OBSERVATIONS ON THE RECURRENCE OF DIPHTHERIA IN CAMBRIDGE IN THE SPRING OF 1901.

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THE outbreak of Diphtheria which occurred in Cambridge and Chesterton last October and November has already been the subject of a paper in this Journal, which dealt with the facts observed up to January 5th, 1901. The present communication deals with a return of the disease in the Spring of this year.

The force of the autumnal outbreak fell in the last two weeks of October and the first week of November, during which period 50 cases were notified and 5 deaths occurred. The prospect was disquieting, but the disease quickly subsided. In the course of the next week there were only 8 notifications; and from this time onwards until Jan. 5th but 8 cases occurred, 6 of these about the end of December.

During the six weeks which followed January 5th 5 cases of diphtheria were notified in Cambridge and Chesterton. In the week ending February 23rd there were four, but they were not confirmed by bacteriological investigation. After this a few cases continued to be notified each week, a maximum of eight being reached in the week ending April 6th.

Since April 15th up to the time of writing (Aug. 7th) there have been 7 notifications only, 3 unconfirmed and 4 confirmed by bacteriological investigation, the latter including a nurse in the diphtheria ward of Addenbrooke's Hospital, and one imported case.

The Spring outbreak may therefore be considered to have begun with the cases notified on February 19th and to have ended with that notified on April 15. The following table shows its progress.

TABLE I.

	Cases notified	B. Δ found	B. Δ not found		
Week ending Jan. 12	1				
19	1				
26	0				
Feb. 2	2				
9	0				
16	1				An imported case. Not including two country cases in Addenbrooke's Hospital
23	4	0	3	1 fatal	
March 2	1	1		1 fatal	Died after recovery from diphtheria of operation for removal of the tracheotomy tube
9	3	1	2		
16	3	3		1 fatal	
23	0				
30	4	3	1		
April 6	8	8		1 fatal	
13	3	2	1		Not including a country case in Adden. Hosp.
20	1		1		
27	0				
May 4	0				
11	0				
18	0				
25	1		1		
June 1	0				
8	0				
15	1	1			Nurse in the diphtheria ward Adden. Hosp.
22	1		1		
29	0				Not including a country case in Adden. Hosp.
July 6	1	1			Probably an imported case
13	2	2		1 fatal	Not including a case notified as probably diphtheria and not confirmed by bacteriological examination
20	0				
27	0				
Aug. 3	1		1		
	39	22	11		

The Spring outbreak produced in all 27 notified cases of diphtheria. All were bacteriologically investigated. By this means the diagnosis was confirmed in 18 cases (in 7 by microscopic examination of cultures only, and in 11 by the complete investigation of isolated cultures). In 8 it was not confirmed, though two or more cultures from each were examined[1].

Out of these 8 unconfirmed cases, one was probably a true case of

[1] From one patient who was dying when first brought under observation no swab was obtained.

diphtheria, for a brother and a sister at home who remained well, were found to have diphtheria bacilli in their throats. The remaining 7 were not clinically very typical, and may probably not have been true cases of diphtheria.

Among the 18 notified cases in which diphtheria bacilli were found were three deaths; but one of these was caused by an operation for removal of a tracheotomy tube long after recovery from diphtheria. If this one be excluded the case mortality was 11 per cent.; and this remains nearly the same if we include the 8 cases unconfirmed by bacteriological examination, of which one proved fatal.

During the Spring outbreak the same measures which had been used, as was thought with success, in the Autumn, were again put into practice.

(*a*) Antitoxin was supplied free for prophylactic use, in the case of those who had come into contact with the actual cases of diphtheria, or with those who, not being ill, were known to be harbouring the diphtheria bacillus. And in the case of the poorer classes prophylactic injections were offered and given by a medical man acting under the authority of the Medical Officer of Health.

(*b*) Swabs were supplied to medical practitioners, and bacteriological investigations of their poorer patients made at the public expense. Moreover, the medical practitioners were requested not to certify convalescents as free from infection until three consecutive negative examinations should have been obtained.

(*c*) Whenever diphtheria was known to have broken out in a school and the school had been accordingly closed, the children who had been attending, or such of them who belonged to the classes more particularly affected, were visited in their own homes by the Medical Officer of Health or his representative. And with the consent of the parents a bacteriological examination was made of the throats of them and of other children, if any were living in the same houses. The brothers and sisters of actual cases were sought out and examined as well as those who were in the habit of associating with the latter in work or play. When diphtheria bacilli had been found in any of those thus examined, the parents or guardians were told that the infected child was a source of danger and might communicate diphtheria to those with whom it came in contact, and they were advised to allow it to be isolated in a Home which was opened for the purpose. As nearly all the healthy persons found to be infected were children of school age or

less, it was not difficult to get consent to isolation[1]. Seventeen healthy persons with diphtheria bacilli were discovered. Of these three were not isolated, because the Home was not then open, one because he was suffering from another contagious affection, and two only refused to go to the Home. The remaining eleven voluntarily submitted to isolation.

Besides the home examinations, on two occasions swabs were taken from children at schools where a notified case had occurred. In each instance, only those children attending the classes most implicated were examined, and no diphtheria bacilli having been discovered, these schools were not closed.

The work of visiting the school children in their own homes, of talking to parents, and getting them to consent to the examination of their children was very laborious, and required both tact and patience. And owing to the fact that the staff of helpers which was got together in October last was not available in the Spring, the work could not be carried out so thoroughly as was desirable. Nevertheless a large number of people were examined and the total number of swabs from all sources received since February has amounted to 466 (not including 153 from a country village). If we add those belonging to the Autumn outbreak, the total exceeds 1600, and 172 cultures have been isolated and tested on animals.

The following is an account of the distribution of the cases among the schools affected and the steps taken to prevent the disease spreading.

King Street School, Girls and Infants. Two children attending this school having been notified as suffering from diphtheria, 9 others belonging to the class affected were examined on February 20 with negative results. No diphtheria bacilli were found in the notified children nor in their brothers and sisters. The school was not then closed.

St Giles's Boys' School. A case of diphtheria having occurred in a boy attending this school, and another in the infant brother of a scholar, 32 boys were examined at the school on March 12, and cultivations made from their throats. In none was the diphtheria bacillus found. In no less than 17, however, were Hofmann-like forms present. Of these one, which more closely resembled the diphtheria bacillus, was isolated and tested for acid production and for virulence, with negative result. Those living in the same houses as the two patients, to the

[1] It was not thought expedient, as a rule, to examine the parents or bread-winners, on account of the impossibility of isolating them without provision being made for the support of those dependent on them.

number of nine, were also examined, with the result that the infant patient's brother who had been attending the school, and a brother and a sister of the other case, were found to be infected with the bacillus, though they remained well. These three children were supposed to be isolated in their own homes, the Isolation Home being as yet not available.

The school was not closed and no further cases occurred in it, nor in any persons connected with the patients or infected children.

King Street School, Girls and Infants. Several cases of diphtheria having occurred in this school since the examination mentioned above, the school was then closed and it was decided to make a bacteriological examination of the children in their own homes.

Owing to the difficulty of finding suitable assistants, this could not be completely or expeditiously carried out, and we had to be content with examining 63 out of the 160 children. As the cases were scattered widely throughout the school, it was impossible to select any particular classes as having been more exposed to infection than the rest. The result of this investigation was the discovery of three clinical cases of diphtheria not under medical treatment, and 10 healthy children with diphtheria bacilli in their throats. Cultures from 10 of these were isolated and tested, with the result that 6 were virulent to guinea-pigs, including those from the clinical cases. The other 4, which in their mode of growth on various media, in their reaction to Neisser's stain and in the production of acid when grown in glucose-broth, were identical with the diphtheria bacillus, nevertheless did not kill guinea-pigs in doses of 2·0 c.c. 48 hour old broth-cultures.

The cases and the infectious persons thus discovered were all isolated, either in the Hospital or the Home for persons infected with the diphtheria bacillus. No further case of diphtheria occurred at this school nor in any of those connected with the patients. It is, however, probable that the cessation of outbreak among the children of this school was not entirely due to the measures adopted. For since the investigation of about one-third of the school had revealed so many infected persons, it cannot be doubted that there must have been several infected persons also among the unexamined who were allowed to go free. That diphtheria stopped at this time is probably, therefore, to be attributed in a large measure to the closure of the school, and possibly also to the time of year[1]. There were in all 13 cases of diph-

[1] The last case belonging to this school was notified on April 3. After this only five cases, two alone confirmed by bacteriological investigation, were notified in the

theria among the children attending this school, 3 unconfirmed by bacteriological examination, the rest all confirmed by complete investigation of isolated cultures.

A case of diphtheria occurred in a teacher in a High School for Girls. From this patient during the early stage of her illness a culture of non-virulent diphtheria bacilli was isolated.

Paradise Street School. Two notified cases occurred, but these were not confirmed by bacteriological diagnosis. Nine of the other children of this school were examined, but no diphtheria bacilli found.

The school was not closed; no further cases occurred.

St Barnabas. One unconfirmed case was notified.

British School. There were two cases, both confirmed, one fatal.

The Isolation Home.

The Home was opened primarily to accommodate those who, without being ill, were found to be carrying about the diphtheria bacillus. Eleven such were isolated. Lest any of them should at the time when they were examined have been passing through the incubation stage of diphtheria all received a prophylactic injection of antitoxin. In addition, owing to lack of other accommodation, two mild clinical cases of diphtheria and five convalescents from the Addenbrooke's Hospital were also admitted.

This association of healthy persons with cases of diphtheria was not undertaken without due deliberation. It was felt that the bacteriological examination could be firmly relied upon to exclude all except those who were harbouring the true diphtheria bacillus, and that such persons were not likely to be harmed by diphtheria bacilli received from others. Moreover, since Wasserman and others have shown that many human beings have in their blood a considerable amount of diphtheria antitoxin, it was thought that those who carry about the bacillus in their mouths without being ill, were probably protected in this way.

At the same time it was fully recognised that this argument does

town. The last confirmed case was notified on April 9th: the last case (unconfirmed) on April 15th. The weather, which had been cold and wintry, was very wet from the 10th to the 16th. After this it cleared up and became fine and dry, and for a few days very hot; so that we passed abruptly from winter to summer. The diphtheria, however, had ceased to spread a week before the change in the weather took place. The cessation of the outbreak therefore cannot be attributed to the change of weather, though it is not improbable that it was connected with some more subtle seasonal influence.

not necessarily apply to those persons who are found to be harbouring the non-virulent diphtheria bacillus. It may be questioned whether it is necessary to isolate these persons, and whether, if isolated among those who carry about the virulent diphtheria bacillus, they are not liable to catch diphtheria. In practice, however, the virulence of the bacillus is only determined after isolation has been carried out; and accordingly in our Home five of these persons lived for some time (see Table II.) in close contact with twelve others who were infected with diphtheria bacilli, known to be virulent in the case of eight. This action was followed by no bad results, no case of diphtheria or even of sore-throat occurring among the healthy persons in the Home.

From seven of the persons isolated in this Home, the bacilli were twice or oftener isolated and tested for virulence on the guinea-pig. The result was striking. Those admitted with a non-virulent diphtheria bacillus were never found to have acquired a virulent bacillus during their stay in the Home, nor was a non-virulent diphtheria bacillus ever found in a child in whom virulent bacilli had once been found. In the case of E. J. the bacilli were isolated and tested 10 times in the course of the 15 weeks she remained in the Home. During 5 of these weeks her little sister V. J. was with her constantly, and on three occasions the bacilli were isolated from her and proved fully virulent. Moreover from another girl, G. B., who remained in the Home almost as long as E. J., diphtheria bacilli were isolated and proved fully virulent no less than 6 times. The same evidence, though less strong, is afforded by the rest of the seven cases mentioned above. (See Table II.)

The conclusion seems to be either:

(1) that no transmission from one child to another occurred while they were in the Home;—and in this connection it must be remembered that antiseptics were in daily use by everyone, except for 24 hours before the taking of each swab; or else,

(2) that certain persons have the power of rendering a virulent diphtheria bacillus non-virulent when it gets upon the surface of the pharyngeal mucous membrane. And if we admit this, we ought also to admit that an attenuated bacillus recovers its virulence when it gets into the mouth of an ordinary individual.

This conclusion is supported by the fact that in two instances non-virulent diphtheria bacilli were found in a healthy elder sister of patients with actual diphtheria, and from whom virulent bacilli were isolated. It is tempting to conclude, either that the younger children suffered from diphtheria because they caught a non-virulent bacillus

Table II.

Examination of Notified Cases, and Healthy Persons found to be Infected.

Δ = Diphtheria bacilli seen on microscopic examination.
Δ = Diphtheria bacilli isolated and proved virulent.
Λ = Diphtheria bacilli isolated and proved non-virulent.
O = No diphtheria bacilli seen on microscopic examination.
\+ = Death of patient.

(A) *Notified Cases.*

Reference number and initials of patient		Date of notification	February					March									April												May				
			2	12	18	19	25	4	10	11	13	15	20	25	29	30	1	2	6	8	10	15	17	18	24	27	30	3	6	13	16	
	H. N.	2. II	Δ	O	-	O	-	O																								
	E. M.	2. II	Δ	Δ	-	O	-	-	O																							
990	F. W.	1. III	-	-	-	-	-	Δ	-	-	-	-	Δ	-	O	O	-	-	O													
939	M. A.	6. III	-	-	-	-	-	-	Δ	Δ	Δ	-	O	O	O																	
991	L. A.	10. III	-	-	-	-	-	-	-	Δ	-	-	Δ	-	-	-	-	+														
937	M. A.	6. III	-	-	-	-	-	-	O	Δ	-	-	Δ	-	Δ	-	Δ	O	O	Δ		} For further examinations in Isolation Home see below										
998	H. A.	26. III	-	-	-	-	-	-	-	-	-	-	-	Δ	Δ	-	**Δ**	-	-	-	O											
938	R. A.	1. IV	-	-	-	-	-	-	O	-	-	-	-	-	-	-	-	Δ	-	-	Δ											
981	Miss B.	12. III	-	-	-	-	-	-	-	-	Λ	Δ	-	-	-	-	-	-	-	-	O											
1012	F. S.	29. III	-	-	-	-	-	-	-	-	-	-	-	-	-	**Δ**	-	Δ	-	-	Δ	-	Δ	-	Δ	-	Δ	-	Δ	O	O	
1013	E. S.	1. IV	-	-	-	-	-	-	-	-	-	-	-	-	-	**Δ**	-	Δ	+													
1015	J. M.	29. III	-	-	-	-	-	-	-	-	-	-	-	-	-	**Δ**	-	-	O	-	O	-	O									
1023	E. T.	1. IV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	**Δ**	-	-	-	O	-	Δ	-	Δ	-	-	O	Δ	O	Δ	O
1039	V. J.	1. IV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	**Δ**	-	O	-	For further examinations in Isolation Home see below										
1038	J. H.	2. IV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	**Δ**	-	-	O	-	Δ	-	Δ	-	-	Δ	Δ	-	Δ	
1047	M. S.	3. IV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	**Δ**	Δ	-	O	-	Δ	-	O	-	O	O				
1066	M. M.	3. IV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	**Δ**	} For further examinations in Isolation Home see below											
1043	E. T.	4. IV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	**Δ**	-	}												
1101	Mrs G.	7. IV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Δ	Δ	-	Δ	Δ	Δ	-	Δ	Δ	Δ	Δ	Δ	
1105	E. W.	9. IV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Δ	O	-	O	-	O							
	E. B.	19. II	-	-	+																											
898	C. B.	,,	-	-	O	O	O																									
899	P. B.	,,	-	-	O	O	O																									
901	T. B.	,,	-	-	O	-	O																									
923	A. E.	6. III	brother of 926 and 928					O	O	O	-	O	O	O																		
1005	H. R.	27. III	-	-	-	-	-	-	-	-	-	-	-	O	O																	
994	G. Br.	6. IV	-	-	-	-	-	O	-	O	-	O	-	O																		
1047	S. W.	11. IV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	O	O									
1158	Mrs M.	15. IV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	O	-	O								

Most of the examinations of patients in Addenbrooke's Hospital were made by Mr T. Strangeways-Pigg, Pathologist to the Hospital.

(B) *Healthy persons found to be infected, but not removed to Isolation Home.*

(*a*) Because the Home was not ready in time. (*b*) Refused to be removed.
(*c*) Because suffering from contagious eczema.

			March		April						
			7	9	1	2—3	4—5	8	10	15	17
923	A. W.	(*a*) brother to 990	Δ	Δ	O						
926	J. E.	(*a*) brother and sister	-	Δ							
928	N. E.	(*a*) to 923	-	Δ							
1025	M. R.	(*b*) - - - -	-	-	-	Δ	-	-	O	-	O
1054	A. C.	(*b*) - - - -	-	-	-	Λ					
1118	M. S.	(*c*) - - - -	-	-	-	-	-	Δ			

(C) *Persons removed to the Isolation Home.*

(*a*) Notified cases. (*b*) Convalescents. (*c*) Healthy persons found to be infected.

Reference number and initials of patient			April										May								June							July									
			3	6	8	10	15	17	22	24	26	27	30	3	6	13	16	18	23	25	28	1	5	7	10	16	24	26	28	1	3	5	9	10	13	19	22	23
1066	M. M.	(*a*)	-	Δ	-	-	-	-	O	O	Δ	-	O	Δ	-	O	O	O																				
1043	E. T.	(*a*)	Δ	-	-	-	-	O	O	O																												
937	M. A.	(*b*) continued from A	-	O	Δ	-	-	Δ	Δ	O	O	O																										
998	H. A.	(*b*)	-	O	Δ	-	-	O	O	O	O																											
938	R. A.	(*b*)	-	-	-	-	-	Δ	O	O	O																											
1039	V. J.	(*b*) sisters - - -	-	-	-	-	-	-	O	Δ	O	O	Δ	Δ	Δ	O	Δ	-	O	Δ	O	O	Δ[1]															
1034	E. J.	(*c*)	Λ	-	Δ	-	Δ	-	Δ	Λ	O	Λ	-	O	Λ	O	Δ	-	O	Δ	O	O	Λ	Λ	Λ	Δ	O	Λ	Δ	Λ	Δ	Λ	Δ	Δ	O	O	O	
1099	G. B.	(*c*) - - - - - - - -	-	-	Δ	Δ	Δ	-	Δ	O	Δ	-	-	Δ	Δ	O	Δ	-	O	Δ	Δ	O	Δ	Δ	Δ	Δ	Δ	Δ	Δ	Δ	Δ	Δ	O	-	O	O		
1026	Fl. S.	(*c*) sister to 1012 & 1013	Δ	-	Δ	Δ	Δ	Δ	-	O	Δ	Λ	-	Δ	Λ	Δ	O	O	Δ	O	O	O																
1028	L. W.	(*c*) - - - - - - - -	Λ	-	Δ	-	O	O																													
1087	G. G.	(*c*) - - - - - - - -	-	Λ	-	Δ	Δ	-	Δ	-	O	Δ	-	Δ	Λ	O	Δ	-	O	O	O																	
1082	E. D.	(*c*) - - - - - - - -	-	Δ	-	Δ	-	-	O	O	O																											
1050	A. T.	(*c*) sister to 1023 - -	Δ	-	-	Δ	Δ	-	Δ	O	Δ	-	-	O	Δ	-	O	Δ	O	O	Δ	O	O	O														
1090	M. H.	(*c*) - - - - - - - -	-	Δ	-	-	-	O	O	O	O																											
1093	W. S.	(*c*) - - - - - - - -	-	Δ	-	-	-	O	O	Δ	O	O	O																									
1117	M. H.	(*c*) - - - - - - - -	-	-	Δ	-	-	-	Λ	O	O	O																										
1124	E. R.	(*c*) - - - - - - - -	-	-	Δ	-	-	O	O	O	O																											

[1] This culture was more than once examined and no suspicious micro-organisms were seen: the child was consequently sent home. At a subsequent examination of the tube, however, one colony of diphtheria bacilli was found.

which regained its virulence when it entered their mouths, or that the elder girls caught a virulent bacillus from the children and caused it to lose its virulence. Either conclusion, however, would be at variance with the well-known stability of virulence, or want of virulence of the diphtheria bacillus[1].

On the other hand, if we conclude that those who are found to have the non-virulent diphtheria bacillus have acquired a bacillus already attenuated, we shall have to regard these persons not only as harmless to others, but as themselves liable to catch diphtheria when they come into contact with those who have the virulent diphtheria bacillus, for there would be no reason to regard them more than others as possessing a special resisting power. Neisser[2] indeed has recently found a high degree of antitoxic power in the serum of two girls who suffered from recurring sore throat and from whom the non-virulent diphtheria bacillus was isolated. But since diphtheria antitoxin is found in the serum of many ordinary people, it may in these cases have been quite unconnected with the fact that they harboured the non-virulent diphtheria bacillus. Lubowski (*loc. cit.*) attempted to produce antitoxin in rabbit with these same bacilli, but did not succeed.

While within the Home, those found to be harbouring the non-virulent diphtheria bacillus were not at any time separated from those who harboured the virulent bacillus.

Orders were, however, given that as soon as bacteriological examination had shown a child to be free from one or other of these bacilli, he should be removed to another part of the building and put with others in like case as himself, until three consecutive negative examinations had set him free, or the reappearance of the bacillus caused his return to the general part of the Home.

The experience gained during the Spring outbreak of diphtheria here, has tended to confirm the opinions arrived at during the Autumn outbreak.

I shall briefly refer to three of them.

(1) "Experience of the outbreak of diphtheria in Cambridge gave no reason for thinking that the pseudo-diphtheria bacillus is other than perfectly innocuous to man."

[1] Lubowski working in Ehrlich's laboratory (*Zeitschr. f. Hygiene*, Leipzig, Bd. xxxv., p. 87) found that he could not make non-virulent diphtheria bacilli virulent for guinea-pigs by repeatedly passing them through those animals.

[2] *Deutsche med. Wochenschrift*, 1900, Hf. 32.

During the Spring, as also in the Autumn examinations, Hofmann's bacillus was very frequently found. I do not know whether all bacteriologists would regard all the micro-organisms which I am accustomed to class under this head, as pseudo-diphtheria bacilli. Some, as they first appear on the original serum culture, are far more than others difficult to distinguish on morphological grounds from true diphtheria bacilli, and in not a few instances I have been in doubt until pure cultures had been isolated; but this I can affirm, that of all those isolated by me and tested on animals (17 since the beginning of March, and 69 last year), none form acid out of glucose nor produce any but a very transient local swelling when 2·0 c.c. of a well-grown 48 or 72 hour broth-culture is injected into the guinea-pig, and they do not give Neisser's reaction when grown for 22 hours on Löffler's blood-serum (ox). Moreover, however much they may have resembled the diphtheria bacillus at the start, they come in sub-cultures closely to resemble what I regard as the typical Hofmann form.

It has been thought better, for the sake of simplicity, to omit from Table II. all reference to the finding of Hofmann's bacillus, but it may be stated that it was frequently found, and that too, often at the time when the diphtheria bacilli were disappearing, and consequently not found without careful search. The two bacilli were often associated together and always with all their distinctive characters quite marked. From a child in whom the diphtheria bacillus had been found no less than 20 times, frequently isolated and tested for virulence, the diphtheria bacillus was found after prolonged search on the last occasion on which it appeared, and with it was the bacillus of Hofmann. Both micro-organisms were isolated. The Hofmann was typical in form, formed no acid, and was perfectly harmless to a guinea-pig which received 4·0 c.c. of a 48 hour broth-culture; while on the other hand 0·1 c.c. of a similar culture of the diphtheria bacillus killed a guinea-pig as usual within the 48 hours. There was therefore no evidence of the diphtheria bacillus becoming gradually changed into the pseudo-diphtheria bacillus just before its disappearance.

(2) It is, I believe, an error to conclude that diphtheria bacilli are distributed among the healthy members of a community free from diphtheria. These investigations have been made principally on children attending schools in which diphtheria had broken out, and on others who had been in more or less direct contact with actual cases. And so far as this was the case they afford but little evidence bearing on this point. But they include also the examination in November of

43 children attending a school in which there had been no case of diphtheria, and in March of 32 boys attending a school in which there was but one case, and of 9 boys attending another school in which there were two notified cases, neither of which was confirmed by bacteriological examination; and in none of these 84 children were diphtheria bacilli found. On the other hand, all the healthy persons who were found with the diphtheria bacilli in their throats had been in contact more or less directly with clinical cases. Thus of the 17 infected healthy persons discovered during the Spring, six were brothers and sisters of cases, two were girls employed at needlework in the same room as an infected person sister of a clinical case, nine were girls attending a school in which eleven cases of diphtheria had recently occurred. Thus all could be accounted for. And this remark is equally true of the healthy persons discovered to be infected with the bacillus during the Autumn. It may therefore be stated that *diphtheria bacilli were found in the healthy throats of those only who had come into more or less direct contact with actual cases of diphtheria.* On the other hand the bacillus of Hofmann was found quite as frequently among those who had never come into contact with cases of diphtheria as in those who had done so.

(3) Partially attenuated diphtheria bacilli have not been found.

As in the Autumn, so in the Spring, the cultures have either killed guinea-pigs within 48 hours, or three days at latest, the dose injected being 0·1 c.c. of a 48 hour broth-culture (or in some cases 0·5 c.c., this being the smallest dose injected), or 2·0 c.c. of a well-grown 48 or 72 hour broth-culture has produced nothing more than a trivial local lesion. The only exceptions to this rule have been two, and in each of these cases when the injection was repeated with a new culture, death took place within the usual time. I do not deny that diphtheria bacilli may become attenuated, but think it interesting to note that in a somewhat extended experience partially attenuated bacilli have never been found. Fifty-five diphtheria cultures have been separated and tested for virulence during the spring, making with the 24 isolated and tested during the autumn and winter, 79 in all.

It is also worthy of note that in no case, as far as is known, has a virulent diphtheria bacillus been replaced by a non-virulent diphtheria bacillus before its final disappearance. Reference to Table II. will show seven cases where the virulence of the bacilli present on from two to ten occasions in each case was tested and found constant.

The non-virulent diphtheria bacilli. Non-virulent bacilli were found during the Spring in one clinical case during the early stage of the

illness, and in 6 other persons who remained well. These bacilli were microscopically typical diphtheria bacilli and showed no points of distinction in their modes of growth on culture media. They gave Neisser's staining reaction. Only on the injection of animals did the difference show itself[1]. The guinea-pig experiments were in the case of many of them repeated so as to leave no doubt as to the reality of the want of virulence. The animals injected with 2·0 c.c. of broth-culture suffered very little local swelling, and a small abscess about as big as a pea was the principal result[2]. From these little abscesses the bacilli in pure culture were several times obtained and tested on guinea-pigs to see if they had gained in virulence. One of them was passed through four animals in succession. But in each case the injection of 2·0 c.c. of 48 hour broth-culture produced no more effect than at first.

It has already been stated that a harmless diphtheria bacillus was found during the early part of the illness in one case. A similar observation was made during the October outbreak, and in another case which occurred then, a non-virulent diphtheria bacillus was obtained from a patient examined for the first time during convalescence. Neisser[3] points out that one cannot infer anything as to the virulence of a bacillus for man from observations on the guinea-pig, and refers to the culture of *Streptococcus* which Koch and Petruschky obtained from a woman who died of puerperal peritonitis, which as it was exalted in virulence for the rabbit, lost its virulence for man. On the other hand, I do not think it permissible to draw from experiences with the *Streptococcus*, inferences as to the diphtheria bacillus, which, unlike the coccus, forms *in vitro* a powerful poison which affects alike man and many animals. In Cambridge the non-virulent diphtheria bacillus has been found in 3 only of the 31 clinical cases which have been fully investigated since last October, while it has been found in no less than 8 out of the 18 persons who remained well, and from whom cultures of diphtheria bacilli were isolated. It would appear therefore that

[1] With two avirulent diphtheria bacilli of this kind Lubowski, *Zeitschr. f. Hygiene*, Bd. xxxv. p. 87, in Ehrlich's laboratory succeeded in immunising animals and producing a serum which agglutinated not only these bacilli but also 23 different races of quite typical diphtheria bacilli, but which had no action on pseudo-diphtheria bacilli.

[2] I have more than once seen similar abscesses form in guinea-pigs treated with large doses of virulent bacilli together with antitoxin. And also in an immunised horse treated with living bacilli. In the latter case the bacilli obtained from the abscess had retained their virulence.

[3] Zur Differentialdiagnose des Diphtheriebacillus, *Zeitschr. f. Hygiene*, 1896, Bd. xxiv., p. 453.

the bacillus which is non-virulent for guinea-pigs is non-virulent also for man.

The non-virulent diphtheria bacillus occurred twice only among the seven diphtheria bacilli which were isolated from healthy persons in the Autumn, and the virulence of which was determined; while on the other hand it occurred 6 times out of 11 cultures of this kind obtained during the Spring. This may perhaps be due to some seasonal influence.

Should persons who without apparent illness are found to have the diphtheria bacillus in their throats be notified as cases of diphtheria?

Early in the course of the autumnal outbreak this question arose in Cambridge and was decided in the negative. The question may seem to some superfluous; the obvious answer being that diphtheria is a disease, and therefore a person cannot be held to have diphtheria, who remains well. But it has been urged on high authority, that these persons should be notified.

The question therefore seems worth discussing and that chiefly on the ground of expediency. It has been pointed out that without notification the Medical Officer of Health has no power to deal with these persons, but that armed with this instrument he can compel them to be isolated. In answer to this, it may be said that he could only compel the removal of those for whom it could be shown that isolation was impossible at home, and that too on the receipt of an order from a magistrate; that home isolation of a healthy person in a family which did not believe in its necessity could of course be nothing but a farce. Moreover compulsion in a few instances would raise a general opposition to isolation, and the taking of swabs, which could not be enforced, would be largely resisted.

On the other hand, when diphtheria is prevalent, the failure once and again to isolate a person in whom diphtheria bacilli have been found is not of great importance. It is clearly impossible to bacteriologically examine everybody who may have by some chance caught the bacillus. And since some such persons must inevitably remain at large, one more or less will not greatly signify[1].

Nevertheless it is worth while taking a considerable amount of

[1] This applies only to times when diphtheria is prevalent: at other times when none but sporadic cases occur it is possible, no doubt, to examine every 'contact,' and very desirable to isolate all infected persons.

trouble if we can only isolate a good proportion of these infectious persons, or at any rate keep them from school. In that case we should congratulate ourselves on our success and not grieve too much that some have escaped. The truth is we can do nothing unless the people back up our measures. Compulsion is fatal to success. If it were a case of dealing with our Public Schools and the class of people who send their sons to them, there would be little or no difficulty in carrying out bacteriological examination of contacts, and the parents would see to the isolation of their infected children, for they would at once recognise that the measures proposed were in their own interest. The poorer classes will take the same view if the matter is fairly explained to them. We must therefore in such matters act by persuasion rather than by force, and offer bacteriological examination as a privilege which it would be wise for them to accept, and let them refuse it if they will. That such a course is not barren of results is, I think, shown by the fact that we only once or twice met with a refusal to make an examination of children's throats, and that of the thirteen children whom we sought to isolate, permission was refused in the case of two only. One was the child of an ignorant woman who had strong opinions on the subject of compulsory vaccination. The other was a girl of 18 who would not be isolated because her people were just expecting visitors at Easter[1]. Now had the Medical Officer tried compulsion, it is doubtful whether he would have succeeded in isolating these people. And the application of pressure would doubtless have stirred up to resistance others who were quietly complying with his recommendations.

[1] From both these persons who refused to be isolated, the bacillus in question proved to be a non-virulent diphtheria bacillus; and it is interesting to note that no case of diphtheria was known to arise from contact with either.