reactors.

Description of Outbreak

The institution under consideration is a modern private day school for girls of all ages, run on up-to-date lines with good hygienic facilities. The buildings are airy, on two floors, and there is no overcrowding. The children come from a number of adjoining districts. The school has three divisions—senior, junior, and infants. Among the infants are a few small boys. The three divisions are mainly separate, but there is a small amount of mixing between the senior and junior schools in the main building. The infants' department is situated in a separate building which was formerly used for residential purposes, and, with the exception of a few children who stay for midday lunch, the infants do not mix with the other divisions. Dinners are not provided at the school, but about 20% of the children bring midday lunch and mix in one room during the lunch hour. The approximate numbers in the divisions are: seniors, 160; juniors, 70; infants, 100. The teaching staff numbers 15.

First Phase

The school was closed for half-term holiday from March 1 to 5 inclusive. On the 3rd information was received from an adjoining district that a child (Case 2) attending the senior school had been removed to hospital with diphtheria. Owing to the school being closed it was not possible to inspect the children in school, but a list of class contacts was obtained and the names were telephoned to the various districts on the same day. As a result of this information two more cases (Case 1 and Case 4) from the same class were discovered in an adjoining area. As soon as the school was reopened on March 6 all the children were inspected and swabs were taken from class contacts

and from any children showing the slightest suspicion of a pathological condition in the nose or throat. The number of children swabbed amounted to about 10% of those attending school, and all these results were negative. On this and ensuing days lists were prepared of children absent from school, and these were circulated to the medical officers of health of the districts where the children lived. This proved a very useful measure in the recognition of doubtful or missed cases.

The position on March 6 was that all the children attending school were well, and so far as was known they had not been in contact with a possible case for six days. In view of the fact that the great majority of the children (94%) gave a history of immunization, there appeared to be no urgent need for anything but continued observation at this stage.

In the meantime home inquiries brought to light several other pupils who had sickened during the holidays. The total number of cases belonging to this phase was eight (see Table I). Seven of these were senior girls and one was a junior girl. The infants' school was not affected. Seven of the cases became ill during the holiday week-end between Feb. 27 and March 3. One of the cases (Case 1) developed what was apparently a mild tonsillitis on Feb. 22, and this was followed by heavy nasal diphtheritic infection. This was the first case in point of time.

Second Phase

On Sunday, March 24, notice was received that a further case of diphtheria (Case 9) had occurred in one of the senior classes (Form IV) which had been involved in the previous outbreak. The date of onset in this case was given as March 22. This was 22 days after any of the previous cases had attended school. On March 25 a case (No. 10) was reported from another senior class (Form III) which had been previously affected. On the same day the whole school was inspected and Schick testing was carried out in the two classes involved. In the meantime arrangements were made to obtain the parents' consent for Schick testing and combined active and passive immunization where considered necessary for the whole school.

On March 26, with the exception of six objectors, the whole of the remaining school-children and staff were Schick-tested. Controls were used for the staff only. The intention was to give combined active and passive immunization to Schick-positives only, but as it was not considered justifiable to wait longer than 24 hours before adopting this treatment an early reading was taken, and this meant the inclusion of a considerable number of children with doubtful reactions among those who received immunization. Fifty-three per cent. of the children had this treatment, which consisted of the injection of 0.3 ml. of A.P.T. into the deltoid in the left arm and 500 units of diphtheria antitoxin similarly into the right arm. Six Schick-positive members of the staff were given 1 ml. of T.A.F. instead of A.P.T. A Schick reading of the children after an interval of five days showed that actually only 20% were positive.

During the ensuing days throat and nasal swabs were taken from the whole school, including staff. On March 26 four more children went down, two of whom were in the junior school, but the infants' division was clear. The total number of carriers found without symptoms or signs was eight. Five children had positive throats only, two had a positive nose only, and the other had a positive nose and throat. A type report was available for seven out of the eight carriers, and all of these were gravis. Four carriers were in the senior division, one in the junior, and three in the infants (see Table III). Naturally, all of these

children were excluded from school. For various reasons general swabbing was not completed until April 6.

The school broke up for Easter on April 11 and four further cases were reported during the holidays. One case (No. 15) developed on April 9, 14 days after she had received 500 units of antitoxin and 0.3 ml. of A.P.T. Another case (No. 18) was taken ill on April 16, 21 days after similar treatment. The other two (Cases 16 and 17) were Schick-negative children who had not received any further injections, and they developed their illness on April 9 and 15 respectively. The number of clinical cases associated with the second phase of the outbreak now totalled 10 (see Table II).

During the week before May 2, the date on which the school was due to reopen, a further complete swabbing of

immunized, the degree of virulence must have been very high. The development of symptoms and membrane was in a number of cases extremely rapid. The virulence was such that a guinea-pig was killed in 24 hours. At some previous time all except two, or possibly three, of the 18 cases had received immunization which was probably adequate, and at least four were Schick-negative just before the onset of the illness. This probably accounts for the fact that there were no deaths. The state of immunization of the children was comparatively good, 94% having been immunized at some time previous to 1946. This was reflected in the Schick-negative rate, which amounted to 80%.

Analysis of the cases shows that three occurred among 23 children who had never been immunized (a case rate of

TABLE I.—Cases of Diphtheria: First Phase

Case	Age	Form	Date of Immunization	Prophylactic Used	No. of Injections	Schick Test	Date of Onset	Date Last in School	Remarks
1	15	IV Sen.	1940	Not known	2	Not done	22/2/46	22/2/46	Mild tonsillitis and heavy nasal infection
2	15	IV Sen.	1937	T.A.F.	3	" "	27/2/46	28/2/46	Severe
3	14	III Sen.	1942	Not known	?	" "	2/3/46	28/2/46	Mild, slept with Case 2
4	15	IV Sen.	1938	T.A.F.	3	" "	3/3/46	28/2/46	Severe
5	15	III Sen.	1941	A.P.T.	2	" "	3/3/46	28/2/46	Mild
6	14	III Sen.	1941	"	2	" "	3/3/46	28/2/46	Severe
7	8	Prep. I Jun.	1941	"	2	" "	1/3/46	28/2/46	Moderate
8	12	I Sen.	1941	"	2	" "	2/3/46	28/2/46	Mild

TABLE II.—Cases of Diphtheria: Second Phase

Case	Age	Form	Date of Immunization	Prophylactic Used	No. of Injections	Schick Test	Date of Onset	Date Last in School	Remarks
9	15	IV Sen.	Not done	—	—	Not done	23/3/46	22/3/46	Severe
10	14	III Sen.	" "	—	—	" "	23/3/46	22/3/46	" "
11	13	II Sen.	" 1940"	A.P.T.	2	Neg. 26/3/46	26/3/46	26/3/46	Mild
12	12	I Sen.	1941	"	2	Slight pos. 26/3/46	26/3/46	26/3/46	Moderate
13	10	Prep. I Jun.	1941	Not known	?	Pos. 26/3/46	26/3/46	26/3/46	Severe
14	9	Prep. II Jun.	1944	A.P.T.	2	Neg. 26/3/46	26/3/46	26/3/46	Mild
15	14	III Sen.	1935	"	1	Pos. 26/3/46	9/4/46	10/4/46	Moderate
16	12	I Sen.	1942	"	2	Neg. 26/3/46	9/4/46	9/4/46	" "
17	12	I Sen.	1941, 1944	"	2, 1	Neg. 26/3/46	15/4/46	10/4/46	Mild
18	14	III Sen.	1939	Not known	?	Pos. 26/3/46	16/4/46	10/4/46	Very mild (not typical)

TABLE III.—Diphtheria Carriers

Case	Age	Form	Date of Immunization	Prophylactic Used	No. of Injections	Schick Test	Date Last in School	Remarks
A	17	V Sen.	1934	T.A.F.	3	Neg. 26/3/46	19/3/46	Throat negative, nose positive
B	14	III Sen.	1941	"	2	Neg. 26/3/46	28/3/46	Throat positive, nose negative
C	8	Prep. I	1942	A.P.T.	2	Neg. 26/3/46	5/4/46	" "
D	6	Infant B	1942	"	2	Neg. 11/3/46	5/4/46	Throat "negative, nose" positive
E	13	II Sen.	1943	"	?	Neg. 26/3/46	5/4/46	Throat positive, nose positive
F	13	IIB Sen.	1943	A.P.T.	?	Neg. 26/3/46	5/4/46	Throat positive, nose negative
G	8	Inf. trans.	1942	"	2	Neg. 26/3/46	8/4/46	" "
H	6	Infant A	1943	"	2	Neg. 26/3/46	8/4/46	" "

all the children and staff was carried out at the school by special appointment; the results were negative. At the same time a further 0.5 ml. of A.P.T. was given to children who had been Schick-positive and a boosting dose of 0.5 ml. was given to Schick-negatives. No further case occurred after April 16.

Discussion

A notable feature of the first phase was the explosive nature of the outbreak. Reviewing the cases in retrospect, it will be seen that one patient (Case 1) became ill about a week before the others, her illness having started on Feb. 22, the date she was last at school. It may be that the closing of the school for the half-term holiday period was instrumental in preventing further spread during this phase.

The reason why the infection remained quiescent for some three weeks and then flared up again is not clear. Where typing was carried out (12 cases and 7 carriers) the organism was of the gravis type. It is therefore a fair assumption that this type of organism was responsible for the whole occurrence. Judging by the severity of the illness in some of the children who had been previously

13%), while 15 occurred among 299 immunized children (a case rate of 5%). One case included in the first group received one injection more than 10 years before, and is not regarded as having been immunized. Dividing the immunized children into two groups—those immunized within five years and those before that period—it was found that the percentage of cases was approximately equal. It appeared, however, that with regard to clinical severity those patients more recently immunized had some advantage over the others. Bearing in mind that the numbers involved are small, the following table is given for what it is worth:

	Severe	Moderate	Mild
Cases immunized within five years	2 (20%)	3 (30%)	5 (50%)
Cases immunized longer than five years	2 (40%)	1 (20%)	2 (40%)
Cases not immunized	2 (66.6%)	1 (33.3%)	

There was an anomaly in the infants' division. Taken by itself, although the immunization rate was 96% the Schick-negative rate was only 69%. It is rather striking that no cases occurred in this division, although there was evidence of a carrier condition in three cases. It is possible that there is a more rapid response of the protective mechanism to a secondary stimulus in the younger age groups.

The second phase of the outbreak was dealt with in general on the lines advocated by Fulton, Taylor, Wells, and Wilson (1941), with the exception that combined active and passive immunization was confined in the main to Schick-positive reactors. Four cases developed after this procedure; two were Schick-positives (Cases 15 and 18) who had received 500 units of antitoxin and 0.3 ml. of A.P.T. 14 and 21 days, respectively, before the onset of their illness, and the other two (Cases 16 and 17) were Schick-negative children. In view of the fact that four cases went down in the 24 hours intervening between Schick testing and reading it is clear that it is inadvisable to wait even 24 hours for Schick-test results before carrying out immunizing measures in the face of virulent infection. Furthermore, four of the cases were Schick-negative reactors. The repeat swabbing and boosting doses to Schick-negatives before readmission after the Easter holidays were carried out as additional safety measures. A difference of opinion exists as to the value of general swabbing, and it is true that most of the carriers gave only one positive result, although a few were more persistent.

In this district, where the average incidence of diphtheria is low and the diphtheria carrier is almost non-existent, it has been the policy to swab close contacts and to take measures to restrict their movements when positive. In an episode such as this it would be difficult to ignore the possible danger to others from unknown carriers of virulent organisms, and universal swabbing, with full recognition of its limitations, should be employed. It should, however, be completed in the shortest possible time so that all infected children, whether carriers or cases, may be excluded without delay.

It is clear from this experience that even a highly immunized community as judged by present-day standards is not entirely safe against a very virulent type of organism. It is also clear that immunization is of limited value unless it is maintained by boosting doses at regular intervals during the whole of school life. Opinions will differ as to how much of this work is necessary or practicable in order to reach the desired end. Parents do not take kindly to over-frequent injections for their children, and after infancy the frequency of sharp reactions with A.P.T. has a bad propaganda value for the whole scheme of immunization. Even T.A.F. is not without its quota of discomfort. The Schick test is not reliable enough to justify the omission of immunizing injections in negative cases, but serves a useful purpose in measuring the conversion rate of various batches of antigen. In the present state of our knowledge it is suggested that the normal immunizing course in infancy should be followed by a boosting dose of selected antigen every three years irrespective of Schick-test readings. The antigen selected and the dose given will be a matter of individual choice.

Summary

An outbreak of diphtheria is described which occurred in a day school where 94% of the children had a history of previous immunization and 80% were Schick-negative.

The necessity for repeated doses of antigen during the whole of school life is emphasized. The interval suggested between doses is three years.

The limited value of the Schick test as a measure of immunity is pointed out.

I should like to express my gratitude to Dr. Stone, of the E.M.S. Laboratory, Epsom, for her most valuable help in carrying out the bacteriological work, and to the medical officers of health of adjoining districts—Dr. Ellis, Dr. Ive, Dr. Johns, and Dr. MacIntyre—for their enthusiastic co-operation.

REFERENCE

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FAUCIAL DIPHTHERIA AMONG ARMY PERSONNEL IN BELGIUM, 1945

AN ANALYSIS OF 122 CASES

BY

J. H. BOLTON, M.D.

Lieut.-Col., R.A.M.C.; Officer in Charge of a Medical Division at a General Hospital

AND

M. J. PIVAWER, M.B., Ch.B.

Major, R.A.M.C.; Pathologist of a General Hospital

The purpose of this paper is to discuss certain aspects of the diagnosis and management of diphtheria in circumstances a little different from those usually obtaining in civil life. It was known before the invasion of Europe that diphtheria was prevalent in German-occupied Belgium and Holland, and it was recognized that when this part of the Continent was reached the disease might become a major medical problem. Consequently, compulsory lectures and demonstrations were arranged for medical officers of adjacent units. Prompt administration of serum was stressed and the admission to hospital of doubtful cases was encouraged. It followed that a very large number of patients who in normal circumstances would never have got beyond the stage of ambulant treatment were admitted to hospital for a brief period and had a thorough bacteriological investigation of their throats.

The Investigation

Bacteriology.—The absence of facilities for testing the virulence of organisms limited the scope of the investigation, and the bacteriological diagnosis has depended upon assessments from the point of view of morphology, cultural characteristics, and biochemical reactions of the organisms. The following bacteriological technique was employed: Preliminary throat swabs were plated on: (1) tellurite plates (Hoyle's modification)—it is better to avoid human blood in this preparation as it is less inhibitory to organisms other than those of diphtheria; (2) blood-agar plates, 5% blood; (3) Loeffler slopes. A smear was stained with methylene blue and examined for Vincent's organisms. No attempt was made to diagnose diphtheria on the direct smears. The next day a combined smear was made from the Loeffler slope and the blood-agar plate and stained with Albert's stain. The blood-agar was also examined for haemolytic streptococci and the Hoyle plates were inspected for growth. If the slide was positive a diagnosis of morphological diphtheria was made and the result was immediately sent to the ward. The Loeffler slope which showed a morphological diphtheria bacillus was retained. If there was no growth on tellurite in 48 hours the Loeffler slope was subcultured to another tellurite plate. The following day the Hoyle plates were examined. Colonies were studied macroscopically and microscopically. All those showing a rod form were subcultured to a medium which was found to have an advantage over a Loeffler slope.

The medium consisted of 10% serum (animal sera were better than human); 100 ml. of agar; 0.50 ml. of neutral red as supplied for MacConkey's medium; and 1% saccharose. The last three were heated together until the agar was melted, and on cooling to 45.5° C. the serum was added and it was then poured into Petri dishes. This medium was found to be of more value than subculturing back to Loeffler slopes, for the following reasons: (1) Colonies on this medium could be viewed and easily manipulated. (2) Frequently when using Loeffler slopes cocci were found as a contaminant on subculturing