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A CLINICAL STUDY OF AN OUTBREAK OF DIPHTHERIA OCCURRING IN AN ORPHANAGE.

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During the autumn quarter of the year 1905 there was a considerable prevalence of diphtheria in the city of Hull. The estimated population of the city being close upon 260,000, the notifications of this disease rose from 34, 20 and 36 in July, August and September respectively to 110, 68 and 156 in the months of October, November and December[1]. Study of the Report of the Medical Officer of Health for the city shows moreover, that if a curve were drawn representing the quarterly diphtheria notifications in Hull during the five years 1901 - 1905, it would reach its acme in the quarter under consideration

The disease was especially epidemic in certain districts of the city. From one school alone situated in the midst of an infected area thirty cases were reported during the months of November and December. The outbreak was not traced to any definite source such as a contaminated milk supply, but its spread

was in all probability materially aided by the non recognition of very mild cases of the disease.[2]
The Orphanage outbreak with which these notes deal, was included within the circle of this wider epidemic and, as will be seen there was some reason to suspect that it owed its origin to a similar cause.

The Institution stands in a main thoroughfare leading towards the outskirts of the city. It accomodates two hundred children, boys and girls, of ages ranging from six to fifteen.
The building itself consists of two wings, a boys' and a girls' united by a central dining-hall: the separation of the one wing from the other is complete enough for all ordinary purposes but not sufficiently complete to exclude the possibility of the propagation of an infectious disease from one to the other.
The boys and girls have meals together and are taught in the same school rooms, otherwise there is no inter-communication.
They have no opportunities as a general rule of mixing with the outer world except during the July holidays.
During September 1905 however one of the Orphanage girls was permitted to spend part of a day with friends residing in one of the suburbs of the city, it being afterwards ascertained that though cases of diphtheria had occurred in this neighbourhood none had been

definitely met with in the house visited by this girl. Be that as it may, about a week after her return this girl suffered from symptoms attributed to cold, amongst other things she complained of slight sore throat. Her ailment appearing trifling she did not come under medical observation but was sent to the sick-ward, as is the custom of the Institution in all cases of even slight illness

She remained in the sick-ward until October 1st., Six days later a boy presented himself with definite membrane in his throat though the actual onset of symptoms was probably a day or two prior to this discovery. The possibility that Laura S. was the source of infection was not entertained at the time and her throat was not examined. About three weeks later however diphtheria bacilli were recovered from the throat and nose of this girl, although she then exhibited very slight manifestations of ill-health. There is of course no positive proof that this girl suffered from mild diphtheria in September though the circumstances of her illness may at least be regarded as suspicious

When the first case of diphtheria was recognised on October 7th, the disease had already got a hold upon the Institution, as several cases were discovered almost simultaneously and others followed in quick succession. Between the

beginning of October 1905 and the middle of April 1906 forty seven cases of illness were treated as diphtheria. One of the masters also developed the disease.

Considering the universal prevalence of diphtheria and the volume of literature which has been written around it, the record of forty-seven cases cannot form a basis for any general conclusions as to the events commonly occurring during the progress of the disease. From the circumstance of their consecutive occurrence under one roof however these cases have a certain collective interest apart from the individual. Moreover in many of them the disease was of that mild and doubtful type which does not often find its way into hospitals, but is none the less of considerable importance in its relationship to the health of the community at large.
As the patients were further under observation for indefinitely prolonged periods a complete record of their illnesses could be obtained

The forty-seven cases were distributed over three periods in the following order:-

	Cases
1905, October 7th - Dec 4th.	29
1906, Janry 2nd - Jan 14th.	16
.. April 14th - Apl.16th.	2
	47

Table I.

Age Last Birthday.	Boys.		Girls.		Total.		Percentage.
	Number in Institution.	Diphtheria Patients.	Number in Institution.	Diphtheria Patients.	Number in Institution.	Diphtheria Patients.	
6	—	—	5	2	5	2	40
7	5	1	3	2	8	3	37·5
8	11	1	6	4	17	5	29·5
9	13	2	12	6	25	8	32
10	23	6	11	3	34	9	26·5
11	16	2	14	3	30	5	16·6
12	22	3	14	5	36	8	22·2
13	19	1	7	2	26	3	11·5
14	4	—	15	3	19	3	15·7
15	—	—	1	1	1	1	100
	113	16	88	31	201	47	23·38

It will be seen that during December there was a lull in the storm but that the interval between the two 1906 groups was of still longer duration.

All the patients recovered with one exception.

On October 7th., when the outbreak commenced two hundred and one children were resident in the Institution; one hundred and sixteen boys and eighty eight girls

In Table I. they are shown classified according to age and sex and the precentage incidence of the diphtheria patients at the different ages is given.

The numbers are too small to form a basis for calculations but setting aside the misleading 100% at 15 years, it will be seen that most of the cases occurred in children under eleven years of age.

This is in accordance with common experience. In 1904, 5234 of the 7,073 cases of diphtheria admitted into the Metropolitan Fever Hospitals occurred in children under ten, and 2,284 between the ages of five and ten.[3] According to this showing diphtheria was slightly more prevalent in children under five years of age, but much more common between the ages one and ten than at any other period of life

Statistics of the mortality rate from diphtheria at the different ages point to the same conclusion. The disease is most fatal between the second and fifth

years of life, the fatality being less during the first year and diminishing again after the fifth.
The following figures show the mortality rate at the different ages amongst patients admitted into the Metropolitan Asylums Board Hospitals during 1904.[4]

Under 5 years of age	14.45 %
From 5 " to 10	8.16 %
" 10 " " 15	4.09%
" 15 " " 20	2.55 %

The fatal nature of diphtheria during the early years of life is largely due to the frequent occurrence of the laryngeal form of the disease in young children.
In the Hospitals alluded to the operation of tracheotomy was required for laryngeal obstruction in 246 cases of primary diphtheria during 1904, 219 of the patients being under six years of age.[5].
To the regulation which forbade the entrance of any child under six into the Institution we probably owed the absence of laryngeal complications during the outbreak and the associated fact of a low death-rate.

SEX OF THE PATIENTS:

Although the number of boys in the Orphanage exceeded that of girls, the latter were attacked by the disease in greater relative proportion.
The actual figures were 14.10 % of the former and

35.1% of the latter. This is in accordance with general experience. Of 700 cases for example notified in Hull during 1905, 286 were males and 414 females, and in every year since 1901 the same proportion as to sex was observed.[6] Sir R Thorne Thorne[7] attributed this numerical disparity to personal habits more common amongst girls, and to their more probable association in the nursing of younger children sick with the disease.

The Orphanage boys certainly spent more time in the purer air of the play-grounds than the girls, as the latter performed a considerable part of the domestic service of the house.
This circumstance in itself might expose the girls to risks of infection, by bringing them into contact with articles of household use possibly contaminated by some unrecognised case of the disease, otherwise there seemed on the surface, no explanation of their greater relative liability.

PREVENTIVE MEASURES:

Effective methods of checking the spread of an infectious disease can only be undertaken if we have a clear conception of the nature of the contagium the progress of which we wish to check, and a knowledge of the most usual channels of its transmission.
The nature of the contagium of diphtheria has now been

established and in the presence of any accompanying inflammation the discovery of the Bacillus diphtheriae in an exudation, or in the secretions of the affected part, constitutes a certain proof of the specific nature of the disease. If inflammation be absent, the individual who harbours the bacillus may at least be regarded as potentially capable of infecting others. Certain conditions must therefore obtain before an individual can contract diphtheria. A receptive surface for the pathogenic organism must be provided, and a suitable medium for its transmission to this surface must exist. Under ordinary circumstances, the mucous membrane of the upper respiratory or alimentary tract of a susceptible person forms the receptive surface, and a fragment of discharge or secretion from a diphtheric patient the ordinary medium of transference of the infective agent.

We have next to consider that this particle of infectious material may be conveyed in two ways from patient to patient:

(1) It may be carried by indirect means, or

(2) by direct personal contact.

Of the indirect methods, one of the most important is the contamination of some article of food by the discharges of a person suffering from diphtheria. Milk has been specially studied in its capacity as a vehicle of diphtheric infection. Well-authenticated

instances are now on record of milkers and others with diphtheria bacilli in their throats spreading the disease throughout the areas supplied by their farms, and of the immediate cessation of the epidemic when these persons were isolated. The circumstances of the milk supply of the Orphanage were investigated but were not regarded as suspicious. Moreover the entire quantity of the milk taken in for the day had always been boiled immediately after its arrival at the Institution

A second important group of infection-carriers is constituted by articles of household or school-room use brought into contact with infectious persons. Suspicion has also fallen upon the dust of rooms inhabited by patients, as the bacillus has been found capable of considerable endurance. Muir,[8] says that in dried membrane kept in the dark and at the room temperature bacilli may retain their vitality and virulence for several months. Pugh[9] does not consider that the organisms in dust, exposed as they are to the influence of light and air are often received in doses capable of producing the disease.

During this outbreak, precautions were continuously taken to prevent if possible the conveyance of infection by such means.

There was not much difficulty in dealing with articles

brought into contact with acute and recognised cases of the disease, as these patients and their effects could be rigidly isolated

It was less easy to hinder children suffering from latent forms of the disease or incubating it from transmitting infection by such indirect means while they continued to eat and sleep in company with their fellows.

To prevent this occurrence, articles of school and table use were reserved for the separate use of each child as far as possible, and care was taken that eating and drinking utensils should not be mixed in the process of cleansing, by enforcing a rule that each article should be washed separately and replaced on the table ready for the next meal.

As the children did a large part of the housework of the Institution, however, & constant supervision of each child was out of the question, it is easy to see that such measures may only have met with partial success, and that there was no certainty that infected articles did not occasionally pass from child to child.

As the purity of the air breathed is of great importance in maintaining health at a high level and enabling the organism to resist diseases, the drainage was investigated to make sure that there was no escape of sewer gas. Further, open windows in school-room and dormitories were insisted upon.

The direct personal contact of sick or infectious individuals with the healthy and susceptible is, however, the most important means by which diphtheria is spread. When such sources of infection are recognised and isolated, the indirect agents which we have been considering soon become impotent from lack of a fresh supply of infectious material. This is well shown by the immediate cessation of the spread of mild-borne diphtheria after the contaminating individuals are recognised and isolated, and as Hutchens[10] showed, sometimes without suspension of the milk-supply even for a single day.

During an outbreak of diphtheria, three classes of infectious individuals have to be considered:

I. Persons suffering from the disease in its acute form.

II. Persons very mildly ill, but in whom certain local or constitutional manifestations of diphtheria infection are found.

III. Persons who act as hosts for the B.diphtheriae, but in whom clinical evidences of the infection are practically absent.

The members of Class I. give rise to little difficulty. During an epidemic of diphtheria at least no one is likely to fail in the diagnosis of frank cases of the disease and their opportunities of

infecting others can be speedily curtailed.
Members of Class II & III are in a different category. While they themselves run comparatively little risk of death they are a source of danger to the community, in asmuch as their symptoms being latent, they may escape recognition altogether, while no supervision, however strict, can put a check upon the spread of the disease through such slight cases unless ordinary clinical methods are supplemented by bacteriological examinations.

In dealing with this outbreak, we had to face the problem of how best to weed these ambulatory cases out of a collection of two hundred children.

Such cases would probably have been most effectively deprived of their power to do harm, and a check most successfully put upon the spread of the epidemic by them and other agents, had it been possible to combine the methods of prophylactic injection of antitoxin, bacteriological examination, and subsequent isolation upon the results of the same.

The immunization of contacts by injection of antitoxin has been practised on a large scale with excellent results, and the circumstances of Institutional life, where all are 'contacts' after one case of diphtheria has occurred in their midst, appear specially favourable for its successful adoption.
In the New York Infant Asylum[II], for instance, of 224

children immunized one only developed the disease within thirty days from the date of injection, and six after thirty days had elapsed. Previous to the adoption of immunization, one hundred and seven cases had occurred in one hundred and eight days. Ibrahim[12] employed this method on the brothers and sisters of hospital patients, and found that not a single child contracted the disease in its own home. He employed the same method in his wards with the same successful result, and believes that an immunized child can be safely admitted into a diphtheria ward. The period of immunity thus conferred does not probably last longer than three weeks. The important point to remember in connection with this method is that children protected by it should not be allowed to mix freely with the unprotected unless the clean condition of their throats has been bacteriologically proved.

Unfortunately, certain considerations, chiefly of a financial character made it impossible to deal generally with the Orphanage outbreak in this way, though immunization of contacts was practised in certain cases. No child thus protected contracted diphtheria, but my numbers are too small to warrant conclusions being drawn from them.

For prevention of the spread of diphtheria

amongst these children we fell back upon bacteriological examination coupled with isolation, but even in carrying out these methods difficulties had to be faced. The facilities for isolation in a building, not erected for the purpose of dealing with infectious disease on a large scale were necessarily limited. Had the nares and fauces of every child in the building been submitted to bacteriological examination on one day, there was no guarantee, while unavoidable intercommunication existed, that the same condition as to infectivity would prevail in any one throat on the subsequent occasion when the results of the culture tests were received.

If the cubicle system had existed instead of that of long dormitories it would have been much easier to deal with the outbreak and to separate the 'clean' from the infected.

The following plan finally adopted was somewhat in the nature of a compromise:-

The fauces and nasal passages of all the children in the Institution were not submitted to bacteriological examination but only of those in whom systematic inspection discovered signs of local inflammation of any degree. When possible the children thus separated were isolated pending the result of examinations. In 'swabbing' a special point was made of

examining the nasal passages of every child who had even slight coryza, or who was found to have a frequent pulse, a look of illness, or an elevated temperature. This method of procedure was defective in that it ignored the members of Class III, the contacts with no local lesions but in whose throats bacilli might nevertheless be present.

The proportion of persons without signs of diphtheria from whom diphtheria bacilli can be recovered has been variously estimated, and probably depends upon the closeness of the contact of such persons with actively infectious diphtheria patients.

Hewlett & Murray[13], for example, working amongst hospital patients, found bacilli present in the fauces of one out of every seven sick children in the Chelsea Hospital for Sick Children. During the period over which their observations extended, they were able to prove the presence of the bacilli by culture tests in the fauces of 58 children, seven of whom only had clinical evidences of diphtheria. Probably these bacilli are virulent in at least a proportion of the cases and may aid in spreading the disease. Yet Watson Williams[14] states, that in dealing with an epidemic occurring in a Bristol Institution, he allowed 19 such bacteriologically diphtheric children to mix with the healthy, and in spite of free intercommunication no further spread of the disease

occurred. He took the precautions of giving to each child in the Institution 500 units of antitoxin by the mouth and of ordering the throats and noses to be sprayed with anti-septics.

In addition to systematic inspections we ordered, (during the 1906 series only) the temperature of every child in the Institution to be taken morning and evening, and if any degree of fever was thus discovered to exist, it was regarded as an indication of danger, and held to necessitate re-examination. This method of routine temperature-taking proved more helpful than was anticipated when it was commenced, and, by means of it, children were on different occasions isolated prior to the appearance of membrane on their throats.

The 'swabs' were sent to the Pathological Department of the University of Leeds.
The reports received from the laboratory merely indicated in most cases the presence or absence of the Bacillus diphtheriae. Hoffmann's bacillus being regarded by the bacteriologist, as a normal inhabitant of the throat, no note of its presence in any throat was made

Of the total number of swabs sent up for examination (about two hundred including those sent from the acute cases), forty-four results were returned as positive. This meant that three cases treated

treated clinically as diphtheria did not yield the specific bacillus. Of the forty-four cases, eighteen at least could not have been diagnosed with any degree of certainty on clinical examination alone.

An attempt was further made to attack the bacilli which might be present in unrecognised cases and contacts, by gargling and spraying the fauces and nasal passages of all the inmates of the Institution.

This antiseptic treatment was continued from October to April. As the superintendence of these measures devolved upon officials of the Institution who were without special training, it is obvious that solutions of the mildest antiseptics only could be safely employed.

CLINICAL & BACTERIOLOGICAL DIAGNOSIS.

The relationship of the clinical to the bacteriological diagnosis of these forty-seven cases demands some consideration.

The cases fell into three groups:

I. Cases in which bacteriological diagnosis was identical with the clinical.

II. Cases clinically diphtheritic but not bacteriologically so.

III. Cases bacteriologically diphtheritic but without conclusive clinical evidences of the disease.

CLASS I. In all these cases, which were tonsillar in type, definite membrane was present and the clinical diagnosis of diphtheria was verified by the report of the bacteriologist. Twenty-five cases fell into this group. Twenty-one of them were plainly typical cases of moderately severe tonsillar diphtheria and were easy to diagnose. Four cases (Cases 4, 7, II, I5 Table 2) were more doubtful from the clinical standpoint, but in all four the provisional diagnosis of diphtheria was made and isolation enforced before the confirmatory report arrived.

Case 4 & 7. Each had a small yellowish patch on one tonsil and slight evidences only of illness.

Case 11. Was discovered during a systematic examination. There was a definite patch of membrane on the tonsil, but it was far down on the surface of the gland and only detected when the child drew a deep breath.

Case 15. Had more constitutional disturbance than the others, she was pale and her pulse frequent. Her local lesion was not very pronounced.

CLASS II. Four cases came within the definition of this class. They appeared to have clinical diphtheria but the bacillus was not recoverable from their throats.

The twenty-nine cases belonging to Classes I and II are shown in Table II.

Table II.

General Data.				Clinical Conditions.				Bact. Report.		Complications and Sequlae.					Anti-toxin.	Remarks.
No.	Name.	Sex.	Age.	Local Signs in Throat.	Nasal Discharge.	Glandular Swelling.	Temperature. (Initial).	Throat.	Nose.	Vomiting.	Cardiac.	Albumin.	Paralysis.	Other Complications.	Dosage.	
1	J. B.	M.	10	Moderate redness and swelling. Memb. both tonsils.	Serous. Moderate.	Moderate.	102	P.	O.	..	..	..	..	..	Units 2000	
2	C. R.	F.	8	Moderate redness and swelling. Memb. both tonsils and soft palate.	Yellowish. Crusts. Slight.	Moderate.	101	P.	O.	..	Frequency of pulse. 2nd pulm. sd. accentuated. Systolic murmurs apex and base.	Trace.	Palatal. Much wasting of limbs.	..	Units 2000	Nasal speech and regurgitation of fluids first noticed on 37th day. Duration of paralysis 20 days.
3	F. H.	M.	13	Much redness and swelling. Memb. both tonsils.	Slight.	Moderate.	104	P.	O.	..	Frequency of pulse. Duration 6 weeks.	..	..	..	Units 2000	Heart perfectly normal on discharge.
4	T. H.	M.	12	Slight congestion. Memb. on R. tonsil.	None.	Slight.	101	P.	O.	..	Systolic murmur apex and base. Old standing endocarditis.	..	..	..	Units 2000	Heart condltion apparently unaffected by diphtheria.
5	A. T.	M.	11	Moderate redness and swelling. Memb. both tonsils and post-pharyngeal wall.	Slight. Serous.	Moderate.	102	P.	O.	From 9th to 16th day at intervals.	Weak, frequent irregular pulse. Cardiac dilatation and alteration of rhythm. Death on 16th day.	Present.	Return of fluid through nostrils.	Much pallor.	Units 2000 + 2000	Very little urine passed during last two days of life.
6	H. L.	M.	7	Moderate congestion. Memb. both tonsils.	Slight.	Slight.	104	P.	O.	..	Weak and frequent pulse during several weeks.	..	..	..	Units 2000	Heart normal on discharge.
7	E. M.	F.	10	Slight redness and swelling. Memb. right tonsil.	None.	Slight.	101	P.	O.	..	..	..	..	..	Units 2000	
8	E. H.	F.	11	Moderate injection. Memb. left tonsil.	None.	Slight.	102	N.	N.	..	..	..	..	..	Units 2000	Discharged in beginning of December. B. diph. absent on every examination.
	2nd attack.		,,	Memb. both tonsils.	None.	Moderate.	102	P.	O.	..	Slightly irregular and frequent pulse. Systolic murmur apex and base.	..	..	..	Units 2000	Second illness commenced January 12. B. diph. present.
9	F. T.	F.	6	Slight redness & swelling. Memb. R. tonsil.	Thick and yellowish.	Moderate.	102	N.	N.	..	..	..	..	..	Units 2000	Antitoxin rash.

Note.—P. = D. B., found. O. = no report. N. = D. B., not found.

Table II. (*continued*).

General Data.				Clinical Conditions.				Bact. Report.		Complications and Sequlae.					Anti-toxin.	Remarks.
No.	Name.	Sex.	Age.	Local Signs in Throat.	Nasal Discharge.	Glandular Swelling.	Temperature (Initial).	Throat.	Nose.	Vomiting.	Cardiac.	Albumin.	Paralysis.	Other Complications.	Dosage.	
10	E. A.	F.	14	Slight injection of tonsils. Memb. right tonsil.	Slight.	Moderate.	102	P.	O.	..	..	..	..	..	Units 2000	No complaint of illness. Discovered on systematic examination.
11	C. S.	F.	13	Very slight redness. Small patch on left tonsil.	None.	None.	98·4	P.	O.	..	..	..	..	..	Units 2000	No complaint of illness. Discovered on systematic examination.
12	W. B.	M.	11	Much swelling and injection of fauces. Memb. left tonsil.	Slight.	Moderate.	103	P.	+	..	Weakness and frequency of pulse.	..	..	Pallor.	Units 2000	
13	M. B.	M.	10	Redness and swelling. Memb. left tonsil.	Considerable muco-purulent.	Moderate.	98·4	P.	+	..	..	..	..	Much pallor.	Units 2000	No complaint of illness. Discovered on systematic examination.
14	W. M.	M.	12	Much injection of tonsils. Memb. both tonsils.	Moderate.	Moderate.	101	P.	O.	..	..	..	..	..	Units 2000	Antitoxin rash.
15	M. S.	F.	9	Slight redness and swelling. Small patch right tonsil.	None.	Slight.	100	P.	N.	..	Frequent and irregular pulse. Systolic murmurs apex and base.	..	..	Pale.	Units 2000	Vomiting commenced on 42nd day. Was slightly sick almost daily during nearly a month thereafter.
16	E. S.	M.	9	Very little injection. Memb. both tonsils, chiefly left.	None.	Moderate left side. Some tenderness.	100·2	P.	O.	..	Frequent pulse of low tension.	..	..	..	Units 2000	Heart normal on discharge.
17	A. L.	M.	10	Injection & moderate swelling. Memb. both tonsils. Foetor of breath.	None.	Moderate.	100	P.	O.	..	Systolic murmur. Accentuation of 2nd pulm. sound.	..	..	Pallor.	Units 2000	Heart normal on discharge.
18	E. F.	F.	13	Little injection. Patch on right tonsil.	None.	Slight.	100·4	N.	N.	..	..	..	..	..	Units 2000	Discovered on systematic examination. Slight antitoxin rash.
19	D. L.	F.	14	Much redness and swelling of fauces and tonsils.	None.	Slight, chiefly on left side.	102	N.	N.	..	..	..	..	..	Units 2000	Antitoxin rash.
20	W. B.	M.	9	Redness and swelling. Much mucus in pharynx. Memb. both tonsils.	Moderate. R. nostril. Crusts.	Moderate tenderness left.	102	P.	O.	..	Pulse infrequent during early convalescence.	..	..	..	Units 2000	
21	A. T.	M.	10	Much redness and swelling. Foetor. Memb. both tonsils.	Slight.	Considerable.	100	P.	O.	..	Infrequent pulse during early days of convalescence.	..	..	..	Units 2000	Reduplication of 2nd pulm. sound.

Note.—P. = D. B., found. O. = no report. N. = D. B., not found.

Table II. (*continued*).

General Data.				Clinical Conditions.				Bact. Report.		Complications and Sequlae.					Anti-Toxin.	Remarks.
No.	Name.	Sex.	Age.	Local Signs in Throat.	Nasal Discharge.	Glandular Swelling.	Temperature (Initial).	Throat.	Nose.	Vomiting.	Cardiac.	Albumin.	Paralysis.	Other Complications.	Dosage.	
22	M. L.	F.	9	Very much swelling of tonsils. Memb. both tonsils. Much mucus.	Moderate.	Considerable.	104	P.	O.	..	Frequent pulse. Alteration in cardiac rhythm during the acute attack.	Trace.	..	..	Units 2000 + 2000	Frequent pulse (150) during acute stage of illness. Good recovery.
23	G. F.	M.	10	Little redness. Patches on both tonsils. Trifling.	Slight.	Slight.	100	P.	O.	..	..	..	..	..	Units 2000	Discovered on systematic examination.
24	L. B.	F.	11	Slight injection of fauces. Memb. both tonsils.	Slight.	Slight.	100	P.	O.	..	Systolic murmurs apex and base. 2nd pulm. sound accentuated.	..	..	..	Units 2000	Temperature found to be elevated. No voluntary complaint of illness.
25	L. C.	F.	11	Slight redness. Memb. both tonsils.	None.	Slight.	100	P.	O.	..	..	..	..	..	Units 2000	Herpes on lips.
26	E. S.	F.	8	Much redness and swelling. Memb. both tonsils.	None.	Moderate.	100	P.	O.	..	Slight irregularity of pulse. Pulmonary second sound accentuated.	..	..	..	Units 2000	Heart normal on discharge.
27	E. F.	F.	7	Moderate redness and swelling. Memb. right tonsil.	None.	Moderate.	102	P.	O.	..	..	..	..	..	Units 2000	Antitoxin rash.
28	A. F.	F.	12	Much redness and swelling. Memb. on both tonsils.	None.	Considerable.	101	P.	O.	..	..	..	..	..	Units 2000	
29	M. O.	F.	12	Moderate swelling. Dark red injection. Memb. both tonsils.	None.	Moderate.	102	P.	O.	..	..	..	..	..	Units 2000	

Note.—P.=D. B. found. O.=no report. N.=D. B., not found.

I.

CASE 8. TABLE II.

ELSIE H -. aet 11.

The clinical evidences of diphtheria in this casewere the following: On October 9th complaint of sore throat, look of langour and illness.Temp.102° glands beneath the angle of the jaw moderately swollen especially the left. Pharynx and tonsils red and swollen, greyish-white firm patch on left tonsil. The pulse unduly frequent. Coryza absent. Bacteriological report was negative on three occasions. Antitoxin (2000 units)was injected. During convalescence the child was anaemic and pulse-rate continued above normal.
Returned to school, December 11th.

This was the first attack of illness.
On January 11th she was found on "routine"temperature taking to be feverish (Temp.102°) and was isolated. Her history continued as follows: Complaint of headache made but not of sore throat. Pulse was unduly compressible and frequent. Glands beneath the jaw were swollen. She was pale and depressed, Soft palate fauces and tonsils were red,and on the left tonsil a large tough patch of greyish-white membrane. Two smaller patches present on right tonsil.

Coryza absent. Anti-toxin injected.
Bacteriological report positive. During convalescence, undue pulse-frequency was associated for a time with irregularity: after fourteen days systolic apical and basal murmurs developed.

If this child suffered, as I am inclined to think she did, from diphtheria on both occasions the immunity conferred by an attack of the disease did not last beyond three months. It may, of course, be argued that her former illness was tonsillitis, not diphtheria, and that she owed her immunity during two months' residence in an infected ward to anti-toxin.

In addition to the appearance of the tonsil, the look of depression and illness on this patient's face, and her soft frequent pulse appeared to me to justify a diagnosis of diphtheria in October as well as in January.

2.

CASE 19. TABLE II.

DORIS L. - aet 14

Complaint of sore throat on November 27th Temperature 102° . The glands at the angles of the jaw slightly enlarged, especially on left side.

The soft palate and tonsils much injected, the left tonsil 'juicy' and swollen and on its inner surface partly hidden by the swelling of the anterior part of the gland a firm patch of a greyish-white colour. No coryza. Pulse rate 136. Anti-toxin was injected. Bacteriological report was negative. Convalescence was uneventful. It is of interest to note however that on January 2nd, after isolation (during fourteen days) in a ward with 'clean' convalescents, diphtheria bacilli were for the first time recovered from this girl's fauces. This necessitated a return to the sick-ward where she remained until her bacteriological reports were again negative. Contamination before she left the infected ward on the first occasion may possibly explain this circumstance. Her throat to all appearance was healthy on the occasion of the positive report

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3.

CASE 18. TABLE II.

This was clinically the most doubtful case of the four.

ETHEL F. - 13.

No complaint of illness, on occasion of systematic examination of contacts found to be pale, glands

beneath the jaw slightly swollen and temperature 100·4. Fauces rather red, not much swollen. On right tonsil friable, yellowish patch. No coryza. Pulse rate slightly above normal. Anti-toxin injected. Bacteriological reports remained negative. No complications nor sequelae occurred.

In less pressing times this patient might certainly have received the benefit of the doubt which existed. But during an epidemic of diphtheria any case with definite patching, is best treated on the graver supposition unless it is possible to arrange for adequate quarantine.

4.

CASE 9. TABLE II.

FLORRIE T. - aet.6.

Complaint of sore throat on October 13th. Pallor and depression present. Temperature 102°, pulse frequent and weak. Distinct rhinorrhoea. Soft palate and fauces injected. Definite, sharply defined patch of membrane on the right tonsil. Anti-toxin injected. Bacteriological report negative. Remained for some time with a frequent pulse, otherwise made a good recovery.

It is to be regretted that the nasal discharge in this

case was not submitted to bacteriological examination. Owing to this omission, the report stating the failure to find the bacillus loses a considerable part of its significance

The disagreement between clinical and bacteriological findings may arise in various ways. Another condition may be mistaken for diphtheria. I have seen patches on the tonsils of patients suffering from scarlet fever in its early stages, or on the day following tonsillotomy which bore a strong resemblance to the diphtheritic membrane. That this state of things is sometimes present after tonsillotomy was impressed upon my mind by an incident which occurred when I was house-surgeon in a Childrens' Hospital. The day after an excision of adenoids and tonsils was performed on an out-patient, a message was conveyed to me through the telephone to the effect that the child had developed diphtheria, and was thought to have contracted it during the course of his operation, or, at any rate, at the hospital. Fortunately for my peace of mind the appearances on the throat sometimes present after tonsillotomy were familiar to me.

In the present series of cases, such conditions as scarlet fever and an antecedent excision of the tonsils could be excluded.

The throat affection which is probably most

often wrongly diagnosed as diphtheria is tonsillitis especially the follicular variety.
During 1904 no fewer than 902 patients were sent into the Metropolitan Fever Hospital certified as diphtheritic but afterwards discovered to be suffering from some other disease.

The ultimate diagnosis after admission in 614 of these cases was tonsillitis.[15]

In another class of cases the explanation of the difference between the clinical and bacteriological opinions lies in the failure to catch the bacilli on the 'swab', either because the organisms are few in number, or because the pledget of wool has not been brought into sufficiently accurate or vigorous contact with the diseased parts. Either of these two events may have happened in the case of one negative bacteriological report received during the outbreak. —

A boy complained of illness and was seen by me because I chanced to be in the building at the moment. On examining him I found a small patch of membrane on one tonsil and 'swabbed' with the above result.
On the fourth day of his illness a supplementary swab, not taken by me, was sent up. The report on the second occasion confirmed the clinical diagnosis of diphtheria.

Table III.

General Data.				Clinical Conditions.				Bact. Report.		Complications and Sequalae.			Anti-toxin.	
No. of Case.	Name.	Age.	Sex.	Condition of Throat.	Coryza.	Glandular Swelling.	Temp.	Throat.	Nose.	Heart.	Albumen.	Other Sequalae.	Dosage.	Remarks.
1	E. S.	12	F.	Redness & swelling of tonsils.	Considerable discharge. Crusts.	Slight.	100	P	P	... ...	Trace.	...	...	B. diph. persisted on 66th day.
2	E. R.	8	F.	Slight redness of fauces.	Moderate serous discharge.	...	98·4	O	P	... ...	...	...	...	B. diph. found on 54th day.
3	F. M.	8	M.	No redness.	Moderate sanious discharge. Crusts.	...	98·4	P	P	Frequency of pulse. Slight cardiac dilatation. Systolic murmur.	Trace.	...	...	Murmur musical. Heart normal on discharge.
4	R. V.	9	F.	Slight catarrhal tonsillitis.	... ...	...	98·4	P	N	... ...	...	...	...	... ...
5	A. F.	12	F.	Redness. Much mucus in pharynx.	... ...	...	98·4	P	N	... ...	...	...	...	... ...
6	L. S.	15	F.	Big red tonsils. Mucus.	Slight.	Slight.	98·6	P	P	... ...	...	...	...	... ...
7	A. S.	10	F.	Slight catarrh.	Slight.	...	98·4	P	P	... ...	...	...	...	... ...
8	A. H.	10	F.	Redness & slight swelling of tonsils.	... ...	Slight.	98·4	P	P	... ...	...	...	...	... ...
9	M. G.	9	F.	Catarrh. Mucus in pharynx.	Slight.	...	98·4	P	P	... ...	...	...	...	... ...
10	G. C.	7	F.	Very slight redness of fauces.	Considerable serous discharge. Crusts.	...	98·4	P	P	... ...	Trace.	Pleurisy with effusion.	...	B. diph. again found 14 days after discharge. Persisted 60 dys.
11	F. H.	14	F.	Large tonsils. Redness.	Muco-purulent discharge. Sanious.	...	98·4	P	P	... ...	...	...	...	... ...
12	E. S.	12	M.	Not much redness. No swelling.	Considerable purulent.	...	100	P	P	... ...	Trace.	...	2000 units.	... ...
13	E. M.	12	F.	Catarrh of fauces.	... ...	...	101	P	N	Old-standing heart disease. Loud apical systolic murmur.	...	...	500 units.	Heart condition not altered on discharge.
14	E. H.	9	F.	Slight redness. Mucus.	... ...	...	99·6	P	O	Pulse infrequent. Regular. Pulm 2nd sd. accentuated.	...	...	...	B. diph. present on 60th day.
15	H. H.	9	F.	Fauces very slightly red.	Moderate. Tinged with blood.	...	99·4	P	P	Systolic murmurs, apex and base.	Trace.	...	...	Heart normal on discharge. Slight weakness neck muscles.
16	F. D.	8	F.	No redness.	Serous discharge.	Slight.	100	...	...	Systolic murmurs, apex and base.	...	Otorrhœa.	...	Murmurs persisted on discharge.
17	C. O.	6	F.	Slight redness.	Slight muco-purulent.	...	100	N	P	Systolic murmurs, apex and base.	...	...	...	Murmurs persisted on discharge.
18	T. R.	10	M.	Redness.	Profuse discharge. Much swelling nasal mucous membrane.	Slight.	100	O	P	... ...	...	...	2000 units.	... ...

P = D.B. present. N = D.B. not found. O = no record.

Points of importance to bear in remembrance are that one negative result is not conclusive evidence of the absence of B.diphtheriae in a given case, and that, unless the immediate course of an illness disproves it completely, the clinical diagnosis (in membranous cases') ought to be accepted as the basis of treatment.

CLASS III.

As before stated, there was bacteriological evidence of diphtheria in the patients who came under this heading, though the clinical manifestations of the disease were not typical and the diagnosis could not have been made from them alone. In all, eighteen patients were included in this group(Table III) These cases were discovered either on systematic examination of contacts, or through the presence of some degree of fever. In none of them was definite diphtheritic membrane found on the tonsils or other parts, but in all, local lesions with or without general symptoms of illness were present.

The local indications varied from a mere redness and succulent condition of the tonsils, or slight catarrh, to a considerable degree of rhinitis, associated in two cases with oedematous swelling of the nose.

CASES 4. - 9., TABLE III. require special notice as they almost deserve to be put in a sub-group by themselves. In these six cases the local lesions were trifling and practically no constitutional symptoms existed.

In only three of the six was coryza associated with the faucial catarrh, but in four, cultures from the nasal mucous membrane were positive. In all of them, cultures from the throat yielded positive results. One of the members of this sub-group was Laura S. - the girl whose illness in September may have set the ball of infection rolling. Another of them - Ada F. (Case 5, Table III) reappears again as Case 28, Table II. In April this child developed definite membranous diphtheria, bacteriologically verified. This lends colour to the opinion that the presence of B. diphtheriae in her throat during October may have been accidental.

In all the eighteen cases belonging to Class III, the bacteriological report was recognised as the ultimate Court of Appeal, and the cases were accordingly isolated and treated as true diphtheria. In some of them, this isolation determined by culture tests, had to be prolonged.

It was in members of this class that the phenomenon of protracted infectivity occurred, to which reference

will afterwards be made.

Notwithstanding precautions, it was, I believe, to a recrudescence of infection in one of these cases, or to a failure to recognise her infectivity, that the fresh outbreak of January at least owed its existence.

It may be objected that all such non-membranous cases were not truly diphtheria. But from a practical point of view, the definition of the disease had to be broadened to include them, for under suitable conditions they were surely capable of infecting others. From the laboratory standpoint they were diphtheria. Clinically, the supervention in some cases at least of certain sequelae, to be afterwards described, appeared to justify the inference that the bacilli recovered from their noses and throats were not inert.

LOCALIZATION OF THE LESIONS.

There was much uniformity in the location of the membrane when present in my cases.
The exudation was situated on the tonsils in the twenty nine cases characterized by the presence of deposit. Both tonsils were involved in seventeen cases, one alone in twelve.
In two of the seventeen there was a slight extension

on to the soft palate in one, and to the posterior pharyngeal wall in another. Of these two cases, the former developed palatal palsy later on in her illness. The latter died of heart failure.
The patches were usually greyish-white or pale wash-leather colour. In the most characteristic cases they were sharply defined, as if laid on with one stroke of a brush. As most of the cases were seen and treated early, the membrane had not generally become closely adherent when a part of it was removed for examination.
Coryza was present in fifteen out of the twenty-nine acute cases; in most of them the discharge was insignificant. In one it was profuse and more prominent than the small patch on the tonsil.

The boy did not appear to be ill enough to justify the assumption that the membrane had extended from the nose to the throat, nor could definite patches be seen on his nasal surfaces. This case was discovered during a systematic examination, and though he looked ill made no complaint of any sort.

In the eighteen non-membranous cases, the indications of diphtheritic infection were chiefly located in the nose. Nasal discharge was present in thirteen out of the eighteen cases, and the five remaining exhibited merely a catarrh of the fauces

and tonsils. In the thirteen nasal cases the discharge was profuse and purulent in two only. In the others it was sero-purulent, tended to dry up into crusts, and was apt to cause slight excoriation of the upper lips and edges of the nostrils. The appearances did not differ materially from those present in a 'stuffy cold' in the head. There was no tendency to sneeze, but slight 'snuffling' resulted from the degree of nasal obstruction present.

The course of the disease in these catarrhal cases was almost invariably mild, though certain sequelae developed in a third of the patients so affected. Watson Williams, [16] says that "primary nasal diphtheria is usually a purely local affection". He adds however that bacilli virulent to guinea-pigs have been recovered from such cases, from which it may be concluded that diphtheria can be disseminated by some of them at least.

Naturally this mild form of nasal diphtheria attracted little notice before the etiology of the disease was understood.

Trousseau [17] regarded nasal symptoms as indicative of serious disease, and usually characteristic of the malignant form of the disease, his illustrations being drawn from cases in which the pharyngeal membrane may have been supposed to have secondarily extended to the nares.

CHARACTER OF THE ONSET.

Diphtheria is not usually a disease of sudden and tempestuous onset, though the urgency of the initial symptoms varies in degree. It is certain that grave pharyngeal disease may exhibit considerable latency of symptoms. Trousseau [18] gives instances in support of this, cases having come under his personal observation in which the sudden onset of laryngeal symptoms first drew attention to the existence of membrane in the pharynx. He depicts in vivid words the manner in which diphtheria first showed itself in a woman who had walked to Mass in the morning, and in the midst of her preparation for Vespers, was seized with a fit of suffocation. Her throat on examination was found to be thickly covered with membrane, and in spite of immediate tracheotomy the patient died next day. Henoch[19] lays stress upon the insidious nature of the disease in young children who may complain only of feeling 'poorly' when there is extensive formation of membrane on the fauces. On the other hand, Shech quoted by M^{c}Bride,[20] considers that in young children the disease is apt to come on acutely with rigors, sickness, and pains in the head and limbs.

Gee[21] believes that lassitude and digestive disturbances as well as fever are often prodromal symptoms of the disease. The latency of symptoms

and the danger to the community accruing therefrom were well illustrated by the case of a lady who consulted me the other day. She was a teacher, and complained that for two years or so her throat had "felt tired", and her voice weak at the end of the day's work. I noticed a slight swelling beneath the angle of the jaw on the left side, but was somewhat astonished to find a white patch on the left tonsil on examination of her throat. She was unaware that her throat was much worse than usual, and hads been teaching a class of sixty girls during the whole of that day. The diagnosis of diphtheria in this case was bacteriologically confirmed.

Of the twenty-nine acute case in the Orphanage series, fifteen only made a complaint of discomfort referable to the throat. "Lumps in the neck" and 'swollen neck' were the expressions commonly employed by the children in describing their symptoms.

Eight had headache and lassitude, three of these were actually sick.

One lad of thirteen was seen at an early stage in his illness, and was able to describe what he felt with intelligence. On the morning of October 23rd. he was 'shivery' but felt able to go to school. He had no sensation of pain in his throat, but his head felt heavy. At midday he reported himself as he felt

considerably worse. His face was then bluish-white and drawn, the surface of the body cold, the temperature in the mouth 101°, the pulse 120 and compressible. There was slight serous discharge from both nostrils, the fauces and soft palate were injected and on the surface of the right tonsil was a small sharply-defined patch of membrane not larger than a pea. In an hour the temperature was 104°.

In two children the prodromal symptoms as indicated by their temperature charts were apparently of longer duration

ELIZABETH B. - aet 11.

(CASE 24, TABLE II)

On January 4th she was isolated on account of an evening rise of temperature. On January 5th and 6th the temperature remained above normal (100°- 101°), she had headache and a red throat. On January 7th. she was sick two or three times the temperature was 101°, the throat red and membrane present on the left tonsil

ELSIE F - aet 7

(CASE 27, TABLE II)

Isolated on account of pyrexia (102°) on Janry 10th, Janry 11th complained of headache felt'tired'. The throat was red. Janry 12th, Membrane present on the right tonsil

Doris. L. Age. 14.

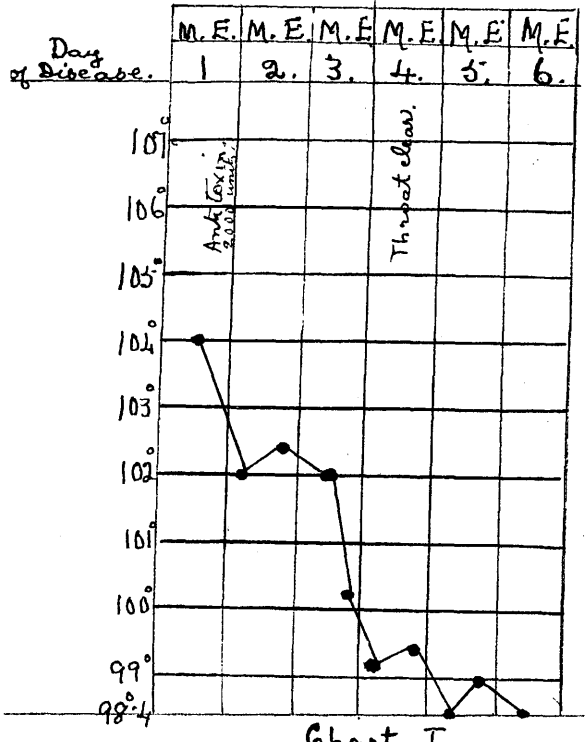

Chart. I.

Ethel H. Age 13.

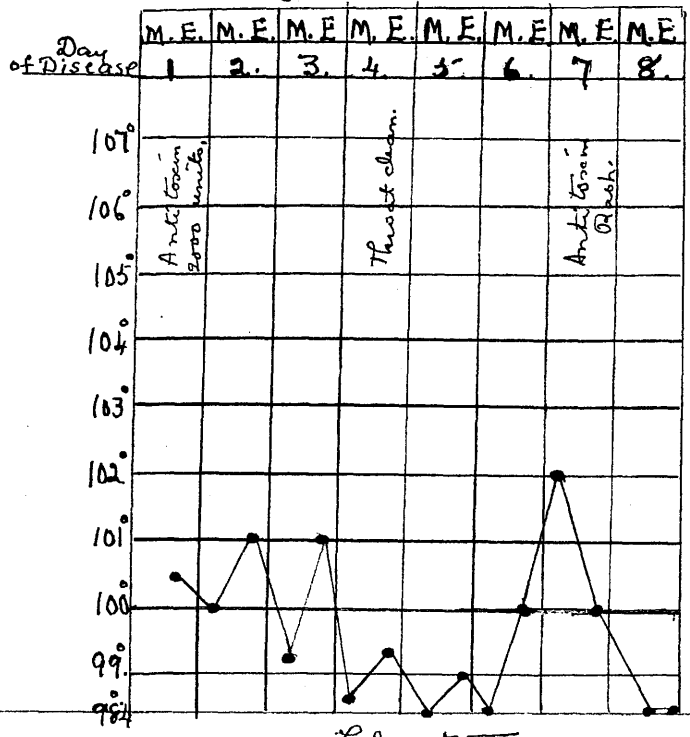

Chart II.

Charlotte R. Age 8.

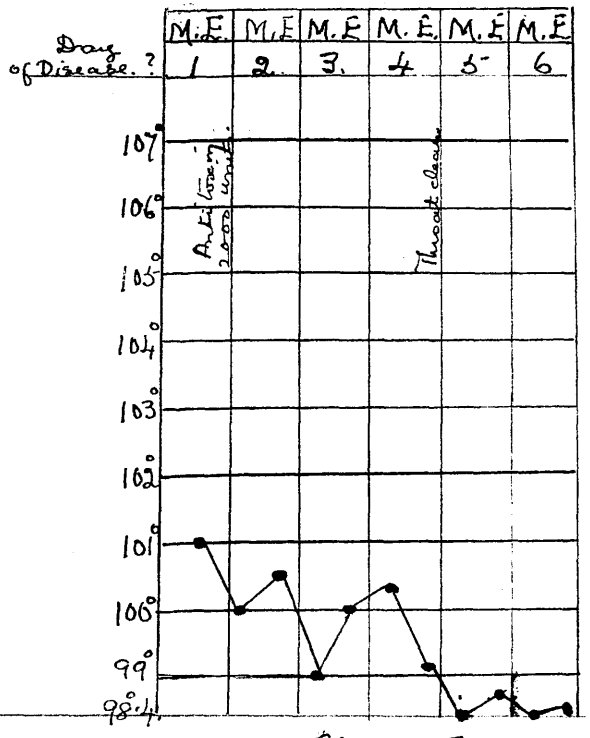

Chart III.

Marcella L. Age 9.

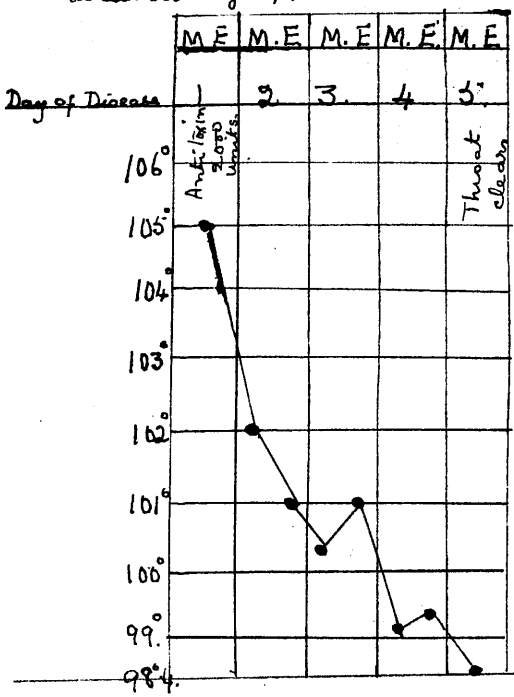

Chart IV

Arthur L. Age 10.

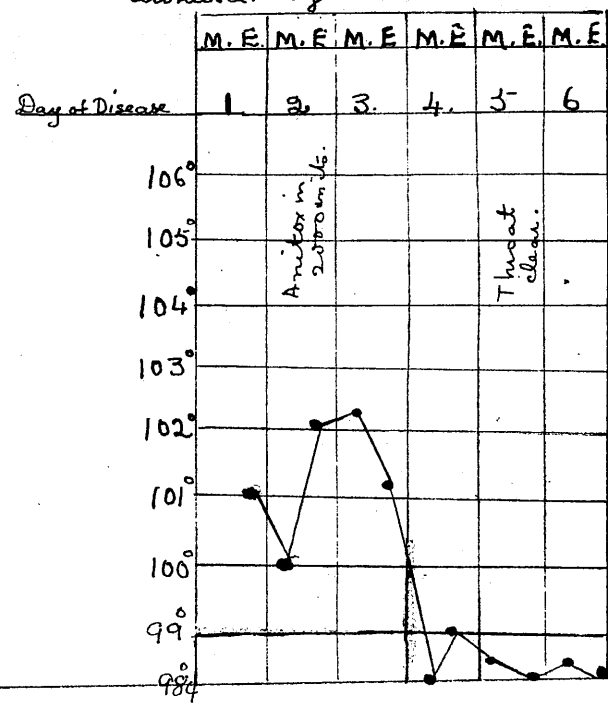

Chart V.

Walter B. Age 9.

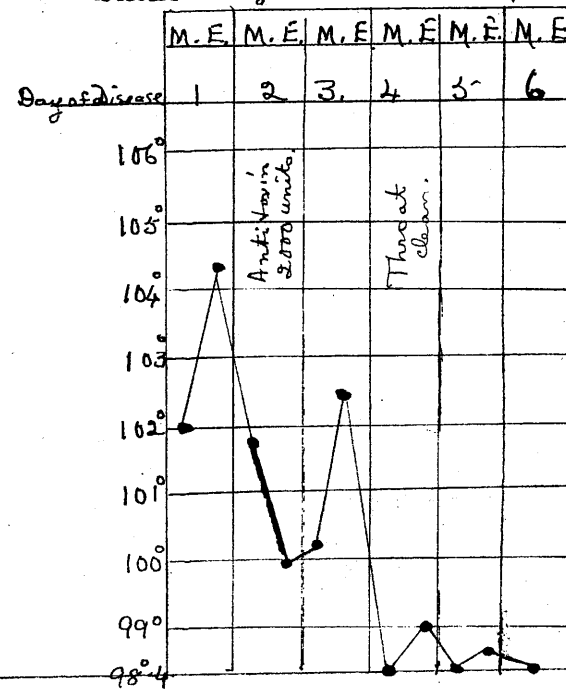

Chart VI.

Neither of these children had been in contact with a case of diphtheria after isolation.

The non-membranous cases gave no assistance in the diagnosis of their malady for not one of them made any definite complaint of illness, but when questioned most admitted such symptoms as headache and weariness.

COURSE OF THE TEMPERATURE.

Some elevation of temperature was noted in all the membranous cases, the variations ranging from 90° to 104°. One child had a temperature of 105° on the evening of her first known day of illness, but as a rule the limit of moderate fever was not greatly exceeded. Commonly the temperature fell to normal on the fourth day.

The accompanying Charts showing the course of the temperature in some of the cases are more descriptive than any words.

In Ethel F -'s Chart (II) the rise on the seventh day coincided with the appearance of a localized antitoxin rash.

The temperature in the non-membranous cases did not exceed 101° on any occasion of the primary illness: but in the case of one child during the progress of a complication pleurisy there was considerable pyrexia.

GLANDULAR SWELLING.

Swelling of the glands beneath the angle of the lower jaw on one or both sides occurred in all the cases of pronounced diphtheria and was present to a slight degree in some of the others. The swelling was insignificant or moderate in most cases, in some of the non-membranous cases it was barely perceptible. In three patients with foetor of the breath and considerable swelling of the tonsils, the glandular enlargement was noted as 'considerable', but not even in these did it assume marked proportions. Very few of the children admitted that they had much feeling of tenderness on pressure over these glands. The swelling subsided after the acute symptoms had passed off. In no case did adenitis or suppuration ensue.

ALBUMINURIA.

Albuminuria is of common occurrence in diphtheria of any severity. During 1904, of 4,639 patients treated in the Hospitals under the Metropolitan Asylums Board[22] this complication was noted in 31·98%.

It occurred in eight cases only of the present series, and five of these suffered from the nasal form of

the disease. The amount did not exceed a "slight cloud" on boiling in any of them, and neither blood nor casts accompanied it

The comparative infrequency of this symptom in my cases may be in part accounted for by the moderate severity of the attack in most of these patients, but may also be more apparent than real, and attributable to the difficulty in making accurate observations on this point. The quantity of albumen in diphtheria varies from day to day, and being frequently present in the urine as a transient condition only, may escape detection if observations are not very frequent.

Two of the three acute cases in which albuminuria occurred were, as will be seen on reference to Table II, of a severe type judged in the light of subsequent events.

CARDIAC COMPLICATIONS IN DIPHTHERIA.

Case of acute Heart failure

Death on the sixteenth day of illness.

ARTHUR T. - aet 11.

(Case 5. Table II).

This boy complained on October 19th of sore throat and headache.

He was puny and under-sized and looked very pale and depressed. The temperature was 101° with evening rise to 102°, Pulse 120, regular but compressible. Pharynx and tonsils moderately injected and swollen, on each tonsil a thick white patch the size of the finger nail, there was a strip of membrane on the posterior pharyngeal wall. Serous discharge from both nostrils, trace of albumen in the urine.

Anti-toxin injected (2000 units)

October 21st. Injection repeated, as although the membrane had not spread and most of it had peeled off, a small patch persisted on one tonsil

October 22nd. Although the temperature was normal and throat clean the boy's condition was not satisfactory. Undue pulse frequency persisted, and the area of deep cardiac dulness was increased (half finger's breadth) towards the left.

The first cardiac sound was weak and the long pause

shortened. He was exceedingly pale, but not apathetic. He had disinclination for food.

October 28th: No improvement in patient's condition. Regurgitation of fluid through the nostrils reported to have occurred on the preceding day. Speech not nasal. Palate not definitely immobile.

Sick once or twice after food, which he took badly, though no actual dysphagia present.

October 30th: Condition had altered for the worse. Pallor amounting to actual blanching of the body present. Complained of great weariness, but was perfectly alive to his surroundings, irregularity of the pulse noted. Cardiac rhythm distinctly "tic-tac". Vomited once or twice.

November 1st: Progressive failure of the heart's action, weakness very pronounced, complained constantly of feeling "very tired".

November 2nd: Obviously worse. Vomiting occurred at fairly frequent intervals, the pulse was very weak, the rate over 160. The heart sounds could not be differentiated, there was no murmur, neither dyspnoea nor cyanosis present. Towards the evening he became very restless and moaned constantly, but was conscious, recognised his mother, and complained of great weariness. Very little urine passed.

November 3rd: Died at 4.pm. The breathing was Cheyne Stokes in type before death, and there was one

slight convulsive moment shortly before the end.

No post-mortem was obtained.

The history of this patient's illness furnishes a sufficiently typical clinical picture of diphtheria in one of the fatal forms in which failure of the heart is the most prominent symptom. Authorities are not yet entirely agreed as to whether nerve or muscular degeneration plays the more important part in the production of this cardiac failure to the occurrence of which diphtheria owes much of its sinister reputation. Clinically it is not possible to distinguish certainly between [illegible] conditions arising from toxic involment of the vagus or cardiac nerves and those accruing from degeneration of the heart muscle itself. Probably in most cases both causes are operative.

Poynton[23], who lays special stress upon the occurrence of degeneration of the heart muscle in diphtheria, gives particulars of the case of a child of five who died on the seventeenth day of her illness, with symptoms leading up to the fatal issue practically identical with those which developed during the course of the illness of Arthur T.

POSTMORTEM: The chief changes found were those of severe degeneration of the essential elements of the heart wall.

Poynton compares the poison of diphtheria with the

poison of rheumatism, and concludes that their effects upon the cardiac muscular substance are so manifested that, while in diphtheria the dilatation of the heart observed clinically is not so great as in rheumatism, the tendency to a fatal issue is greater.

The poison of diphtheria has, he finds, a more destructive effect on the muscle fibres than the poison of rheumatism.

The symptoms manifested in such a case as that of Arthur T - are commonly described by writers as 'cardiac paralysis', and, if the term has not an exact pathological meaning, it has at least the sanction of continued clinical usage. It is, however, not always applied by all writers to describe the same group of symptoms, being used to designate any heart failure occurring in the course of diphtheria by some, while by others it is employed in a more restricted sense.

Turner & Beggs[24], in examining the returns of the Metropolitan Fever Hospitals for the purpose of determining the causes of death from diphtheria during 1904, were met with the difficulty arising from this difference in nomenclature. They found that in most of the hospitals 'cardiac paralysis' signified heart failure occurring not only after the throat was clear, but, generally at least, after a short period of

convalescence had ensued. Patients who died within the first two or three days of illness were entered as having succumbed to 'toxaemia' or the 'primary disease'. In two of the hospitals, however, the two classes were not distinguished, all cases belonging to either class in one hospital were having returned as 'cardiac failure', and in another as 'cardiac paralysis', and with this explanation, the tables thus compiled showed that 347 patients (of a total of 4,639 cases) died of the primary disease and 'cardiac paralysis', 188 being within the former class, and 159 coming under the latter heading, 68 deaths were due to pulmonary complications, including laryngitis.

These facts are somewhat opposed to the findings of White and Smith[25], who state that in 946 cases of diphtheria studied by them, half the fatal cases were due to broncho-pneumonia, and a quarter only to heart-complications.

The severe cardiac failures of diphtheria usually have their date of onset within the first three weeks of illness, and commonly prove fatal within a few days. If a date were to be given to the onset of acute cardiac failure in Arthur T's case, it would be October 28th, the tenth day of illness, as on that day some slight temporary palatal paresis probably occurred and vomiting first commenced. The duration

of his life (six days) after the commencement of acute symptoms was somewhat more prolonged than appears to be usual.

White and Smith[26] found that when gallop rhythm of the heart was present and vomiting had set in, the patients usually only lived from one to three days.

During eight consecutive years, states Bolton,[27] the records of University College Hospital showed that death from heart complications took place on a average on the tenth day of illness, the earliest record being the eighth, and the latest the fifteenth.

In Rolleston's[28] series of nearly 500 cases, the average day on which cardiac paralysis occurred was noted to be the eighth. Stanley[29] in twenty-two cases of acute heart failure found the ninth, the average day on which death took place

It is, therefore, reasonable to assume that a patient who survives the third week of his illness is beyond the most urgent danger of death from this form of heart failure.

Cardiac complications of this type are naturally most often associated with a severe form of the primary disease.

White & Smith[30] with Rolleston[31], however, believe that the day on which the patient first comes under treatment is of great importance. The former state that four-fifths of their fatal cases had no treatment

before the fourth day of the disease. The boy, whose case I am considering, was examined with other children the day prior to his complaint of illness. He had then no membrane on his tonsils. He was injected immediately after his disease was discovered. Late treatment was therefore not responsible for the fatal termination of his illness; nor were the physical signs in his throat of more than average severity. He had nasal discharge it is true, but not of a profuse character, and the glandular swelling was only moderate. The early signs of grave import in his case appeared to be the blanching of the skin, to which Trousseau[32] drew attention as occurring in 'malignant' types of the disease, and the weakness and frequency of the pulse. He was probably very susceptible to the action of the diphtheritic poison, and his family history is instructive, if considered as having a possible bearing on this point, as his father died of heart disease, and a sister aged eight, of diphtheria in the Hull City Hospital, after three days' illness.

At a later stage of his illness, the marked disturbance in the cardiac rhythm, the feeble and irregular pulse, the vomiting and scanty urine, the epigastric pain, the great exhaustion, and the striking pallor were all characteristic of the gravest type of cardiac complication. Great

variations in the pulse rate have been described as occurring in the majority of these fatal cases, but accurate observations on this point require very constant supervision of the patients and were difficult to obtain under the circumstances of this case.

I have no note of the occurrence in this case of that enlargement of the liver which is said to be often present in severe forms of diphtheria. Rolleston[33] found this hepatomegaly (Marfan's hépatomégalie) in 70·5 % of the 'very severe' cases in a series of 310. He considers the sign of prognostic import and an index of the severity of infection

The Prognosis and Treatment of these cases of cardiac failure are not hopeful. No treatment adopted after the collapse has once set in appears to do much good. Probably the prophylatic measure of early and adaquate doses of anti-toxin, coupled with the enforcement of absolute rest, are the most reliable means at our command. Injections of strychnine and atropine combined with active stimulation by brandy and ether were tried in the case of Arthur T., but did not apparently influence the progress of the malady. Morphia was injected to control the restlessness which developed at a last stage of the illness.

MINOR CARDIAC COMPLICATIONS.

The cardiac complications of diphtheria are not always of this impressive character. Many patients during the course of the disease, exhibit minor degrees of cardiac disorder, which manifest themselves in such signs as an unduly frequent, perhaps irregular pulse, and accentuation of the second pulmonary sound, occasionally in association with the development of cardiac murmurs, and moderate increase in the area of cardiac dulness. In my series of forty-seven cases twenty-three cases showed some evidences of circulatory disturbance. One of these cases has already been described under the heading of acute heart failure. In fourteen of the remaining twenty-two patients, membrane had been present on the tonsils during the acute stage of illness, in five the signs of infection had been faucial and nasal catarrh only.

In eleven of the twenty-two, the most prominent feature of heart disturbance was an unduly frequent pulse. The normal pulse-rate in a child of six is about 90, from eleven to fourteen years the rate averages 85 to 75.[34] In the eleven cases mentioned above, the rate ranged from 110-150. In some instances this abnormal condition did not persist longer than a week or ten days, in two boys it was

noted during eight weeks, and in one girl from the outset of the illness in October till her discharge in April. In one other case, the initial frequency was high, and was associated with severe illness, but recovery after the acute stage had passed was complete:

The details were the following:

MARCELLA L. Aged 9.

Case 22. Table II..

Complaint of headache and sickness on Janry 2nd:, On Janry 3rd. had 'sore throat'. On examination was found to be flushed, the conjunctivae injected, the breath offensive and the glands beneath the angle of the jaw considerably swollen. There was no coryza. Pulse rate 150. Temperature 104°. Tonsils much swollen meeting in the middle line. Much membrane on both . Anti-toxin (2000 units) was injected. The evening temperature was 103°,

January 4th: Had passed a restless night, semi-conscious, moaning as she dosed. Temperature 102°. Pulse 140 and weaker. Area of cardiac dulness not enlarged but the first sound indistinct and the long pause shortened. Tonsillar swelling and foetor of breath less. Liq. Adren. Chlor. m.V. given in Camphor water every four hours as recommended by Rolleston[35].

Janry 5th. Pulse rate 133, quite regular. Membrane

appeared to be deliquescing but a patch was now present on anterior faucial pillar

Janry 7th: Small patch still present on the tonsil Glandular swelling subsiding.

Pulse rate 116, heart's action much more forcible and the sounds clear. Rhythm normal. Patchy papular rash (probably due to an enema) on the knees and thighs. Taking food well, Liver not to be felt

Janry 8th: Temperature normal, pulse-rate 96 Throat clean

Janry 12th: A trace of albumen present in urine for the last time.

Her further convalescence was uneventful.

Irregularity of the pulse was noted in three cases only: in two it was a passing condition, In the third it was more persistent and associated with more marked signs of ill-health.

This child suffered from a mild attack of tonsillar diphtheria commencing on October 30th. On Nov 25th her pulse was first noticed as 'irregular', on Nov 29th the pulse-rate was 92, but on auscultation over the heart it was found that about eight beats in the minute failed to reach the wrist.

Nov 30th. the pulse was of the 'bigeminus' type

Dec 6th: The condition of intermission was passing off. The pulse was 124 and of low tension.

On Dec 11th: systolic murmurs were noted at the apex and pulmonary area

She was sick once or twice. This condition of sickness persisted for about a month from this date and was associated with much pallor and an appearance of ill-health.

Her condition on discharge was only fairly satisfactory.

In ten cases, soft systolic murmurs were heard at the apex and over the pulmonary area. In the case of one boy, the murmur was loud and musical, was conducted into the axilla, and persisted for six weeks. At the end of that time the heart sounds were clear. In this boy's case, and in four other cases, the evidence of initial illness had been practically confined to the nose. In none of the five was the coryza very profuse nor accompanied by redness and swelling of the nose. These murmurs, in both membranous and non-membranous cases, persisted for variable periods; in one case the murmur was only heard during one week, but in most, they persisted during at least three or four weeks, and in some were heard on discharge. They gave rise to no symptoms of heart disturbance such as dyspnoea and cyanosis.

On May 5th an examination of all these cardiac

patients was made for the purpose of ascertaining in how many of them signs of cardiac disturbance were still present. Excluding two cases in which the murmurs were apparently of pre-diphtheritic and probably rheumatic origin, three had some signs of heart disorder. One was a little girl who had exhibited an abnormally frequent (130) but regular pulse throughout the entire period of her isolation, and the condition was still present on discharge. In two others, systolic murmurs could still be heard at the apex and pulmonary area, but in none of the cases were any symptoms of cardiac trouble present; all three children looked in excellent health and were attending school as usual.

It may be noted that the disease did not appear to increase the embarrassment of the heart in the two children with signs of old endocardial mischief. In the girl's case there was a strong family history of rheumatism, and a systolic murmur had been previously noted on the occasion of another illness.

The prolonged recumbency was probably rather a benefit to these children that otherwise, and thus diphtheria wrought them good rather than evil.

Of the late and often fatal heart-failure of diphtheria we had no instances during this outbreak. This form of syncopal attack appears to be often induced by some unwonted strain, and is probably best

prevented by the avoidance of premature attempt to rise from bed and resume the habits of ordinary life.

DIPHTHERITIC PARALYSIS:

The relative frequency of paralysis as a sequel of diphtheria has been put at different figures, a circumstance which can partly be explained by the unobtrusive characters of some forms of the affection, and by the lateness of its incidence as a whole.

Paralysis (all forms except the cardiac included) developed in 690 (14·87%) of a total number of 4,639 patients treated during 1904 in the Metropolitan Fever Hospitals[36]. Gowers[37] states that the percentage has been estimated at figures varying from 8 to 66. In a series of 1382 cases quoted by Taylor[38], it occurred in eleven per cent.

Paralysis is most usually consecutive to the pharyngeal form of the disease. Henoch[39] indeed says he has never seen it follow any form of diphtheria except that affecting the throat. It is said to be infrequent after the purely laryngeal type of the disease, but it must be remembered that fewer patients survive this more

fatal affection and live to attain the period of convalescence at which palsy commonly supervenes. It has been known to follow cutaneous diphtheria. Trousseau[40] relates the history of a case in which membrane formed on the surface of the chest which had been recently blistered. Extensive paralysis occurred one month later

Palatal paresis is the most common form of the affection, it is usually the first to appear and may be the sole evidence of poisoning of the peripheral nerves. It is occasionally noted during the acute attack, but this early type, which is indicative of a severe infection, has been ascribed to a local myositis[41].

During 1896, 823 cases of paralysis after diphtheria occurred in the Metropolitan Fever Hospitals[42]; of these 393 were cases of paralysis of the palate alone.

Palatal palsy was the only paralytic sequel which occurred amongst my series of cases, and this was observed in one patient, the history of whose illness was as follows:-

CHARLOTTE R -, Age 8. (Case 2 - Table II)

This child was the second case in the series. She was first seen on October 8th. Membrane was present on both tonsils which were moderately

injected and swollen. There was a small patch on the left side of the soft palate. She had slight coryza, moderate glandular swelling, a temperature of 101° and a pulse rate of 120. She was pale and languid looking,- she stated that she had had "lumps in her neck" but little pain during two days. She received 2000 units of antitoxin. In three days the throat was clean and her condition fairly satisfactory. The pulse-rate was persistently high. It did not vary within wide limits but at every observation was from 120 - 130. There was moderate increase in in the area of cardiac dulness, a diffuse pulsation in the third, fourth and fifth inter-spaces, accentuation of the second pulmonic sound and after the third week a systolic murmur best heard at the apex was intermittently present. A trace of albumen was present in the urine until the twenty-fifth day of illness. She was not allowed even to sit up in bed. This strict recumbency was enforced right up to the onset of paralysis and of course during the continuance of that sequel. She took iron and strychine after the acute stage of the primary illness was over. She took food well.

Novr.6th: (29th day) Much wasting of the lower limbs was noted. As far as could be judged there was no actual paralysis and no anaesthesia. The knee

jerks were not active, but were present

Nov 14th (37th day) The wasting had perceptibly increased. She now coughed when drinking. The temperature was 100°. The pulse rate was 130. The breath sounds over the left front of the chest were weaker than on the right side and a few râles were heard. The speech was nasal There was absolute immobility of the soft palate in phonation. Fluid regurgitated through the nostrils on drinking. The knee jerks were absent. She looked pale and rather distressed. Fluid food was stopped and nourishment of a gelatinous or semi-solid consistency administered.

Nov 17th (40th day) From this date until Decr Ist (54th day)her condition remained unimproved.She became more pinched and pallid. The wasting of all four limbs but especially of the lower was marked. The hand-grips were feeble. No attempt was made to test her powers of walking on account of her cardiac condition. She could however draw her legs up and had fair power of resistance. Knee jerks were absent but the plantar and abdominal reflexes were brisk The palate was motionless and its reflex contractility abolished. Its surface appeared to be anaesthetic. She could blow out a candle and read small print. Her voice was rather husky and most pronouncedly nasal. When she tried to speak the marked contraction of the brows accompanying the effort gave an impression of

strain painful to witness.

She swallowed very fairly well her food being of semi-solid consistence. She was fed at frequent intervals. Albumen was present in the urine

On Decr. Ist (54th day) The nasal twang was less pronounced.

Decr 4th (57th day) The soft palate moved slightly on phonation and the left knee jerk was present.

Decr 6th (59th day) There was already a great improvement in the aspect and nutrition of the patient. Both knee-jerks were present. The speech was natural. The palatal movements were apparently normal. She took ordinary food, solids or liquids, well.

Decr 18th. The alteration in this child's appearance was striking. She was now plump and her colour was rosy. She was animated and happy. No other paralysis followed this attack. On account of her cardiac condition, she was kept in bed for a considerable time, but her ultimate recovery was excellent.

The onset of the paralysis in the case just detailed was somewhat delayed. Signs of disturbed innervation of the palate commonly precede all other forms of diphtheritic palsy. They are most frequently first noted about the end of the third week or during the fourth.

In Rolleston's [43] series, the average day of the disease on which palatal paralysis appeared was the twenty-fourth

The severity of the preceding illness in my case was not more than moderate, though the extent of surface covered by membrane was probably greater than was observed in most of the patients of this series.

The visible involvement of the soft palate was of trifling extent, but in this case alone during the outbreak did the exudation appear on that part.

The occurrence of this form of post-diphtheritic paralysis is frequently the first event which calls attention to the antecedent throat affection and on that account it has been supposed by some authorities, Henoch [44] amongst others, to be in proportion more often consecutive to the milder forms of diphtheria. This inference from clinical observation is not confirmed by the teaching of experiment, for the larger the dose of toxin introduced into a susceptible animal the greater the liability to paralytic sequelae. Unfortunately this child was in all likelihood walking about for a day or so with membrane in her throat, as it will be remembered she was an early victim of the epidemic, and admitted that she had felt a 'lump in her neck' for at least two days before complaining of

illness. She was thus placed under conditions favourable to the development of complications and sequelae in that her treatment was commenced after the first or second day of illness.

To counterbalance this unfavourable circumstance however, she had been kept strictly in bed during the entire period of convalescence antecedent to paretic developments.

The wasting of the limbs was a marked feature in this case and occurred prior to the onset of definite palsy of the palate. Probably had the child been out of bed, staggering gait and weakness of the lower legs would have been the first thing to draw attention to the nerve affection.

The palatal paralysis could not have been overlooked in her case, as the nasal speech was so exceedingly pronounced. The initial coughing with food was probably consequent upon an anaesthetic condition of the mucous membrane in the epiglottic region, and the physical signs in her chest, noted at the same time, appeared to indicate that some particlesof food had found their way into the air-passages.

The continuance of the paralysis in her case was of about average length. The prognosis in uncomplicated palatal palsy is good, and the patients appear to recover without special treatment. In this child's case, careful administration of nourishment and strict

avoidance of exertion were chiefly relied upon as aids to recovery. Iron and strychnine were given with the food. The improvement in nutrition after the disappearance of the palsy was very striking. Curiously enough this child who exhibited the greatest degree of wasting ultimately gained more weight in proportion to her size than any one of her fellow-patients.

The knee-jerks of every child who contracted diphtheria during the outbreak were carefully tested on many occasions both during the height of the disease and during convalescence

They were however only definitely abolished in the case just considered. In the majority of the patients they were noted as 'brisk'.

In no case during the outbreak did [illegible] dimness of vision nor other evidence of ocular affections occur. The children were examined as to their ability to read small print in the sick-ward, and after their discharge, no complaint was received from their school-teachers who had been warned as to the possible occurrence of some interference with vision.

Two children exhibited a slight weakness of the neck muscles, not amounting to paresis, when they first rose from bed. They were also observed to be rather clumsy in their gait. The knee-jerks were however present, and the conditions became normal after a week or so had elapsed

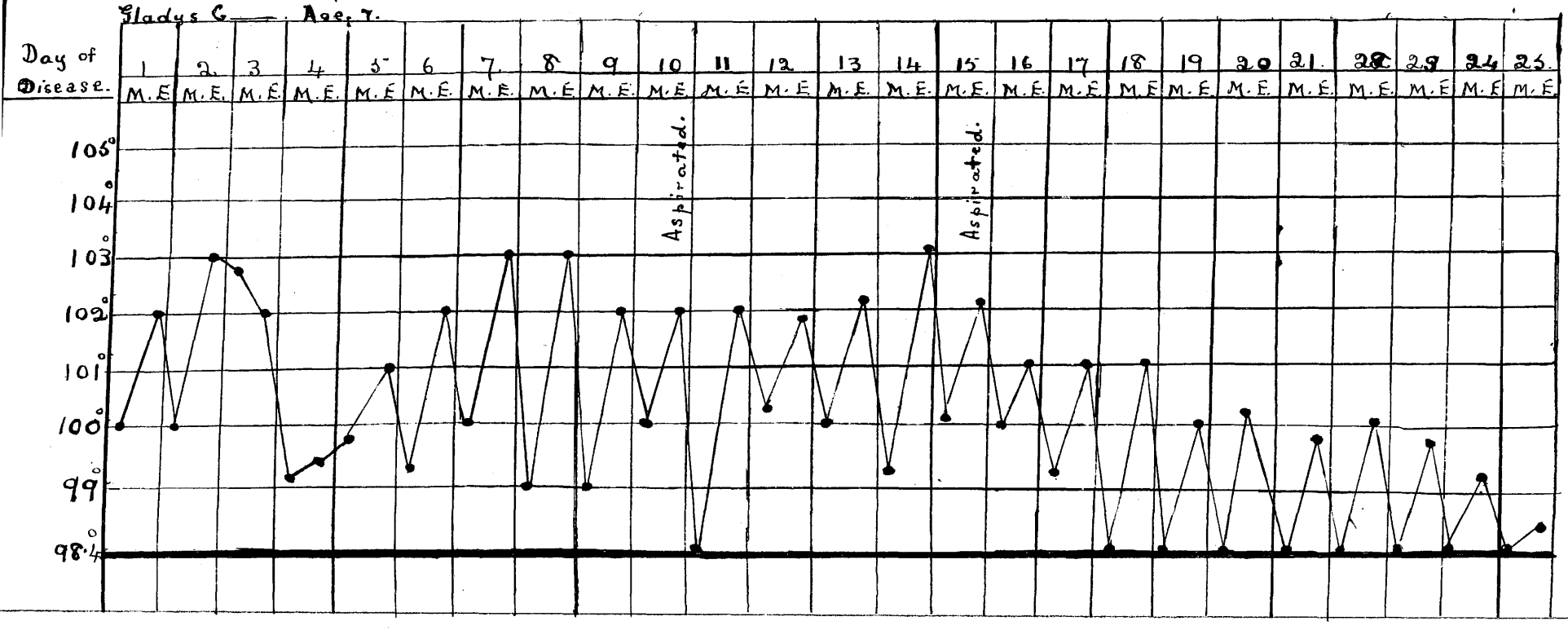
Gladys G——. Age, 7.
Day of Disease.
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
M.E. M.E. M.E. M.E. M.E. M.E. M.E. M.E. M.E. M.E. M.E. M.E. M.E. M.E. M.E. M.E. M.E. M.E. M.E. M.E. M.E. M.E. M.E. M.E.
105°
104°
103°
102°
101°
100°
99°
98·4°
Aspirated.
Aspirated.

Chart VII.

PLEURISY OCCURRING DURING CONVALESCENCE.

Pleurisy with serous effusion is not often found in clinical association with nasal and pharyngeal diphtheria. It is not mentioned in the tabular statement of the complications ensuing during the course of the disease in the 4,639 cases treated during 1904 in the Metropolitan Fever Hospitals. Pneumonia was noted amongst the complications in ·47% and broncho-pneumonia, a frequent sequel of laryngeal diphtheria, in 1·12 %, Holt [45] says that pleurisy with serous effusion may occur in connection with diphtheria complicated by severe nephritis.

Watson Williams[46] incidentally mentions a case of pleurisy occurring in a child with nasal diphtheria. The boy of whom he speaks had diphtheria affecting the nose in December and returned to school after three negative cultures, in February: he then developed an attack of pleurisy but throat and nose cultures made during its progress were negative. Four months after the attack of diphtheria the nose again yielded positive cultures.

The history of the case in my series in whom pleurisy occurred bears a certain analogy to the above. She was first known to have diphtheria bacilli in her throat and nose at the end of October

and pleurisy developed in January. Her figure appeared to occupy the foreground during every stage of the outbreak. Some details of her illness are the following:

GLADYS C -. Age 8.

On January 11th. she was isolated for the second time on account of a sero-sanguineous discharge in which diphtheria bacilli were shown to be present. Her temperature was 101°. She looked rather pale and perspired readily. There was no membrane on the tonsils.

Her local condition speedily improved under treatment. She remained however quiet and disinclined to talk.

On Janry 18th: her temperature was 100° - next day impairment of percussion was noted over the base of the left lung. Bronchial breathing and bronchophony were heard on auscultation. The child had very little dyspnoea

On Janry 25th: the heart had become displaced to the right. Bronchial breathing and bronchophony were still very marked. An exploring needle was passed into the chest and revealed the presence of fluid. There was a trace of albumen in the urine. The face was a little puffy, but this was explainable by the chest condition.

On Janry 28th & on Febry 1st: I withdrew in all about

two and a half pints of clear straw-coloured fluid. This was tested for diphtheria bacilli, but no growth resulted.

Thereafter the child's condition gradually improved, the temperature ceased to rise at night after Febry 13th, the 25th day of the disease.

A few moist sounds could still be heard at the apex on her discharge in April, and the breath sounds were rather weak over the left base. She gained in weight, however, and became quite lively.

Her sputum (obtained with difficulty) was examined for tubercle bacilli but none were found.

Diphtheria bacilli were last found in the nose on March 11th.

The extreme latency of the chest symptoms in this child was remarkable. Had it not been for the considerable evening rise of temperature her condition might have remained undiscovered. It is impossible to be dogmatic about the actual cause of her pleurisy. At one time I feared some dormant tuberculous infection had been stirred into life by the activity of the diphtheria bacillus, but the later course of her temperature and her greatly improved nutrition are against this. The course of the temperature from January 18th, the day on which the dulness was first noted over the left lung, is shown

in the accompanying chart. After the 25th day, the last recorded on the chart, the slight evening elevation of temperature did not occur, and she had been absolutely free from fever for nearly two months before her discharge on April 14th.

TREATMENT.

The treatment of these patients apart from antitoxin, was conducted on simple lines. During the acute stage of illness no drugs were as a rule required, and were only given under the special circumstances which I have already indicated in discussing the cardiac complications which occurred in some patients.

The use of local applications was also restricted, during the early days of the acute attack, to cases in whom nasal discharge or foetor of the breath was a prominent feature. Under these circumstances the fauces and nasal passages were freely sprayed and syringed with hot solutions of boracic acid or similar mild antiseptic solutions. This had at least a cleansing effect and relieved the discomfort of the patients. It is obvious that under the available conditions the use of topical remedies requiring special skill in their application was impossible as a routine procedure, as the disturbance

of the patient probably caused thereby would have more than annulled their good effect.

When the acute stage was over, and the children were able to help themselves a little, gargling with considerable quantities of warm antiseptic solutions was practised, and, in nasal cases, the nose was syringed and sprayed two or three times daily with warm and weak saline or boracic solutions, and iodoform ointment was applied to the inside of the nostrils to prevent crusting of the discharge. Such measures were chiefly adopted with a view to securing their cleansing effect upon the mucuos surfaces rather than because much benefit from their antiseptic influence was likely to be obtained. Alcohol was only given in two or three cases, and then only to meet a temporary emergency, and when pallor, lassitude, or cardiac disturbance existed during convalescence, general tonics, such as cod-liver oil, iron, and strychnine were prescribed.

More importance was attached to what may be called the hygienic treatment of the disease, a treatment which may be summarized as consisting in the enforcement of a sufficiently long period of absolute rest, in ensuring an adequate supply of nourishing food, and in perfect ventilation of the ward in which patients are nursed. Concerning the first of these requirements - rest - it is obvious

that in a disease like diphtheria during the progress of which the heart is often severely tried, its labours should be lightened as much as possible, and this can best be done by enforcing recumbency for a sufficient period, the duration varying with the needs of the individual case. Three weeks of strict rest at least are necessary in any case of moderate severity, while, if any cardiac symptoms such as weakness or irregularity of the pulse or altered rhythm exist, the necessity for longer rest is absolute. It is also important to re-examine the heart after patients make the first essay of their walking powers, because even moderate exertion may bring into prominence a hitherto latent weakness: frequently, too, the period of recumbency may require to be prolonged, although the patient is to all appearance well.
An incident once related to me by a surgeon impressed this fact on my mind: he had performed tracheotomy on a little girl, and after a severe illness the patient had battled her way back to apparent health, and was allowed to run about with other children, yet it happened, that while she was playing in the ward one day she suddenly gasped and fell back dead.
Lees[47] gives an instance of a child of eleven years of age, who ~~was~~ kept in bed for eight weeks, yet died five minutes after she rose for the first time. ~~and~~
Such examples could unfortunately be multiplied.

During this outbreak all the patients were treated by strict rest in bed with the exception of six girls (Cases 4-9 Table III). The evidences of illness local and constitutional in these girls were so slight that it was not thought necessary to insist upon their absolute recumbency.

The other patients were kept in bed for varying periods, the minimum being twenty-four days and the maximum ninety-three.

Taking twenty-six membranous cases of whose illnesses I have complete records, the average time spent in bed was 39·3 days, and in eleven who displayed evidences of cardiac disorder the duration of recumbency was 50·8 days.

Of the 'catarrhal' and nasal cases, one boy in whom a musical murmur had developed, and who had a weak pulse, was in bed 66 days, Five girls with signs of cardiac disorder for periods ranging from 40-50 days. The patients were not kept in bed until the murmurs, for example, had disappeared, and in several instances slight evidence of cardiac disorder were present on discharge, but the patients came to no ill. They were kept for rather exceptionally long times in the sick-ward, however, as the circumstances of Institution life do not permit of a gradual resumption of ordinary duties after a child is considered well enough to mix with his fellows.

The nourishment of the patients gave rise to little trouble. Children brought up in an Institution are not whimsical and faddy about their food, and are accustomed to eat with relish what is set before them. The boy who died of heart failure was the only patient who had more than a temporary anorexia. It was rather astonishing indeed to find how much milk, custards, and the like, the patients could consume without ensuing digestive derangement: a child of mine for instance would readily drink three pints of milk in the day. Doubtless this co-operation on the part of the patients conduced to their recovery.

It would not have been possible to keep these patients in a sick ward for such long periods to their profit, if adequate ventilation had not been insisted upon. The pallor and depression of convalsecents are often due to the lack of fresh air in their bedrooms, but happily in an Institution there are no superfluous draperies to exclude light and air. During the early months of 1906, the girls' sick-ward was distinctly overcrowded, yet by keeping the windows open night and day the atmosphere of the room remained quite fresh. The bugbears, 'draughts' and 'chills', can be avoided if care be taken to see that the bed covering is warm enough, and that hot bottles are supplied if there is any feeling of chilliness. Fortunately the sick-ward had a sunny exposure, a

matter worth considering in a depressing illness like diphtheria. It would have been well had it been also provided with a balcony on to which the children could have been wheeled during the convalescent stage at least, but, in spite of the absence of this, the patients who left the sick-ward after prolonged detention certainly did the ventilation credit.

TREATMENT BY INJECTION OF ANTITOXIN SERUM.

Antitoxin is the physician's most potent ally in the treatment of diphtheria, and, since 1895, the year in which the antitoxin era properly speaking commenced, a marked lowering in the curve of the diphtheria mortality has vindicated the claims of the remedy to be so regarded

The death-rate from diphtheria in the hospital of the Metropolitan Asylums Board during 1895 (the first antitoxin year) was 22·85. In 1904 it was 10·08. During the five years 1895-1899 the average mortality rate from diphtheria was 18·2 %. During the period 1900-1904 it had declined to an average of 10·08 %.[48]

The weekly bulletin of the Health Department of Chicago[49] contained some interesting particulars in February 1904. The death-rate from diphtheria was estimated for two periods, a pre-antitoxin from 1888-1895 and an antitoxin from 1896-1903. It was found that

the fatality rate during Period II. was 47% lower than during Period I. and further between October 5th 1895 and December 31st, 1903, 6·44% of 7,435 bacteriologically diagnosed serum-treated cases of diphtheria died, while the average mortality of cases not treated with serum remained at 35%

It has been suggested that since the discovery of the bacillus diphtheriæ and the consequent improved methods of diagnosis, many mild throat affections hitherto vaguely classed as 'tonsillitis' and 'catarrh' have been swept into the net of the graver disease. There may be some measure of truth in this contention, but the discovery of the bacillus has also effected the exclusion of certain doubtful throats which would formerly have been regarded as diphtheritic. Moreover, experimental evidence, which is less open to fallacy, supports the testimony of statistics.

It is most essential to the successful employment of antitoxin that the remedy should be given as early in the disease as possible. The already cited Bulletim of the Health Department of Chicago states that of 586 cases treated with antitoxin on the first day of illness two died, a mortality of 0·34 %. Of 936 cases treated later than the 4th day, 216 died or 23 %

The table of Biggs & Guerard, quoted by Northrup,[50] points in the same direction:

	Percentage Mortality
Ist day of disease	3·5
2nd. "	8
3rd. "	12·8
4th. "	23·6
5th. "	35·0.

Unfortunately early injection is not a factor over which the physician has usually much control, as he does not commonly select the time at which his patients first come under treatment. It was otherwise with the patients of the series under consideration; for, with the exception of the initial cases, all appeared to come under notice on the first or at latest second day of illness, a circumstance which must have exercised a favourable influence on the subsequent severity of their disease.

Each of the twenty-nine acute cases received an injection of 2000 units of antitoxin. In two cases only were the injections repeated. Only two of the catarrhal cases were treated with serum, as in these two cases alone did the degree of illness appear to demand it. Comparatively speaking, this dosage was small. In the Metropolitan Fever Hospitals, for example, it appears to be the almost universal practice to graduate the scale of injection from 24,000 units in a very severe case to 6000 and 4000 in those of a more ordinary degree of

severity.

Bolton[51] thinks that 12,000 to 24,000 units should be injected in a bad case, and the dose repeated next day, failing improvement.

Gasparini[52], on the other hand, records that he treated 150 cases with maximum doses of 6000 units and had a mortality of 7·3 %. It must be taken into account that in my series of cases, the doses, being early, acquired from this circumstance a greatly enhanced potency; moreover, all the cases of the series were of the tonsillar type of the disease, and they occurred in children most of whom were considerably beyond the age of greatest susceptibility. The severity of the initial symptoms ought manifestly to be taken into consideration in judging the dose of antitoxin which a case may require. Extensive membranous formation, secondary nasal involvement and much glandular swelling demand massive dosage at any stage. The dosage and date of injection of antitoxin have a special bearing upon the incidence of the complications and sequelae of diphtheria. The introduction of serum treatment may even appear to have increased the frequency of paralysis, as patients suffering from a severe intoxication, who would otherwise have been overwhelmed by the poison, are by its aid enabled to survive the primary disease, but may fail to escape the succeeding paralyses.

Experimental evidence confirms the conclusion drawn from clinical experience, that the best hope of averting such sequelae lies in early and adequate antitoxin treatment.

Ranson[53] found that after intoxication with one quarter to one eighth of the minimal fatal dose, paralyses may supervene in guinea-pigs, but are not constant. With a dosage over one quarter they are certainly to be expected. He adds "antitoxin given 15 to 22 hours after a dose of toxin not greater than the lethal dose exercises in larger doses a mollifying influence on the subsequent paralyses", and this influence he believes to be more likely to manifest itself in the direction of preventing heart failure rather than of averting local paralysis.

The one case of my series in whom palatal palsy supervened came under treatment as already stated, at an uncertain period of her illness. If more weight had been attached to this circumstance and less to the moderate severity of her local lesion, and had more massive doses of antitoxin been given, the prophylaxis of the subsequent palsy would at any rate have been more completely attempted. As for the patient who died of acute cardiac failure, the dose of antitoxin (4000 units in all) was sufficiently potent to arrest further development of the local lesion but was too small to neutralize the poison,

and this in spite of moderate severity of the local lesion & early treatment. Probably the initial pallor of the patient might have suggested more heroic dosage. It must, however, be admitted that there are individuals so suspectible to the toxaemia of diphtheria that a fatal dose may be absorbed within a few hours of the onset of symptoms, and antitoxin subsequently given is then of no effect.

Observations upon the occurrence of the minor cardiac complications of diphtheria do not show that antitoxin has very perceptibly diminished their incidence. Hibbard[54] concludes from his examination of 800 cases that heart complications of a mild type are common enough except in patients who are treated early. Moderate disturbance of the heart was also very frequent in the series of 936 cases studied by White & Smith[55].

It is true that, in most of these, antitoxin treatment was not commenced until the second or third day, in consequence of late admission into hospital, while in two thirds of the severe and fatal cases, it was begun on the fourth and fifth days of the disease. Of my own small numbers, five out of the eighteen nasal cases developed minor cardiac troubles. This showed that systemic infection of a mild degree, at least, existed, although the local and constitutional manifestations of the primary disease were so slight

that it did not seem necessary to inject antitoxin at all. In view of these sequelae the question arises whether it is not better practice to give the benefit of serum treatment to every case, even of mild nasal diphtheria, in older children.

In children under five, considering the possible danger of an extension to the larynx, it should be administered without fail. The difficulty lies in the diagnosis of these 'latent' cases. Unless direct microscopical examination of the discharge can be relied upon, time is lost before the result of culture tests arrives, while in private practice at least, unless a child had been exposed to direct infection, or, during the progress of an epidemic, there would be some difficulty in injecting these cases on the clinical examination unsupported by a bacteriological report. Parents are not always inclined to take a light view of serum-phenomena when they occur even in children who have had pronounced diphtheria.

As regards clinical diptheria, authorities are agreed that when membrane is present on a child's throat and other signs and symptoms point to the diagnosis, antitoxin should be injected without awaiting bacteriological confirmation. It might further be suggested that to the initial cases of an outbreak as to all others of uncertain date of onset

proportionately larger doses than the local signs appear to demand should be given, and if the family history appear to show any light upon the susceptibility of the patient it should have some influence on the dosage.

The immediate effects of the injection of antitoxin were in every case good. On the following day, or even within twelve hours of injection, the expression of discomfort and of anxiety was replaced by a look of well-being and calm. If foetor of the breath were present, it had been sensibly diminished, and the membrane after twenty-four hours showed signs of loosening at its edge. The good effects of the serum injection were especially evident in two of the nasal cases: On the day of treatment there was much purulent rhinitis and an angry swollen look about the nose itself. Next day the redness and swelling of the nose had quite disappeared and there was considerable diminution in the quantity of the discharge, which in three days had practically dried up. As far as could be ascertained, no immediate fall of temperature followed the injections, but in most cases there was a fall within twelve hours of treatment. The patients, however, were not under the most ideal conditions for observation of phenomena of transient occurrence. Thus the profuse sweating regarded by Rolleston[56] as the

TABLE IV.

No.	Name.	Sex.	Age.	Date of Primary Disease.	Date of Injection.	Dosage in Units.	Complications referable to Anti-toxin. Rashes. Date of Onset after Injection.	Character.	Distribution.	Degree of Fever.	Duration.	Joint Pains. Date of Onset after Injection.	Distribution.	Degree of Fever.	Duration of Pains.	Glands. Date of Onset after Injection.	Glands Affected.	Degree of Fever.	Duration of Swelling.	Remarks.
1	E. T.	[illegible]	6	Oct. 14	Oct. 14	2000	13th day	Vivid red circinate erythema.	Trunk and limbs.	99	3 days	10th day	General, joints of limbs and spine.	103	3 days	...	None.	...	...	Coincident with joint pains. Much depression and malaise.
2	[illegible]	M.	3	Oct. 23	Oct. 23	2000	11th day	Dull pink erythema.	Back, chest, and limbs.	99	3 days	11th day	Upper limbs and pain down thighs.	102	3 days	...	None.	...	...	Depression moderate.
3	C. E.	M.	11	Oct. 17	Oct. 17	2000	12th day	Dull pink erythema.	Back, chest and limbs.	99	3 days	...	None.	...	...	...	None.	...	...	Contact bed and diphtheria.
4	[illegible]	[illegible]	[illegible]	Nov. 28	Nov. 28	2000	9th day	Patchy erythema.	Local at site of injection.	102	2 days	...	None.	...	...	...	None.	...	...	[illegible]
5	D. L.	F.	14	Nov. 27	Nov. 27	2000	8th day	Patchy erythema.	Local back where injected.	98.4	3 days	...	None.	...	...	...	None.	...	...	[illegible]
6	E. K.	F.	7	Jan. 12	Jan. 12	2000	12th day	Urticarial rash.	General, trunk and limbs.	99	3 days	14th day	Neck, and joints of limbs and spine.	[illegible]	3 days	13th day	Glands of neck and groin.	[illegible]	[illegible] days	Considerable [illegible]

Table IV.

No.	Name.	Sex.	Age.	Date of Primary Disease.	Date of Injection.	Dosage in Units.	Complications referable to anti toxin.												Remarks.
							Rashes.					Joint Pains.				Adenitis.				
							Date of Onset after Injection.	Character.	Distribution.	Degree of Fever.	Duration.	Date of Onset after Injection.	Distribution.	Degree of Fever.	Duration of Pains.	Date of Onset after Injection.	Glands Affected.	Degree of Fever.	Duration of Swelling.	
1	F. T.	F.	6	Oct. 14	Oct. 14	2000	13th day	Vivid red circinate erythema.	Trunk and limbs.	99	3 days	16th day	General, joints of limbs and spine.	103	3 days	...	None.	...	...	Coincident with joint pains. Much depression and malaise.
2	W.M.	M.	13	Oct. 23	Oct. 23	2000	11th day	Dull pink erythema.	Back, chest, and limbs.	99	3 days	11th day	Upper limbs and pain down thighs.	102	3 days	...	None.	...	...	Depression moderate.
3	S. F.	M.	11	Oct. 17	Oct. 17	2000	12th day	Dull pink erythema.	Back, chest, and limbs.	99	3 days	...	None.	...	...	...	None.	...	...	Contact had not diphtheria.
4	E. F.	F.	13	Nov. 28	Nov. 28	2000	6th day	Patchy erythema.	Local at site of injection.	102	2 days	...	None.	...	...	...	None.	...	...	Complaint of stiffness.
5	D. L.	F.	14	Nov. 27	Nov. 27	2000	8th day	Patchy erythema.	Local, back where injected.	98·4	3 days	...	None.	...	...	...	None.	...	...	Slight irritation.
6	E. F.	F.	7	Jan. 12	Jan. 12	2000	12th day	Urticarial rash.	General, trunk and limbs.	99	2 days	14th day	Neck, and joints of limbs and spine.	100	2 days	13th day	Glands of neck and groin.	103	2 days	Considerable constitutional disturbance, much pain.

normal result of antitoxin injection was only noted in three cases, but may have been present as a temporary condition in others. In twenty-three of the cases in which the date of the complete disappearance of the membrane was noted, it averaged 3·3 days after injection.

The injections were made in the back at the scapular angle. The skin was disinfected, and the syringe and needles invariably boiled. The children did not resent the treatment; only one child made much complaint. One or two of the older children said they felt slight stiffness at the site of the puncture during the succeeding day, but there was an entire absence of that severe local pain which occasionally follows injection in an adult.

No abscesses developed, nor any sign of septic mischief, but 'serum-phenomena' did occur in a certain proportion of cases now to be considered.

SERUM MANIFESTATIONS.

Table IV. shows that phenomena referable to the injection of antitoxic serum developed in six cases of the series.

These sequelae of injection may occur singly or in association. The most commonly observed are:-

(1) rashes

(2) joint and muscular pains.

(3) adenitis

(4) Pyrexia.

The relative frequency of such complications has been variously estimated.

In Stanley's[57] series of 500 cases, rashes occurred in one hundred and twelve, joint pains in none.

In the Metropolitan Fever Hospitals during 1904 43·19 % of the 4,070 injected patients developed rashes, and 5·15 %, joint pains.[58]

Comby.[59] found that eruptions or other complications followed the injection of antitoxic serum in 16 % of his cases

Rolleston's[60] figures for all the serum manifestations are higher. Eruptions occurred in his series in 69 to 8I per cent of different groups of injected patients, joint pains in 5 to 15 per cent, adenitis in 3 to 11 per cent, and pyrexia in 7·5 to 23 per cent. Rashes are thus shown to be the most commonly observed of the serum phenomena, and are in many cases the only undesigned and undesirable effect of injection.

Various factors have been regarded as contributory to the occurrence of these manifestations: the influence of dosage, severity of primary disease, the age and idiosyncrasy of patients have all been

discussed in this connection.

Wright[61], referring to the treatment of these complications, calls attention to recent German observations on 'serum disease', which bring out the fact that these phenomena of rashes and joint pains occur in a process of immunization by which the organism strives to rid itself of the foreign element of the serum.

Holt[62] thinks that such sequels have been less frequent since the introduction of more concentrated serum.

The bulk of serum injected in the cases of my series was invariably about 5 c.c The dosage (2000 units) was the same in all, and the injections were given within twenty-four hours of the first complaint of illness.

Cases I, 4 and 5 exemplify mild tonsillar diphtheria treated early. Case 2. was of a more severe type though the membrane was confined to the tonsils and the boy was injected within a few hours of his first complaint of illness.

Case 6, was in bed and under observation for two days before membrane appeared on her throat: she was then injected.

Case 3. was a contact who did not suffer from diphtheria at all

VARIETIES OF ERUPTIONS.

Antitoxin rashes may be localized to the site of injection or may be general in distribution

They may be erythematous, urticarial, or of the type of the eruptions of scarlet fever and measles.
The local rashes generally make their appearance within ten days of the date of injection. They are usually transient and unaccompanied by constitutional disturbance.
Cases 4 and 5 (Table IV) were of this mild type.

CASE 4.

This child made no complaint of pain or discomfort but on the sixth day after injection she had a temperature of 102° for which no other apparent cause could be found than a local rash round the site of injection. The eruption was dull-pink in colour, patchy and very slightly raised. It covered an area about the size of the palm of the hand. Her throat was not inflamed and she appeared to be perfectly well. Next day only the faintest discoloration of the skin could be made out and her temperature was normal.

CASE 5.

The rash in this case was similar in colour form and localization but unaccompanied by pyrexia or other symptoms. A week later this girl developed a very pronounced scarlet eruption on trunk, limbs and face which lasted two days. It was neither accompanied by fever nor tonsillitis, was ascribed to

an enema previously given and was probably unconnected with the serum administration.

CASE 3.

This was the 'contact' case who was injected because he had been closely associated with a severe case of diphtheria.

On the 12th day after injection the same dull-pink patching was observed in his case round the angle of the right scapula. The area covered by the eruption was slightly larger than in the former cases and on its lower margin which was somewhat sharply defined was a definite wheal. He had slight irritation of the skin. On the following day the original eruption had faded, but a similar rash was present on the chest, and on the 14th day, on the thighs and legs. On the 15th day only a faint mottling of the skin marked the site of the eruption. The temperature did not rise beyond 99° and the boy had neither pains nor depression.

CASE 2.

The rash appeared on the 11th day, and was similar in character and distribution to that of Case 3, the constitutional disturbances were more evident however. There was some irritation of the skin, but the chief complaint was of severe pains along the outer aspects of both thighs and in the right elbow and both shoulder-joints. The temperature was normal. On

the 12th day the rash had faded and the pains were less severe but the temperature was 102°.
On the 13th day the temperature was 100° and there was still a little pain down the shins. On the 14th day he was well.

CASE 6.

This little girl experienced more inconvenience from the effects of the introduction of serum.
On the 12th day after injection, she was found practically covered from head to foot with an urticarial rash. The eruption was of a vivid red colour, and confluent on the back and extensor surfaces of the arms, thighs, and legs. On the knees, ankles, wrists, forehead and chin were some typical single wheals.
The temperature was 99° and the child in no distress. The irritation of the skin was not marked.
13th day. The rash was fading but the temperature was 101° and the patient pale and distressed. She complained of great pain in her neck and was not able to rotate her head nor to raise it from the pillow. There was a little tenderness on pressure, and quite perceptible enlargement of the posterior cervical glands. In the evening, the temperature reached 103°, and the neck was very painful especially on slight movement. The throat was quite clear.

14th day: The pain in the neck was less distressing, but she cried on account of aching in the thighs and legs, and in both hip-joints. The axillary glands could not be felt, but the inguinal glands were definitely enlarged and tender.

15th day: She was much more cheerful. The temperature was little above normal and the pain in the neck slight.

16th day: She was well. There was neither swelling of the glands nor pain on movement

CASE I.

This child displayed more reaction than any of her fellow-patients.

On the 13th day after injection, her back, chest, and and extensor surface of the arms were found to be covered by a vivid red rash, in character a circinate erythema. The rings varied in size, being especially large on the arms where the pale central area was, in most of the 'rings' about the size of a half-penny and the red zone about an inch in breadth.

In a few hours the rings coalesced and the upper part of the body was entirely covered with the eruption.

On the 14th day: The rash had faded from the upper part of the body but was now fully developed on the thighs and legs. The child looked pale and was quiet. Her pulse was 124 and the temperature 99°. The throat was clean.

On the 15th day: The rash had nearly disappeared. She was still pale and languid.

On the 16th day: She complained bitterly of pains down the outer aspects of her thighs and down the front of her legs. She had passed a restless night and looked poorly. She was quite unable to turn over in bed on account of pain in her back. The temperature rose to 103° in the evening and she refused food.

On the 17th day: The temperature was 101° but there was great complaint of pain in her joints and in the muscles of the back. There was little tenderness on pressure but movement was painful She lay with the thighs slightly flexed and rotated out.

18th day: She was much better and could turn over in bed.

19th day: She was well.

Only one of these rashes was definitely urticarial in type, though wheals were associated with the erythema in at least one other, and may have been transiently present in all. Serum from a different laboratory was employed in injecting Case 6. (urticarial rash) The others were treated with serum of the same brand.

Stanley[63] considered the marginate erythema to be the most typical antitoxin-rash and it was the type of

eruption present in fifty-eight of his 112 cases while associated with urticaria it occurred in fifteen. Urticaria alone was observed in thirty. Rolleston[64] found marginate erythema the more common form of the later rashes and urticaria of more common occurrence before the 10th day.

It will be observed that joint pains were only found in my cases in association with a well-developed eruption.

Though these rashes and joint-pains are evanescent and leave no ill-effect they are a decided disadvantage pertaining to serum injection.

The joint pains especially are severe enough for a child to bear. The little girl, Florrie T.(Case I) suffered more acute pain from her antitoxin complication than the average child with rheumatic fever, though the short duration of the affection counterbalanced its sharpness.

TREATMENT.

Treatment was chiefly needed for the mitigation of the joint pains. It was found that wrapping the limbs in cotton wool and supporting them with a light bandage gave relief when the joint and muscular pains were severe. The irritation of the skin was so trifling that the stage of eruption did not call for any treatment at all.

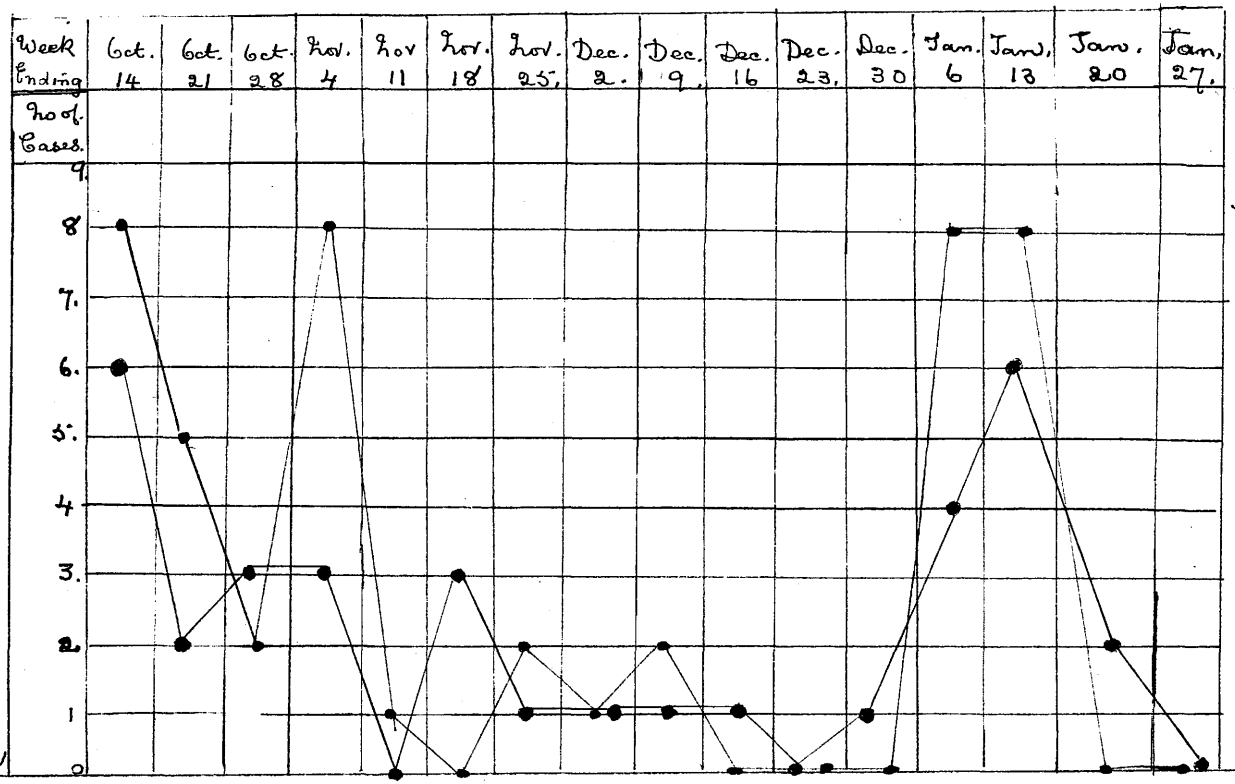

Chart VIII.

Showing incidence of cases of Diphtheria and of "Catarrhal Throats" during the period Oct 1905 - Jan 190

Black line — = Diphtheria

Red line — = Catarrhal Throats.

Wright[65] believes that the development of these phenomena can be largely avoided by the prophylactic administration of calcium salts. He considers tham to be associated with a diminution in the coagulability of the blood a condition which stands in causal relation to "serous haemorrhages" in general. He recommends 30 grains of calcium chloride or lactate to be given to an adult from the sixth to the tenth day after the injection of serum as a routine procedure.

NON-DIPHTHERITIC CATARRH OF THE FAUCES.

Contemporaneously with the cases of bacteriologically-verified diphtheria occurred a number of catarrhal 'sore throats' which failed to yield B. diphtheriae upon repeated culture tests. Reference to Chart 8. shows that there was a striking correspondence in the incidences of these diphtheritic and non-diphtheritic inflammations. During December both were infrequent. In January, with the recrudescence of diphtheria, complaints of these catarrhal throats again became common. Twenty-four of these 'sore throats' occurred in girls, ten in boys. The ages of the children attacked ranged from eight to fifteen. The local conditions present in the throats are shown in Table V. The cases which gave most trouble in diagnosis were those in which follicular deposits were present on

Table V.

Local Conditions present in "Simple Sore Throats."	No. of Cases.
Acute catarrhal tonsillitis...	2
Follicular tonsillitis	3
Mild catarrh of fauces and tonsils ...	22
Mild catarrh of fauces and tonsils with associated rhinorrhœa...	7
Total	34

TABLE VI.

Showing cases in whom "Simple Catarrhal Throats" were followed by Diphtheria.

No.	Initials of Case.	Bacteriological Report. Negative.		Bacteriological Report. Positive.	
		Date.	Clinical Particulars.	Date.	Clinical Particulars.
1	M. L.	October 9	Faucial and tonsillar catarrh. T. 101°. No coryza. Duration of illness 2 days.	January 3	Patches both tonsils. T. 105°. Severe attack.
2	E. H.	October 10	Redness of throat. No coryza. T. 100°. Ill 48 hours.	January 6	Redness of fauces. Mucus. No membrane. No coryza. T. 99·6°.
3	G. C.	October 10	Faucial redness. Looked ill. No coryza. T. 100°. Duration 3 days.	October 28	Coryza. No fever.
				January 11	Red throat. Coryza. Illness followed by pleurisy.
4	H. H.	November 2	Mild faucial catarrh. No coryza. T. 100°. Recovery in 36 hours.	January 9	Redness of fauces. Considerable coryza (sero-sanguineous). T. 99·4°.
5	E. M.	November 17	Follicular tonsillitis. No coryza. T. 102°. Ill 2 days.	January 7	Catarrh of fauces. No coryza. T. 101°.
6	C. O.	November 17	Mild faucial catarrh. T. 101°. Slight coryza. Ill 2 days.	January 9	Catarrh of fauces. Considerable coryza. T. 100°.

enlargement of the tonsils, in ten it was present to a very moderate extent and in four only was there definite enlargement affecting in each case only one tonsil. The temperature with these catarrhal throats reached 104° in three cases, in eight it was 102°, or over it. It averaged 101° or 101°·5 in most. The throat cleared, and the temperature fell to normal in most cases within four days, but in some, slight fever and redness of the throat existed for five or even six days.

Four of the children who had been in contact with acute cases of diphtheria received injections of antitoxic serum. One circumstance of interest is that six of the thirty-four children, as will be seen from Table VI., developed clinical or bacteriological diphtheria at a later period of the outbreak. Bacteriological examinations were repeatedly made in all these cases and on no occasion yielded a positive result. No satisfactory explanation of the etiology of these throats can be given without a complete bacteriological report on the organisms found in them, whereas the only positive statement I can make is that diphtheria bacilli were found in none of them, and 'cocci' were noted to be present in most. The close coincidence between these diphtheritic and non-diphtheritic throats, as set forth in the chart, appears to imply some-thing more than a casual connection between them. The position may of course be maintained that a negative report meant that the bacilli though

really present were few in number and were 'missed'. This interpretation is possible but seems to be controverted by the entire absence of any of the common sequelae of diphtheria in these children, and, further, no charge of infectivity could be definitely brought home to any of them. Between January 14th and 21st. eight of these patients, in some of whom nasal discharge was present, rejoined their healthy companions after periods of isolation varying from eight to fourteen days. Yet no fresh case of diphtheria occurred in the Institution until April 16th.

In two of the patients who had definitely suffered from diphtheria, what was apparently a simple tonsillitis occurred during recovery and while they were still isolated. In one case, a passing suspicion of scarlet fever was aroused, in the other, of a second attack of diphtheria. The details are as follow:-

EVA S. Age 10. had mild catarrhal diphtheria of the fauces with much coryza. Her illness commenced on October 9th. The nasal discharge was somewhat intractable, but had practically ceased at the end of the third week. She was an unhealthy-looking child with many carious teeth. On Nov 6th (33rd day) an erythematous rash of a bright red colour but not definitely punctiform and somewhat patchy in distribution was found to be present over the upper part of her chest and on the neck. The face was flushed, the tongue raw-looking, the throat more

injected than on the occasion of her primary illness and she complained of pain on swallowing and on pressure over her neck especially on the right side. The gland beneath the angle of the jaw on the right side was enlarged. The pulse-rate and temperature were raised. She was not sick .On the following day the rash was fading and the throat less congested. The temperature was 99° On the fourth day she was well. The eruption was not followed by desquamation. The case of pellicular throat occurred in the girl whose primary attack of diphtheria was followed by palatal palsy. She had been isolated in the sick-ward from the beginning of October, and on March 4th while still there was found to have a temperature of 102° and complained of pain on swallowing. On examination the right half of the soft palate was seen to be injected and on the right tonsil there was a white friable patch of exudation about the size of the little finger nail. The tongue was clean. There was no glandular enlargement and no tenderness on pressure Her pulse rate was 138 but this condition of pulse-frequency was not new having been noted since October. Her throat was "swabbed". On March 8th the throat was clean. There had been no spread of the patch and a negative bacteriological report had meantime been received. No antitoxin was given

The case of the first patient did not actually give rise to much difficulty in diagnosis, although a

suspicion of mild scarlet fever did cross the mind on the first day, but the patchy distribution of the rash, its non-punctate character, the evanescence of the symptoms and the absence of sequelae were against the diagnosis, nor did there appear to be any likely channel by which the infection of scarlet fever could have been conveyed to this patient.

The second case presented a more real difficulty. The patch , it is true, did not spread, was friable, and not adherent like the typical diphtheritic membrane, but it bore a close remblance to the exudation seen in many mild tonsillar cases of the disease during this outbreak. It was certainly possible that this child whose throat had yielded negative cultures on several occasions during convalesence, had suffered a re-infection. The nature of the exudation could only have been satisfactorily cleared up by bacteriological examination. A second culture test proved negative like the first.

PERSISTENCE OF DIPHTHERIA BACILLI IN CERTAIN CASES.

The prominent part played by the mild unsuspected cases of the disease in the inception and spread of epidemics of diphtheria has already been indicated. The persistence of bacilli, which are sometimes virulent, in the throat and nasal passages of convalescents is attended with no less danger to the public health. 'Return' cases which come under the notice of

physicians practising in Fever Hospitals are probably in many cases directly attributable to infection carried by discharged convalescents, though it is unlikely that the share of such convalescents in the spread of diphtheria is confined to the comparatively few instances which are thus brought into prominence. From a study of the disease, it is impossible to avoid the conclusion that many diphtheria patients treated in their own homes are at least afforded every opportunity of returning to school and work while they are still capable of imparting the disease to others.

The duration of diphtheria bacilli in the throat can only be ascertained by bacteriological examination in every case, as the period is subject to great individual variations. In some cases it would appear that the organisms disappear almost simultaneously with the membrane; but reports show that no general rule can be laid down as to the time during which the bacilli are persistent. Holt[66] quotes the results of bacteriological examinations of 605 cases investigated by the New York Health Department. In 309 the bacilli could not be found three days after the membrane had vanished from the throat, in more than half of the remaining 301 they had disappeared by the seventh day, In two only did they persist more than sixty days. Caiger[67] says that the period during which the bacilli are said to persist varies from eight to twenty-four days. In his own cases he found the average length

of time twenty days, but in some, the duration of infection thus estimated was two or even three months. He believes the longest time on record is 363 days.

In a certain proportion of cases of diphtheria, therefore, the phenomenon of protracted infection, as it has been called, occurs, and patients in whom it does occur are frequently responsible for the recrudescence of an apparently suppressed outbreak of the disease. Various explanations of this prolongation of the period of infectivity have been offered. Thus it has been suggested that it has its origin in the inadequacy of the means adopted to disinfect the affected parts, an explanation which especially covers the nasal and naso-pharyngeal types of the disease. It is obviously much more difficult to reach the recesses of the nose and the sinuses in connection with it than to apply disinfectants to the more accessible surfaces of the fauces.

Another suggested interpretation, that these cases arise through re-infection, has application only in the case of patients nursed collectively at all stages of the malady in hospitals, or, as in my own series, in the sick-wards of an Institution. It would be interesting to compare with hospital statistics, figures representing the persistence of the bacilli in the fauces or nares of patients in private practice, who are usually shut off from

contact with other cases of diphtheria during the entire time of their isolation. Again, as occurred in at least one patient during this outbreak, bacteriological examination of the throat and nasal secretions, made a reasonable time after the primary disease, may yield negative results, but may be succeeded by a positive result on the occasion of the next test. If this occurrence has no connection with contact with an acute or actively infectious case, one possible explanation of the circumstance may be that the previous negative result or results merely represented a failure to discover bacilli which, though present in the nose or throat, were not numerous. Another explanation may be that the 'swabs' were applied too soon after antiseptic treatment of the mucous surfaces and that in consequence inhibition of the growth of the bacillus resulted.

In addition to these more mechanical views of the causation of prolonged infection, Newsholme[68] has drawn attention to the conception of persistent infectivity occurring as " a phenomenon in the natural history" of infectious deseases.
This hypothesis somewhat discounts the importance of contact with acute cases and of disinfection, as it supposes that the phenomena do not mainly depend upon such conditions, but are events occurring during

the natural progress of some cases of the disease and independent of extraneous circumstances altogether.

The cases in which persistence of infection occur are not necessarilly those in which the primary illness has been a very severe one. During the Orphanage epidemic, our experience on the contrary was that the bacilli persisted most obstinately in cases in which the clinical evidences of diphtheria had not been at any time conclusive.

In four, out of the five in whom this phenomenon was observed, coryza had been the most prominent feature of the primary disease, in the fifth case coryza was never present during observation and the nasal mucous membrane seemed healthy on inspection.

For reasons which were in the main financial, the convalescent patients were not submitted to very frequent bacteriological examinations. The minimum duration of infection can not therefore be accurately stated in any one of them, for the throats may have been free from bacilli before the first negative culture result was received. On the other hand, the last positive result which may be arbitrarily regarded as fixing the maximum duration of infection, if it errs at all, errs in the direction of under-estimating the duration of the time of persistence of infectivity, since bacilli may have remained in the throats subsequent to the date at which it was received.

Table VII.

No.	Name.	1st P.	F. P.	Duration of Infectivity. (In Days.)
1	E. S.	October 9th	December 14th	66
2	E. R.	October 21st	December 14th	54
3	G. C.	October 28th	November 25th	25
	,,	January 10th	March 11th	60
				85
4	F. N.	November 11th	January 4th	54
5	E. H.	January 10th	March 11th	60

Shows cases in whom B. diphtheriæ persisted for more than fifty days.

1st P. = 1st Positive result. F. P. = Final Positive result.

In five cases as has been indicated, the duration of infection calculated from the date of onset of symptoms to the day on which the last positive bacteriological report was received exceeded 50 days.

Reference to Table VII shows the exact duration of the infectivity in days.

As has been said, all these patients suffered from diphtheria in an insidious form, and in all, with the exception of Case 5., coryza was present when they were first isolated, but this had been treated with apparent success, at least when the final examinations with positive results were made.

Case I. had in addition bad teeth and a spongy unhealthy condition of the gums.

Case 4. had adenoids.

Case 2. was a healthy looking child with no discoverable signs or symptoms except a nasal discharge which tended to form crusts.

Cases 3 & 5. deserve rather fuller consideration:

CASE 3. GLADYS C -.

The complicating pleurisy which occurred during one period of this child's isolation has already been described, she will now be considered as a possible link in the chain of infection

She was first discovered to have diphtheria bacilli in both throat and nose at the end of October and was isolated with six other patients, who had very slight

clinical evidences of ill-health and did not during isolation come into contact with any acute case of the disease. On November 25th the faucial and nasal secretions of these seven children were bacteriologically examined with negative results for the others but with positive for Gladys C. She was then removed from this room and isolated in company with one other little girl in whom diphtheria bacilli persisted during convalescence, this other child is referred to as Edith R -. Case 2, Table VII.
Although on the 51st day the report on Gladys C-'s nose and throat was that "no diphtheria bacilli" were present. She remained in isolation until the 65th day which was December 24th, being then free from nasal discharge and faucial catarrh she was allowed to rejoin her healthy companions. The other child Edith R - having still a positive report as to the infectious condition of her secretions was sent back to the sick-ward.
On Janry 2nd the first case of the 1906 series was discovered this being the first notified from the Institution since the beginning of December; on January 11th it was found that something had still to be added to the diphtheritic chapter in Gladys C-'s history, as bacteriological examination of the nasal discharge from which she was then found to be again suffering revealed the presence of diphtheria bacilli. She was immediately sent to the sick-ward with the other cases of diphtheria and was isolated for a

second period which as will be seen was of considerable duration, bacilli being reported present for the last time in her secretions on the 60th day (March 11th) of her second term of incarceration

It may have been coincidence but after this child was set apart from her fellows the outbreak almost immediately ceased to spread, only two cases being notified immediately subsequent to her isolation

If Gladys C -. were not responsible for the January outbreak, then its source remains undiscovered. It is at least reasonable to assume that the initial cases of this fresh series owed their origin to infection conveyed by her in spite of negative bacteriological reports, prolonged isolation, and the apparently healthy condition of her throat and nose on discharge. The circumstances of her infectivity may be accounted for in various ways.

It may be supposed (I) that the bacilli were present and were merely missed on the occasion of the bacteriological examinations in December.

(2) That re-infection from the secretions of the girl Edith R -. occurred before December 24th, and after the last negative examination.

(3) That under the stimulus of some catarrh a "recrudescence" of the original disease occurred after her release in December.

(4) That she became re-infected between Dec 25th and

Jan 11th by some one of the acute cases of diphtheria which then occurred, that the origin of the January outbreak could not be traced to her, but that she was nearly a victim like the rest.

It is idle to make assertions after the event when verification and confutation of the opinions held are alike out of the question, but the speedy cessation of the epidemic after the isolation of the patient appeared at any rate to discount the fourth of these conjectures; any one of the others remained within the limits of possible occurrence.

CASE 5. This patient was regarded with suspicion as the source of the April recrudescence but the evidence against her broke down at a critical point. She was an unhealthy-looking pallid child but there was little clinical evidence of her diphtheritic infection at any time beyond slight catarrh of the fauces when first isolated in January. She had no coryza. At the end of February diphtheria bacilli being still reported to be present in her throat, she was isolated with Gladys C., then the only other patient in the Institution known to be potentially infective. On March 11th bacilli were still present in her throat, but on April 10th, the 94th day of isolation cultures were negative. On April 14th no abnormal condition being apparently present in throat or nose she was allowed to return to the ordinary life of the

Institution after thorough disinfection of her person and clothing. On April 16th a girl who had slept in the same dormitory during these two nights developed unmistakeable diphtheria and on April 18th another girl also from this dormitory contracted the disease. The usual period of incubation in diphtheria is stated to vary from two to six days, it was therefore not unjustifiable to entertain suspicion of a connection between the release of Ethel H. and these incidents, especially as the girl who developed the disease on April 16th had been in exceptionally close contact with Ethel H. Remembering past experience Ethel H. was at any rate again isolated. The chief link in the chain of evidence was however now proved to be wanting. Attempts to cultivate the bacilli from her throat and nasal secretions repeatedly failed; 'swabs' sent to Leeds on two subsequent occasions and to the Laboratory of the Clinical Research Association agreed in obtaining negative reports. It was of course possible that some fragment of discharge adhering to this patient's hair or to some other part of her person or to her clothing may have conveyed the infection in spite of precautions. On the strength of these negative reports she was sent to her own home, and no occurrences of a suspicious nature have since been reported by her friends. It is equally significant, however, that no fresh cases of diphtheria have occurred in the Institution since her departure.

The occasional persistency of infectivity in

diphtheria, exemplified by the five cases we have been considering, raises many practical questions mainly concerned with the school-attendance of children convalescing from the disease. It is obvious that skilled bacteriological examination is the only certain means of determining the period of quarantine necessary in any individual case, nor is one bacteriological examination sufficient. A single negative result ought to be corroborated by a second at least, and further should there be any dubiety as to the typical or atypical nature of the bacilli recovered from the throat of any child the community not the child should have the benefit of the doubt and isolation should be prolonged for the time requisite for the safety of susceptible persons. If this method were carried to its logical conclusion it would mean that no child known to have suffered from diphtheria would be permitted to return to school without certificates of two negative culture tests from nose, throat, or any part from which a discharge existed. In the case of the school attendance of children of wealthier parents, this rule can be carried out without difficulty. It is otherwise with children attending public elementary schools, for unless patients of this class suffer from diphtheria of a severe type necessitating admission into hospital, they are usually unable to command prolonged medical supervision. Many of them return to school at the

end of a period of quarantine arbitrarily fixed, for, as matters stand at present, there is no guarantee that their throats and noses have ever been submitted to bacteriological examination at all. From the standpoint of the community this is of less importance at the acute stage of an attack of clinical diphtheria than during the stage of convalescence, and if the number of bacteriological examinations be of necessity limited it would be better to reserve them for the determination of the period of necessary quarantine and to diagnose and notify on clinical evidence alone. Even in my short series of cases it has been shown that in one out of ten the usual period of quarantine would have been totally inadequate if the persistence of bacilli in the throats and nasal passages were be accepted as a guide to infectivity. It may be objected that, without tests as to virulence, the mere presence of diphtheria bacilli means little, and that bacteriologists are not yet agreed as to the infectivity of morphologically doubtful bacilli. In actual practice, it seems the wisest procedure, however, when a report is received stating without qualification that diphtheria bacilli "are still present" in the throat or nose of a convalescent, to accept the guidance of bacteriology and to prohibit school attendance at least. Moreover, some scheme of home-supervision of these convalescents

would have to be devised for isolation without it would be of uncertain value. Until all elementary schools are placed under some system of medical control, vested with considerable discretionary powers, no check upon the spread of diphtheria by means of convalescents and mild unsuspected cases of the disease is likely to be effective.

Another question which concerns hospital rather than school administration is raised by the prolongation of the period of infection in some cases of diphtheria. At least one instance is known to me personally in which the disease appeared to be definitely conveyed to others in the ward by cases of diphtheritic paralysis admitted into a Childrens' Hospital. If such cases are urgent they ought at least to be isolated provisionally until their throat and noses have been bacteriologically examined, or a small ward in each hospital should be set apart for their reception.

It has been sufficiently shown, even within the limits of my short series of cases, that diphtheria is no longer a disease of uncertain origin, that the key to its nature lying in our hands its treatment has reached that level of simplicity and directness which co-exists with certainty of knowledge.

It is suggested by the progress of an epidemic of even this circumscribed extent that the problems

which press for solution in connection with diphtheria are no longer mainly those of its etiology, nor of the cure of the individual case, but rather are concerned with the still considerable prevalence of the disease.

The difficulties which bar the way to the complete suppression of this infection are no doubt almost insurmountable, but efforts of the future must be directed towards securing a measure of control over its spread commensurate with the definiteness of our knowledge of the methods of its dissemination.

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