

DIPHTHERIA IN SCARLET FEVER.

Being a Thesis for the Degree
of M.D.

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DIPHTHERIA IN SCARLET FEVER.

The association of diphtheria and scarlet fever in the same patient is one of considerable interest and there is already a fairly extensive literature on the subject, but more particularly from the point of view of post-scarlatinal diphtheria. There are also some observations with regard to the percentage of scarlet^{fever} patients who, on admission, can be shown to harbour the diphtheria bacillus, but none, so far as I am aware, in regard to the effect of the combination of the two diseases on the patient. As these observations are somewhat scattered and do not deal with the subject as a whole, it seemed that it might be of value to collect the various facts together and to add to them some further observations on the association of these diseases as seen at this hospital during the past ten years. The subject naturally falls into three sections:-

- (1) Association of scarlet fever with diphtheria bacilli on admission to hospital.
 - (2) Post-scarlatinal diphtheria.
 - (3) Methods of dealigⁿ_^ with the above in hospital practice.
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(1) ASSOCIATION OF SCARLET FEVER WITH DIPHTHERIA BACILLI ON ADMISSION. It is generally known that a small percentage of scarlet fever patients on admission to hospital are found to harbour diphtheria bacilli either in the throat or nose or in both. An even greater percentage harbour Hoffman's bacillus according to Pugh and Garratt and Washbourne and it has been the experience at this hospital that this bacillus is very commonly present in cultures from throats of scarlet patients. As there is no evidence that this organism is pathogenic or related to the diphtheria bacillus (Graham Smith) no further mention will be made of it here, except as will be seen later its atypical forms ^{are} ~~an~~ even greater difficulty in diagnosis in scarlet ^{fever} patients than in uncomplicated diphtheria.

The percentage of scarlet ^{fever} patients showing the presence of B.diphtheriae on admission varies considerably according to different observers.

Goodall found 4.7% in a series of 418 cases.

Sverensen " 2.5% " " " "1547 "

Garratt & Washbourne 1.2% " " " " 666 "

Report M.A.B. found 5.41% " " " " 203 "

Pugh " 4.76% " " " " 418 "

Cumpston " 5.8% " " " "1017 "

Williams examined the throats of 53 scarlet ^{fever} cases some time/

time after admission and found diphtheria bacilli in 11. Beggs (quoted by Ashbourn & Garratt) found diphtheria bacilli in the throats of 51 out of 140 cases of scarlet fever examined, but here also the examination was made at various periods after the admission of these patients. Moreover, post-scarlatinal diphtheria was at the time prevalent in the wards and 14 out of the 51 cases exhibited clinical evidence of the disease. Ranke (quoted as above) at Munich found diphtheria bacilli present to the extent of 53.7%.

It is evident from these figures, that only a small percentage harbour these bacilli in the throat on admission but, that when examination is made later on in the course of the scarlet, the percentage becomes very much greater - as would be expected.

When the nose is examined culturally the number of cases according to all observers is higher.

M.A.B. Report in a series of 202 cases 12.37%.

Bagh " " " 418 " 8.6%

Cumpston " " " 165 " 12.72%.

Williams examined 141 cases of scarlet showing nasal discharge and 57 were found to harbour diphtheria bacilli. Of these cases 36 were found on admission, 7 occurred in first week, 3 in the 2nd, 4 in the 3rd, 5 in the 4th, and 1 each in the 6th and 7th weeks. Todd found 51 cases of rhinorrhoea subsequent to scarlet fever to be associated/

associated with this bacillus out of 365 cases at the London Fever Hospital.

Scarlet^{fever} patients have also been found to harbour the bacillus in discharges from the ear. Otorrhoea is not as a rule present on admission but follows the acute stage of the disease. Williams examined the ear discharges of 63 patients and found diphtheria bacilli in eight (one on admission and the remainder subsequently). Out of 40 cultures from ear discharges of scarlet fever cases in both acute and convalescent wards, Forbes found in 32 bacilli morphologically indistinguishable from diphtheria. His observations, however, were made when the number of cases of post-scarlatinal diphtheria was at its maximum, at the end of November and the beginning of December. The bacilli he states have not usually been found in the ear discharge in the first few days it is present. The earliest day was the second, and their presence on the fifth day was common. Of other observers, Gordon found the bacilli in 5^{out of 7} cases of scarlet fever with discharging ears and Graham Smith found 7 out of 10 cases of ear discharge to harbour organisms morphologically resembling diphtheria bacilli.

During the past ten years records have been kept in the ward journals at this hospital of all cases who on admission were found to harbour diphtheria-like organisms in the throat. No systematic examinations have been made/

made of the nose or ears, and only since the winter of 1914-15 were routine examinations made of the throats. I have examined the clinical notes of all these cases and have excluded those who showed only the presence of B.Hoffmanni or who were admitted after the acute stage of scarlet fever. The following table gives the results of these examinations. The years correspond with the hospital years from 1st June to 31st May.

Yearly Prevalence.

<u>Year.</u>	<u>Scarlet Cases admitted.</u>	<u>Cases harbouring diph. bacilli.</u>	<u>% of admissions.</u>
1910-11	1768	17	.96
11-12	1222	7	.57
12-13	1260	25	1.9
13-14	1930	22	1.1
14-15	2455	32	1.3
15-16	2425	35	1.4
16-17	1181	55	4.6
17-18	475	11	2.3
18-19	512	23	4.4
19-20	1542	56	3.6

1910-14 cases scarlet. 6180
71 - 1.1%
Transition year.

1915-20: 6135:180 = 2.9%

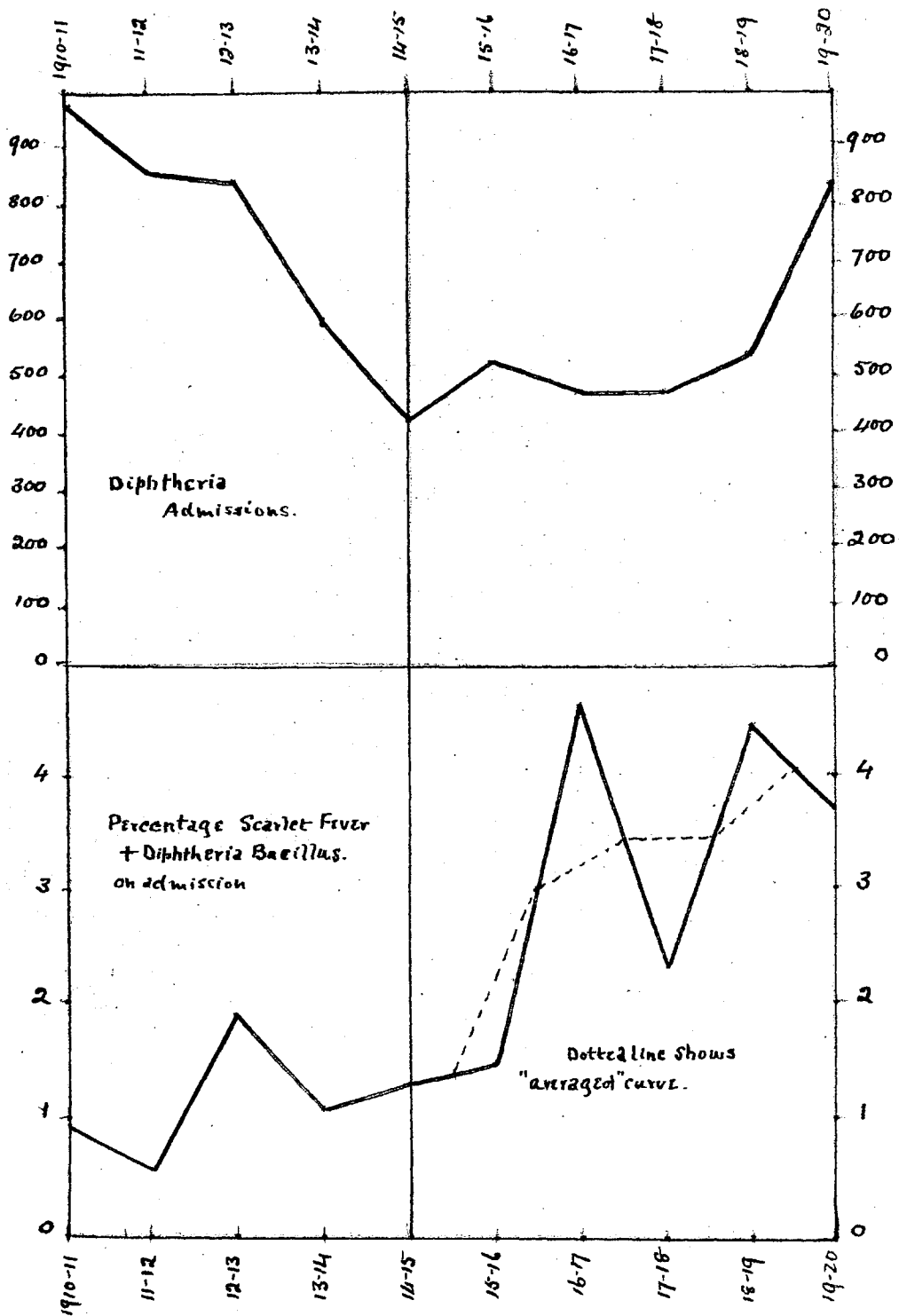
Of the 14,770 cases admitted during these 10 years, 283 are recorded as harbouring organisms morphologically indistinguishable from the Klebs-Koeffler bacillus.

From/

From 1910-14 no routine cultivations were made on admission except from those cases who showed definite diphtheritic membrane on the fauces or whose throats, while not showing this definite evidence, were "suspicious". During 1914-15 routine examination was introduced and has been carried out ever since. The cultures were taken on the day of admission or in some cases on the day following, the medium used being solidified serum. The growths were examined the following day by means of smear preparations stained by Neisser's method (London modification).

It will be seen from the above table, that there is a considerable yearly variation in the prevalence of diphtheria bacilli in scarlet. As would be expected, since routine examination has been carried out, the numbers found are very much larger, an average of 2.9% of admissions from 1915 to 1920 as compared with 1.1% from 1910 to 1914. The figures for the years following the introduction of systematic culturing are in accordance with those found by previous observers. Theoretically it would be expected that the yearly variation in the prevalence of B.diphtheriae in scarlet patients would bear some relation to the prevalence of diphtheria in the district which supplies the hospital. Though it is dangerous to draw conclusions from such a small number of cases, some such relation can be made out. It would obviously be fallacious/

Chart showing yearly Diphtheria Admissions and yearly percentages of Scarlet Admissions harbouring the Diphtheria Bacillus. 1910 to 1920.



fallacious to consider the incidence before 1914-15, as the cases discovered then depended on the opinion of the various medical officers in charge of the wards as to what was suspicious of diphtheria. But if the percentage prevalence since that year be considered, it will be seen that the tendency is upward - specially if the curve be averaged. Compare this with the prevalence of diphtheria for the same years. I have been unable to procure the exact figures for the district which supplies the hospital, but, as in Glasgow very few cases of diphtheria notified are treated at home, the admissions to hospital agree very closely with the local prevalence. It will be seen that the year 1914-15 marks the lowest point of the ten yearly diphtheria cycle and that the prevalence increases from that year.* I have been ^{un}able to trace any other statistics dealing with this point. It has, however, been shown by Richards and others that the prevalence of post-scarlatinal diphtheria varies with the prevalence of diphtheria outside. As the prevalence of post-scarlatinal diphtheria depends upon the number of cases of unrecognised diphtheria admitted to the scarlet wards one would infer that the relation found here holds good elsewhere.

Seasonal incidence. This being so, it would be expected that the seasonal prevalence might show similar relations but when it is considered that the cases of scarlet harbouring the diphtheria bacillus are not for the most part (as will be/

* See Chart

be seen later) cases of clinical diphtheria but are diphtheria carriers who have contracted scarlet, it is not surprising that the figures given below do not bear this out, and although taking them generally there is on the whole a greater prevalence of diphtheria in scarlet fever in the months during which the incidence of diphtheria is greater than during the others. But again one must be chary of drawing inferences from so small a number of cases over so few years.

1915-20.

<u>Month.</u>	<u>June.</u>	<u>July.</u>	<u>Aug.</u>	<u>Sept.</u>	<u>Oct.</u>	<u>Nov.</u>	<u>Dec.</u>
Mean monthly admissions of diphtheria.	29.4	31.4	34.8	46.4	68	57.4	57.2
Mean monthly percentage of scarlet admissions harbouring B. diph.	2.1	3.8	2.1	4.0	2.6	3.0	4.3

Continuation.

<u>Janv.</u> 58.2 4.0	<u>Febv.</u> 54 2.7	<u>March.</u> 54.4 1.6	<u>April.</u> 41.4 2.3	<u>May.</u> 37.6 1.9
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Sex Distribution.

It may be noted in passing that of the 283 cases 120 were males and 163 females - a slight preponderance of females which is in accordance with the sex/

sex distribution of diphtheria itself and with that of post-scarlatinal diphtheria (Pugh).

Previous Diphtheria or Contact. The histories recorded in the journals are those obtained by the nurse collecting the case. In 12 cases of the 283 no history of previous infectious disease is recorded and of the remainder only 17 show a history of having had diphtheria at any time prior to admission with scarlet, and only 5 had a history of contact with a case of diphtheria.

Clinical Conditions. It is well known that in uncomplicated diphtheria it is impossible in many cases to diagnose the presence of *B. diphtheriae* by clinical examination alone. It is even more impossible to do this when dealing with cases of scarlet fever. In Pugh's series of 420 cases certified as scarlet fever and examined for *B. diph.* on admission, 2 were found to be uncomplicated faucial diphtheria. One was scarlet fever associated with a croupy cough and considerable obstruction to respiration: diphtheria bacilli were obtained from the fauces which were inflamed but without deposit. Two were scarlet fever complicated by fibrinous rhinitis. In 3 cases the fauces were merely congested, 9 showed inflammation without deposit and three presented follicular exudation. One case showed ulceration of tonsils and uvula and one case a pultaceous mass of exudate on the tonsils with some ulceration. As regards/

regards the noses of the same series of cases, two showed fibrinous rhinitis. In 33 cases which on careful inspection presented no evidence of either faucial diphtheria or fibrinous rhinitis, morphologically typical diphtheria bacilli were found. The same holds good for the other series of cases recorded - only in very few is there clinical evidence in throat, nose or ear of infection by diphtheria bacilli. Some degree of faucial lesion is characteristic of scarlet fever and rhinorrhoea and otorrhoea are both common, the former on admission and later, the latter after the acute stage is over.

To describe the clinical conditions of 283 cases found to harbour the diphtheria bacillus on admission, it would seem to be best to divide them into groups corresponding to the stages of severity of scarlet throats. All the cases were in the acute stage of the disease. The description of the throat lesions as given by Kerr forms a suitable basis for this classification.

- (1) Throat lesion limited to congestion.
- (2) Further inflammation with oedema and enlarged tonsils covered with sticky mucus.
- (3) "Patching" of inner surface of tonsils. By patching is meant a yellowish scum over the tonsils, either as a continuous pellicle or separate areas of exudation easily removable as a rule, and leaving no bleeding or abrasion on removal.

(4)/

(4) Ulceration of tonsils, pillars of fauces or palate. Three additional groups are necessary to include all the cases in the series.

(5) Cases with diphtheritic membrane on Tonsils, etc.

(6) Cases with congested throats but shewing signs of laryngeal embarrassment. Diphtheria bacilli in throat.

(7) Cases with membrane in nose, throats only congested, diphtheria bacilli from throat and nose.

In the following table the 283 cases are shown classified in this manner, divided into groups corresponding to the years before systematic culturing, the years during which this was carried out, and the transition year.

As would be expected, in the years 1910-14 practically all the cases showed signs which would call attention to the possibility of diphtheria. The 4 exceptions to this in group I were discovered to harbour the bacillus by being sent in as diphtheria, three of them on account of contact with diphtheria, and in the fourth case, whatever exudate may have been present at time of diagnosis outside, had disappeared when the case was admitted. With the introduction of routine culturing there is a great increase in the groups I and II, that is to say of cases which would not suggest infection. Over the whole period only 4 cases of laryngeal embarrassment are recorded and only 1 case of nasal diphtheria. Groups V to VII are cases which showed fairly definite evidence of diphtherial infection and in this series/

series include 70 cases. The remainder, groups I to IV, 213 cases, showed no lesion beyond what might be expected from scarlet fever. It is very evident that it is impossible to diagnose the presence of diphtheria bacilli from clinical examination alone, and that unless some method of routine culturing be adopted many cases will pass into the scarlet wards unrecognized.

	Group I.	II.	III.	IV.	V.	VI.	VII.	Totals.
1910-14	4	-	24	6	35	2	-	71
1914-15	11	2	8	5	6	-	-	32
1915-20	69	36	41	7	24	2	1	180
Totals	84	38	73	18	65	4	1	283

As illustrating the difficulties of diagnosis in these cases it is interesting to note how the 283 cases were certified for admission to hospital.

Number of Cases.	Certified as	Proved to be scarlet and diphtheria bacilli.					Scarlet groups	
		I.	II.	III.	IV.	V.	VI.	VII.
95	Diphtheria.	6	7	38	3	38	3	
21	Scarlet & diphtheria.	2	2	10	1	6		
167	Scarlet	76	29	24	15	21	1	1

The above tables show how the cases were certified and what they proved to be on admission: The large number of cases/

cases notified as diphtheria is probably explained by the rash being absent or ill developed at the time of certification. From the journal notes in the hospital they nearly all showed definite signs of scarlet on admission and only a few were admitted to diphtheria wards before it became evident. The two cases certified as scarlet and diphtheria and proved to be Group I, were so certified because of contact with diphtheria.

The next point to be considered is how many of these cases are to be regarded as instances of double infection, and also what is the effect of double infection on the patient.

The cases under group V. are undoubtedly cases of double infection - and so also those in groups VI. and VII. The throat conditions of the remainder fall into line with scarlet fever. The lesion of these cases may be due to infection by diphtheria but in the absence of further evidence it would seem more reasonable to ascribe them to the scarlet. Even though virulent bacilli were isolated from such cases that would not be definite evidence of double infection for virulent bacilli can be isolated from the throats of healthy individuals. Though the faucial lesions of atypical cases of diphtheria may resemble those of scarlet, the majority of cases of diphtheria do show the presence of definite membrane. Further evidence on this point, however, may be got from the consideration of the after history of these patients. But here again difficulty arises when one seeks to ascribe occurrences/

occurrences in the course of the illness to diphtheria - except, of course, the diphtheritic palsies and cardiac paralysis. Apart from the rash in scarlet and the membrane in diphtheria, the signs and symptoms are somewhat similar, and such phenomena, as the pyrexia, albuminuria, adenitis, and the slighter cardio-vascular disturbances are common to both. Also it must be remembered that many cases of scarlet and diphtheria after the subsidence of the acute stage pass on to an uninterrupted recovery without any complications or sequelae. When the after histories of the 283 cases were examined, it was found that sequelae and complications definitely ascribable to diphtheria did not occur in any of the 213 cases in groups I to IV. In these groups only three deaths occurred, two in group III and one in group IV. and all three are recorded as being due to septic scarlet fever, giving a case mortality for the combined groups of 1.3% which is well within the average case mortality for scarlet fever. While there may have been some cases of scarlet plus mild diphtheria amongst them, it seems most likely that the combination was rather that of scarlet fever occurring in diphtheria carriers, specially when, as will be seen later, the organisms from similar series of cases are for the most part non-virulent. Another argument in favour of this view is when the other groups are considered. In them, when there is undoubted double infection/

infection the course in almost every case was very severe even with slight diphtherial lesions and it would be reasonable to suppose that if the other cases were in reality double infections there would be some indication of this in the after histories. With regard to the 65 cases in group V. all were at least sharply ill on admission and only 11 of them are recorded as having made uninterrupted recoveries. The majority showed a considerable degree of toxæmia while albuminuria rhinorrhoea and adenitis were common, the adenitis going on to suppuration in 4 cases. In the 65 cases, 16 deaths occurred, giving a case mortality for the group of 24%, 11 of the deaths being due to cardiac paralysis and 5 due to sepsis. 17 cases are recorded as having had septic scarlet fever, 5 of them dying; 5 as having septic scarlet and post diphtheritic paralysis, 2 of them dying; and 10 developed post-diphtheritic paralysis (but without sepsis) of whom 9 died. The high mortality, the high incidence of sepsis and post-diphtheritic palsies are all striking. The mortality alone is sufficient to indicate the severity of the course of the combined diseases. The sepsis is probably due to the double faucial infection rendering the patient more liable to invasion by the septic organisms commonly present in the mouth. It is tempting to explain the paralyses on similar lines. In scarlet fever as with all other infectious diseases the nervous system is involved to

a greater or lesser extent according to the severity of the case and it is possible that this might lower the resistance of the patient to the toxins causing paralyses. But in this connection must be considered the day of disease on which serum was administered, counting from the onset of sore throat. In the 15 cases developing post diphtheritic palsies serum was administered as follows:-

1st day	-	1	-	1	died.
2nd "	-	4	-	2	"
3rd "	-	2	-	1	"
4th "	-	2	-	2	"
5th "	-	2	-	2	"
6th "	-	2	-	2	"
7th "	-	1	-	1	"
8th "	-	<u>1</u>	-	<u>1</u>	"
		15	-	12	"

As the majority of the cases were late in receiving antitoxin the explanation for high incidence of paralyses lies probably in this direction.

Of the 4 laryngeal cases in group VI, two had septic scarlet but recovered and one died from cardiac paralysis. The one case in group VII, though showing considerable toxæmia on admission made an uninterrupted recovery.

The same conditions have been found in a series of 43 cases/

cases of scarlet and diphtheria which I have had under my care during the past year. Classified into the 7 groups as before the numbers are:-

Group I.	II.	III.	IV.	V.	VI.	VII.
18	10	4	2	8	1	-

The 18 cases in Group I. ran a mild course, 4 showed early adenitis, and 2 showed late adenitis, going on to suppuration in 1 case. But apart from this no other complications or sequelae developed.

Of the 10 Group II cases two became septic but the others made uninterrupted recoveries. The group III cases also showed no complications, except in 1 case otitis media developed in 2nd week. One group IV was septic on admission and died, the other made a good recovery.

Of the Group V. cases two were septic, one having suppurative adenitis and a superficial mastoid abscess, but both recovered. Two developed post-diphtheritic palsies (palatal) and one died of cardiac paralysis. A second one died of cardiac paralysis four days after admission.

The one case in Group VI. made an uninterrupted recovery.

It would appear from the above that, while cases of double infection showing presence of membrane are to be regarded with concern, the presence of a positive culture without/

without a definite diphtherial lesion is of little significance clinically. That is, of course, in these cases where serum has been given on discovery of the presence of the diphtheria bacillus. Whether they would have developed clinical diphtheria or not later on it is impossible to say. Theoretically that would depend on the susceptibility of the patient and on the virulence of the organism. In Cumpston's series of 75 cases which showed only the presence of diphtheria bacilli on admission, four cases (5.3%) developed clinical diphtheria later, one of them dying. As further evidence of the increased severity of course when the two diseases are combined in the same patient, even when the diphtheria follows the scarlet, may be noted the very high mortality from post-scarlatinal diphtheria in the days before serum treatment, a mortality higher than that for uncomplicated diphtheria (Pugh).

BACTERIOLOGY. While, with those cases showing the presence of membrane in nose or throat or laryngeal embarrassment, we are dealing with true virulent diphtheria bacilli, there remains to be considered the significance of the bacilli found in the other cases, which show no other lesions than those which can be attributed to scarlet fever. From a consideration of the results of previous workers it would appear that diphtheria like bacilli found in the ear discharges are of relatively little importance. In the series of cases mentioned previously, Williams found in 4 strains tested, that though acid was produced in broth they were all non-virulent to guinea-pigs. Of Forbes series 11 were tested but he found them/

them not to be true diphtheria bacilli, and Graham Smith concludes that while diphtheria like bacilli are very common in these conditions, true virulent diphtheria bacilli are rare.

As regards bacilli from the nose, Pugh tested 6 strains from cases showing no evidence of either faucial diphtheria or fibrinous rhinitis. All produced acid in glucose broth but were non-virulent to guinea-pigs. In Williams series, 17 strains were isolated. 11 of these were found to produce acid in glucose broth and of these three were found to be virulent. All the strains from Todd's 51 cases of rhinitis subsequent to scarlet fever produced acid in glucose broth and behaved in all ways like diphtheria bacilli. Out of 7 strains injected into guinea pigs 7 proved virulent.

The only cultural and pathogenicity tests recorded for the series of throat cases are those by Pugh. Five strains were tested. All produced acid in glucose broth and all were non-virulent to guinea-pigs. To this I am able to add observations on 14 strains of bacilli isolated from the group I cases of the series of 43 scarlets with diphtheria bacilli under my care during the past year. It is in the Group I cases that there is least of all clinical evidence of infection and it seemed it would be interesting to test the virulence of the organisms isolated from such cases.

Besides the 18 cases in Group I, 6 others also in Group I were reported to have "positive cultures" but these/

these on further investigation proved not to be diphtheria bacilli. Two were found to be short chained streptococci which, when stained by Neisser's method, very closely resembled the diphtheria bacillus, and one was a streptothrix, showing blue granules when stained with this method. When broken up in the process of making a smear preparation it too closely resembled diphtheria. It corresponded morphologically to the description of the streptothrix recorded by Gordon (p.432) except that while his did not grow on serum this one formed a moist filmy growth on that medium. The three others proved to be Hoffmann's Bacillus. In primary culture from the throat they were very like the barred type of diphtheria bacillus but on isolation and subculturing they reverted to the Hoffmann type and the colonies on serum were also Hoffmann like. To confirm this they were injected into guinea-pigs but had no effect on them and, though they grew in Hiss's serum water medium, no acid was produced from glucose or the other sugars used (see Table 21/)

The 14 other strains of bacilli isolated were morphologically indistinguishable from the diphtheria bacillus and their colonies on serum were all diphtheria like. The bacilli in 4 remaining cases of the 18 in group I were also indistinguishable from diphtheria in primary cultures, but, so few were present, that it was found impossible to isolate them from the numerous other organisms present. Although cultures were taken from these patients repeatedly after the primary culture no diphtheria bacilli were found again.

No.	Morphology.	Glucose.	Galactose.	Lactose.	Maltose.	Dextrine.	Glycerine.	Lactose.	Mannite.	Saccharose.	Pathogenicity for guinea-pig.
1.	Medium length. Polar staining	X ₂ + ₃ C ₆	X ₂ + ₄	X ₂ + ₄	X ₂ + ₄	X ₂	X ₉	X ₂	0	0	No effect.
2.	Long bacilli irregularly beaded.	+C ₂	X ₂ + ₃ C ₃	+ ₂ C ₃	+ ₂ C ₃	X ₂ + ₃ D ₇	X ₉	X ₂	0	0	No effect.
3.	medium length. irregularly beaded.	+C ₂	X ₂ + ₃ C ₄	X ₂ + ₃ +C ₃	X ₂ + ₃ +C ₈	X ₂	X ₉	X ₃	0	0	No effect.
4.	medium length irregularly beaded.	X ₂ +C ₄	X ₂ + ₄ +C ₈ D ₉	X ₂ + ₃ +C ₄	X ₂ + ₄ D ₅	X ₂	X ₆ +C ₉ D ₁₀	X ₂ +C ₆ D ₆	0	X ₄ +C ₆ D ₆	Died in 24 hrs. Local necrosis, congestion of suprarenals.
5.	long bacilli. polar staining & beading.	+C ₂	+ ₂ C ₃	+C ₂	X ₂ +C ₃	X ₂	X ₄ +C ₆	0	0	0	No effect.
6.	Long bacilli. Polar staining & beading.	+ ₂ C ₃	X ₂ + ₃ C ₃	+ ₂ C ₃	X ₂	X ₈	X ₃	N	0	0	Died in 48 hrs. Local necrosis, congestion of suprarenals.
7.	Long bacilli. polar staining.	+C ₂	X ₂ + ₆ C ₆	+ ₂ C ₆	X ₂ + ₇	X ₄	X ₈	X ₄	0	0	Died in 24 hrs. Local necrosis. congestion of intestines, suprarenals haemorrhagic.
8.	medium length irregularly beaded.	+C ₂	+ ₂	+C ₂	+ ₂ C ₈	+ ₂ C ₃	X ₃ + ₈	0	0	0	A little local oedema on 3rd day. No general effect.
9.	Medium length. Polar staining.	+C ₂ D ₃	+C ₂ D ₄	+C ₂ D ₄	+ ₂ C ₃ D ₄	X ₂	X ₄	X ₂	0	+C ₄ D ₅	Died in 48 hrs. congestion of abdominal organs. Local necrosis. Internal congestion of suprarenals, peritoneal effusion.
10.	Medium length. granules large and dark.	+ ₂ C ₄	X ₂ + ₄	X ₂ +C ₆	X ₂	X ₂ +C ₅	X ₃	0	0	0	No effect.
11.	Medium length polar staining	+ ₂ C ₃	X ₂ +C ₃	X ₂ +C ₄	X ₂ + ₄	X ₄	N	0	0	0	Died in 24 hours. Local necrosis. Congestion of suprarenals.
12.	Short bacilli uniformly stained	+C ₂ D ₅	X ₂ +C ₄ D ₃	+ ₂ C ₃	X ₇	0	0	0	0	+C ₃	No effect.
13.	Very long bacilli almost segmented	+ ₂ C ₃	+ ₂ C ₆	+ ₂ C ₅	+ ₂ C ₃	X ₄ + ₆	X ₄ + ₇	X ₄ + ₇	0	0	No effect.
14.	Short bacilli streptococcal form.	X ₂ + ₃ C ₄	+C ₄ D ₈	X ₂ +C ₃ D ₉	X ₃ +C ₄ D ₁₀	0	0	X ₆ +C ₉ D ₉	0	X ₂ +C ₃ D ₉	No effect.
15.	3 strains. Barred from primary culture. Hoffman-like on sub-culture.	0	0	0	0	0	0	0	0	0	No effect.

0 - no effect.

n - slightly acid or neutral.

x - acid.

+ - markedly acid.

c - partial coagulation.

C - complete coagulation.

D.- decolorisation.

Numbers after symbols indicate days of incubation on which change occurred.

The sugar tests given in the above table were carried out in Hiss's serum water medium with 1% of the sugar added. Cultures were examined 48 hours after inoculation and thereafter every day for 10 days. Incubation was then stopped and the cultures were examined for purity. Any found contaminated were rejected and the experiments repeated in a similar fashion. Through the action on glucose alone is usually taken as the criterion of a diphtheria bacillus, the opportunity was taken to compare the action of these 14 strains on other sugars. Graham Smith records that "under suitable circumstances (i.e. such as in Hiss's serum water medium) all strains of diphtheria bacilli produce acid from glucose, galactose, laevulose and maltose, and the majority from dextrine and glycerine. The action on lactose is very variable and only a few strains act on saccharose. All tests on mannite yielded negative results." It will be seen that the results as given in table p21, closely agree with this. All of the 14 strains produced acid in glucose, galactose, laevulose, maltose, 12 in dextrine and glycerine, 11 in lactose, 4 in saccharose, and none had any action on mannite. Coagulation of the medium is also recorded as has already been noticed by Kolmer and Moshage; it occurs more frequently with the readily fermented sugars than with the others. According to them, it is dependent on the amount of organic acids present and it is seen from the above results that coagulation did not occur with anything/

anything less than a markedly acid reaction. In this series decolorisation of the medium has been noticed. So far as I am aware this has not been recorded before. In these experiments decolorisation was found to start at the bottom of the tube where growth was greatest and gradually spread upwards. Decolorisation only occurred in tubes showing a markedly acid reaction and complete coagulation - and not in all of them. The degree of loss of colour varied greatly - being anything from a slight paling of the acid colour to a complete blanching. It was not due to contamination, for as has been stated, all cultures were examined for purity.

VIRULENCE: The method used was the subcutaneous injection of suspensions in normal saline of 24 hour serum cultures, as recommended by Kolmer & Moshage. The guinea-pigs were kept under observation for 10 days and a post-mortem examination was made on death. Of the 14 strains tested, 5 were found to be fully virulent, and 8 totally non-virulent. One produced slight and transient local oedema but without general symptoms and was therefore held to be non-virulent. In all the five guinea-pigs that died the lesions characteristic of experimental diphtheria were found, namely local necrosis with congestion of internal organs, specially of the suprarenal capsules.

As there were five virulent diphtheria bacilli found
in/

in cases showing no faucial lesion beyond congestion, it would have been interesting to have tested the Schick reaction in these cases. Unfortunately I was unable to carry this out. It is only in Group I cases that delay in giving serum to allow this test is at all justifiable, for the lesions in the other groups may be due to diphtheria. Considering the high mortality which has been found in the Group V. cases it would seem to be important for all cases showing lesions to receive serum as soon as possible.

PERSISTENCE OF BACILLI. In the majority of the 43 cases already mentioned the bacilli disappeared from the throat in a very short time - in four already mentioned, the primary throat culture on admission was the only one ever found to be positive. In 13 cases, however, the bacilli were found to persist for unusually long periods.

1 persisted to 5th week of stay in hospital.

4 " " 6th " " " " " (one being virulent on admission).

2 " " 7th " " " " " "

1 " " 8th " " " " " (virulent on admission)

2 " " 10th " " " " " (both non-virulent)

1 " " 11th " " " " " "

2 " " beyond 12th week when patients were dismissed.

(1 was non-virulent and the other virulent on dismissal).

Cumpston also has found the same persistence for long periods in a small number of cases of scarlet fever, and it is in accordance/

accordance with what is known with regard to uncomplicated diphtheria.

Before passing on to the question of post-scarlatinal diphtheria it will be well to summarise the main points that have been discussed so far.

- (1) On admission to hospital, a not inconsiderable number of scarlet fever patients are found to harbour diphtheria bacilli in the throat or nose or both.
- (2) In the majority of these cases there is no clinical evidence of the presence of the diphtheria bacillus, and the combination is in all probability due to scarlet fever occurring in a diphtheria carrier.
- (3) The number of such cases found on admission varies with the prevalence of diphtheria in the district.
- (4) The number with a history of previous diphtheria or having been in contact with diphtheria is very small.
- (5) As with healthy diphtheria carriers, the most of the organisms isolated from such cases are non-virulent, but some are true virulent diphtheria bacilli, and the bacilli may persist for long periods.
- (6) In cases where there is definite evidence of double infection the combined diseases tend to run a very severe course. Sepsis is very prevalent as is also the occurrence of the post-diphtheritic paralyses, due probably to the late administration of serum.

(7) Diphtheria like bacilli are commonly present in the otorrhoea and rhinorrhoea subsequent to scarlet fever. The organisms from the ear are rarely true virulent diphtheria bacilli, but these are more frequently found in rhinorrhoea.

POST-SCARLATINAL DIPHTHERIA.

It is now universally recognised that the cause of post-scarlatinal diphtheria is the introduction of some focus of infection into the scarlet ^{fever} wards. Practically the only means of introducing this infection is by the patients or the hospital staff, and of the two the former is by far the most important. The treatment of the two diseases in the same hospital has been shown by Pugh not to be an important factor in the etiology of post-scarlatinal diphtheria but he gives an instance of infection being carried by a nurse. As he remarks, the medical staff do not come into such close relationships with their patients as to make them a likely source of infection, but it is easily conceivable that a nurse transferred from a diphtheria to a scarlet ward should carry infection in this way. How infection may readily be introduced by the patients has been seen from the previous pages, the wonder is that post-scarlatinal diphtheria is not more prevalent than it is.

PREVALENCE. It is generally stated that scarlet patients are most susceptible to this complication in the third and fourth weeks of disease. This is perhaps rather a loose method of indicating that it is more prevalent in these weeks than/

than earlier or later in the disease, as it is not so much that the patients show an increased susceptibility, as that during this period the opportunities for spread of infection are greater and therefore those who are susceptible at all will be more likely to develop the complication then. During the acute stages of the scarlet fever and up to the third week the patient is confined to bed and the spread of diphtheritic infection would then be only indirectly through the medium of feeding utensils toys etc., but immediately the patient gets up the opportunities for spread are greatly increased, specially if he is transferred to a convalescent ward. Overcrowding of wards is another factor in the spread of infection. Climatic conditions have also been shown to affect the occurrence of Post-Scarlatinal diphtheria, probably due to cold and damp weather setting up catarrhal conditions of the naso-pharynx favouring infection.

As regards the statistics of post-scarlatinal diphtheria Pugh's figures may be quoted as an example, analysing the returns made by the hospitals of the Metropolitan Asylums Board for the years 1891-1900. I have not had access to any satisfactory statistics of a later date. Previous to 1895 bacteriological diagnosis was not used and the figures for 1891-5 may be omitted. From 1896 to 1900 the percentage incidence of this complication, calculated on the scarlet cases completed is in each year 4.6, 5.2, 5.1, 5.1, and 3.7.

In/

In these figures are included all cases of secondary throat illness associated with the diphtheria bacillus including those which would from the clinical appearances alone have been regarded as simple tonsillitis. While such statistics give the actual number of cases developing this complication they do not, specially when used to illustrate the efficacy of preventive measures, give the true state of affairs. For one thing, cases without sore throat but with a positive culture only, are not included and, as Pugh states, "the possible harm which may be done by the introduction of virulent diphtheria bacilli into a ward is to be gauged, not by the number of patients who develop post-scarlatinal diphtheria but by the number infected with the bacillus." Again, the efficacy of preventive measures is not to be estimated so much by the number of cases infected as by the number of outbreaks of post-scarlatinal diphtheria which occur in the wards. For example, in a hospital where isolation of all carrier cases is the rule, one or two outbreaks in large convalescent pavilions might quite well yield a greater number of cases than more outbreaks in smaller wards of another hospital where such isolation is not carried out. It is from this point of view that I have investigated the occurrence of post-scarlatinal diphtheria at this hospital during the past ten years 1910-1920. As during the first four years of this period no systematic bacteriological examination and isolation of positives was carried/

carried out (as was done after 1914) there is an opportunity of discussing the efficacy of this as a preventive measure.

During this period there were 57 outbreaks of post-scarlatinal diphtheria involving 87 cases showing evidence of infection and 137 cases showing positive cultures only. 14850 cases of scarlet fever were completed in these ten years giving an incidence of .3% outbreaks, .5% cases of post-scarlatinal diphtheria, and .9% cases with positive cultures only.

In none of the outbreaks was the infection traced to any definite source (except that mentioned on page 37) nor were any of the nursing staff found to be harbouring the diphtheria bacillus. Of the 87 cases of post scarlatinal diphtheria (which include all those with any faucial lesion however slight,) 82 showed a faucial lesion only, 2 are recorded as faucial and laryngeal diphtheria, 2 laryngeal only, and 1 as faucial nasal and laryngeal diphtheria. This last case died of cardiac paralysis as did also one of the laryngeal cases, but no other deaths occurred, giving a case mortality of 2.3%.

It will be seen from the average of 1.5 cases per outbreak that the outbreaks were for the most part limited to very few cases.

Year.	Cases scarlet completed.	Outbreaks P. scarlatinal Diphtheria.	Cases involved.	
			Clinical Diphtheria.	Positive cultures only.
1910-11	1860	7 .3%	8 .4%	1 .05%
1911-12	1300	6 .4%	17 1.3%	20 1.5%
1912-13	1205	4 .3%	4 .3%	4 .3%
1913-14	1881	3 .1%	3 .1%	7 .3%
1914-15	2473	6 .2%	6 .2%	7 .2%
1915-16	2446	17 .6%	32 1.3%	84 3.4%
1916-17	1335	9 .6%	11 .8%	9 .6%
1917-18	516	3 .5%	3 .5%	3 .5%
1918-19	504	1 .1%	1 .1%	0 -
1919-20	1330	1 .07%	2 .14%	2 .14%

The series of cases is too small to be able to add to already published information on the statistics of the yearly and seasonal prevalence of this complication. However it is interesting to note the yearly prevalence of post-scarlatinal diphtheria with reference to the period of routine culturing which/

which was commenced in 1914-15. Instead of there being a reduction in the prevalence of this complication there is instead a very marked increase specially in the years 1915-16 and 1916-17, in 1915-16 there being also a great increase in the positive culture cases. This is difficult to explain, but there are several factors which may be considered. For one thing, it was in 1916 that the war had most effect on the hospital staff both medical and nursing, and it is possible that in consequence a number of cases of unrecognised diphtheria passed into the wards and that precautionary measures in the wards were not so carefully carried out. Overcrowding of the wards may also have had an effect for in 1915-16 there was an unusually large number of scarlets admitted. But there was an even greater number admitted in 1914-15. However in 1914-15 all the cases harbouring the diphtheria bacillus on admission were isolated, except 5 who had to remain in the wards. In 1915-16, 18 such cases were not isolated but remained in the wards, and it is possible that this, combined with the large number of cases under treatment and the changes in the staff, may explain this increased prevalence of post-scarlatinal diphtheria. Certainly for the past two years, when conditions have been more or less normal, the incidence of this complication has been very low. It is interesting to compare the incidence of post-scarlatinal diphtheria with that of post-diphtheritic scarlet. In speaking/

speaking of the former, Graham Smith states that although patients suffering from diphtheria may subsequently develop scarlet fever, or both diseases appear simultaneously in one subject, in the great majority of instances in which these two diseases occur in the same patient diphtheria follows the attack of scarlet fever. This, however, has not been the experience here. During the same ten years, 71 outbreaks of post-diphtheritic scarlatina have occurred involving 216 patients. During the period 6754 cases of diphtheria have been completed giving an incidence of 1.5% outbreaks and 3% cases involved. The average number of cases per outbreak is 3 - just double that in post-scarlatinal diphtheria. Of the 216 cases 21 died - a case mortality of 9.7%. Compared with the statistics of post-scarlatinal diphtheria, these are in every way much higher.

To turn now to the question of dealing with diphtheria in association with scarlet fever in hospital practice. It is evident from the foregoing pages that ^{if} cases harbouring the diphtheria bacillus on admission were prevented from entering the scarlet wards, post-scarlatinal-diphtheria would be practically eliminated. This however could only be done by isolating all scarlet cases on admission until proved by repeated cultivation of nose and throat (and ear in the presence of discharge) to be free from diphtheria bacilli. Practically it is impossible to carry out this counsel of perfection/

perfection and one must be content with considerably less radical methods. A careful clinical examination of the nose and throat before cases on admission are sent to the scarlet wards will allow of the elimination of those cases showing clinical evidence of diphtheria. In this way too cases with suspicious throats, specially if there is a history of contact with diphtheria, could be diverted to the isolation ward. Even though such cases were proved not to harbour the diphtheria ^{*bacillus,*} there would be no danger to them in the mixed ward if protected by serum. It may be argued that the duration of the immunity afforded by a dose of serum on admission would not be of sufficient length to protect during the whole course of the scarlet fever. However, such has been the procedure here and in no instance has a case so isolated in the scarlet and diphtheria ward developed diphtheria later on.

Having regard to the severity of the combined diseases it would seem advisable that all cases showing definite clinical evidence, or having throats suspicious, of diphtheria should be given large doses of serum; with a view to limiting sepsis it is the custom here to give as well several doses of polyvalent antistreptococcal serum - either subcutaneously or in larger doses per rectum. For the local treatment of the mouths of these septic cases I have found that recommended by Voss for Vincent's Angina to be very satisfactory - namely a 2% solution in glycerin of salvarsan. In many of these cases smears from the throat and mouth show the presence not only of the ordinary pyogenic/

pyogenic cocci but also large numbers of spirochaetes, fusiform bacilli and streptothrices, and it was by finding these that one was led to try this treatment.

With regard to the cases showing no evidence of the presence of B.diphtheria, considerable difference of opinion exists as to whether routine bacteriological examinations to find such cases should be carried out. According to Pugh "on account of the prevalence of the non-virulent bacillus and the fallacies of single cultures, it may be doubted whether a routine bacteriological examination on admission would prove of sufficient value to repay the labour involved. On the other hand, Garratt & Washbourne believe that post-scarlatinal diphtheria can only be obviated by such examinations and by separation of those in whose throats diphtheria bacilli are found.

The occurrence of cross infections is one of the main objections to fever hospitals at the present day and as the diphtherial infection is essentially a preventible one, it does not seem justifiable to allow patients harbouring the bacillus to remain in contact with the others. Even though the most of these organisms are non-virulent and the results of one culture fallacious^u, still many fewer cases would be allowed to pass through under a routine system of culturing than without it. Such routine methods involve very little extra labour, specially, as for administrative purposes, it is not necessary to isolate and test the diphtheria/

diphtheria-like organisms found. The isolation of such patients is ~~an~~ important as, if not more so than, the discovery of the positive culture. As pointed out by Garratt & Washbourne this isolation should not be beyond the resources of most fever hospitals. It has been shown that in this hospital the retention of these cases in the wards was one of the factors leading to an increased prevalence of post-scarlatinal diphtheria during 1915-16. Even though such cases are subjected to bed isolation, as far as can be done in the ward, it is impossible to be sure of preventing the spread of infection. But, besides isolation after the discovery of the presence of the diphtheria bacillus, it is important also to regard all new cases admitted to a scarlet ward as potential sources of infection, and to submit them to a bed isolation as rigid as possible for the 24 or 48 hours necessary to get a result from the cultures taken on admission.

Similarly, any case of scarlet which subsequent to admission develops a sore throat or rhinorrhoea or otorrhoea should be considered as a potential source of infection and be isolated in bed in the ward until proved free from diphtheria bacilli. The reasons for this are sufficiently obvious from what has gone before and they have been fully dealt with elsewhere by Williams.

Of the other factors which have been shown to affect the prevalence of post-scarlatinal diphtheria, little need be said. The harbouring of bacilli by the nursing staff has/

has been seen to be a possible though comparatively rare source of infection. The transference of nurses from the diphtheria to the scarlet wards is unavoidable in hospital practice, and Pugh has pointed out that those who have been working in wards containing diphtheria should not be put on duty in scarlet fever wards unless they have been proved by culturing to be free from the means of infecting their charges with diphtheria. So, too, it would be advisable to take cultures at intervals from the staffs of scarlet wards, to ensure that they remain free from infection, as the nurses when off duty mingle with those from diphtheria wards and are liable to become carriers in this way. The dangers of overcrowding are manifest, not only as regards post-scarlatinal diphtheria but for other cross infections and need not be considered here.

With regard to the means of limiting the spread of an outbreak of post-scarlatinal diphtheria, the same general principles are involved. The case, or cases, developing diphtheria should be removed from the ward as soon as possible and the remainder confined to bed. No new cases should be admitted and no cases should be dismissed till the outbreak has been investigated and dealt with. Cultures should be taken from the nose and throat of all patients and of the staff as well, and owing to the fallacies of the results of one culture only, this should be repeated once or twice. Attention has been directed by Pugh to a supervision over the toys, linen, etc./

etc. under such circumstances as these have appeared to be important factors in stamping out infection. Here it has been the custom to examine the throat only, and with one round of cultures. From the average number of cases that have developed in an outbreak (1.3) it may be considered that the results are satisfactory, and in most cases the ward has been quarantined for a few days only - not more than a week. However, that with this method some cases are missed, is shown by a consideration of some of the outbreaks. In one or two instances further cases of diphtheria have kept cropping up at intervals, showing that the source of infection had not been discovered on culturing after the primary case. Also, cases whose cultures proved negative at the first time of culturing have been found positive a few days later when another round of cultures was made on account of a further case of diphtheria. In one outbreak in the spring of 1920 the original source was found to be probably a patient harbouring diphtheria bacilli in the nose. From this it would appear advisable to carry out the routine recommended by Pugh i.e. cultures from nose as well as throat, at least two rounds of cultures being made. But however efficacious such measures may prove in limiting the spread of infection once an outbreak has occurred, it would seem that the most important point in dealing with diphtheria in scarlet fever is the preventing of unrecognised diphtheria being introduced into the wards, and/

and it has been shown that this is in a great measure practicable.

SUMMARY.

The first part of the paper has been summarised on pages 25-6 and the following points are those borne out by the subsequent pages.

- (1) The most important factor causing post-scarlatinal diphtheria is the introduction of unrecognised diphtheria into the wards.
- (2) Subsidiary factors are (a) introduction of infection by the staff, and (b) overcrowding of wards.
- (3) For prevention greatest importance is attached to systematic bacteriological examination of nose and throat, as well as careful clinical examination on admission together with isolation of all positive cases.
- (4) All cases on admission should be regarded as potential sources of infection ^{and} isolated until proved free.
- (5) Similarly with cases developing sore throat or discharges from nose or ear later on in the disease.
- (6) Precautions should be taken to prevent introduction of infection by the staff.
- (7) For limiting an outbreak of post-scarlatinal diphtheria similar bacteriological methods should be adopted.

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