HIGH AND PERSISTENT CARRIER RATES OF *NEISSERIA MENINGITIDIS*, UNACCOMPANIED BY CASES OF MENINGITIS

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THE investigation with which this paper deals was undertaken in order to discover how prevalent was latent meningococcus infection among a naval community during times of peace when there were no outbreaks of cerebro-spinal meningitis (abbreviated to C.S.M. in the text).

(1) THE PREVALENCE OF C.S.M. AT CHATHAM BEFORE THE PRESENT CARRIER SURVEY

No case of C.S.M. was reported in the Chatham services between March, 1933, and May, 1934, the period of the present investigation. During the 15 months preceding March 24, 1933, there were eleven cases of C.S.M., a few details of which are summarised in Table I.

Table I. *R.N. Hospital, Chatham. Meningitis cases and carriers found between November,* 1931, *and March,* 1933.

C.S.M. cases				"Contacts"		
		Culture from			C.S.M. carriers found	
No. of case	Date of onset	N.P.	C.S.F.	No N.P. swabs	No.	%
1	27. xi. 31	Negative	Negative	—	—	—
2 I	4. i. 32	Negative	Negative	38	0	0
3	6. i. 32	Negative	Negative	30	0	0
4	12. ii. 32	Negative	Negative	13	0	0
5 D	18. ii. 32	Negative	Positive	—	—	—
6	4. iii. 32	Negative	Positive	33	4	12·1
7 S	6. vi. 32	Negative	?	45	6	13·3
8	27. ix. 32	Negative	Positive	49	7	14·3
9	16. xi. 32	Negative	Positive	64	6	9·4
10	17. ii. 33	Positive	Negative	20	4	20·0
11	24. iii. 33	Positive	Positive	34	21	61·6

C.S.F. = cerebro-spinal fluid; N.P. = nasopharynx; I = invalided; D = died; S = septicaemia.

The following points may be noted: (1) After more than a year's freedom from C.S.M., a case was admitted to hospital on 27. xi. 1931, followed by 10 more cases which were spread irregularly over the next fifteen months.

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(2) There was but one death, an exceptionally low fatality. (3) Gram-negative diplococci were present in the stained smears from the cerebro-spinal fluid (C.S.F.) of all cases, except No. 7. This patient never had any symptoms of meningitis. He suffered from purpura and rheumatism with an irregular fever of 4 weeks' duration. He remained mentally alert throughout, and made a complete recovery. Since *Neisseria meningitidis* (Type III Gordon) was cultured from his blood, he was included in this series of C.S.M. cases. (4) The first four cases originated before the authors were appointed to Chatham; and the attempts to isolate meningococci from the C.S.F. or nasopharynx failed. Also the eighty-one contacts to these earlier cases all had negative naso-pharyngeal swabs. In March, 1933, the routine bacteriological technique was revised (see Section 3), and meningococci were recovered from the C.S.F. nasopharynx, or blood, of the remaining seven patients.

This series of C.S.M. cases presents a striking contrast to those seen in the same hospital during the war epidemic. The war cases were much more acute, often dying within 2 days of onset, the mean mortality about 50 per cent., and haemorrhagic rashes were the rule. In the present series rashes were exceptional, the symptoms of meningitis less pronounced, and the C.S.F. was colourless and just turbid, whereas in the war period the C.S.F. was often frankly yellow pus. This contrast is a good illustration of the great variability in the fatality and the clinical picture of outbreaks of C.S.M., from time to time and place to place; an epidemiological phenomenon of which Underwood (1933) has recently published good examples. This clinical pleomorphism makes great caution necessary in using case fatality to estimate the relative therapeutic value of anti-meningococcal sera. However, if treatment is responsible for the low mortality of this recent series of C.S.M. cases, it is fair to state they were all most energetically treated with specific anti-serum on the lines described by Graff (1933). Nine out of the eleven cases were finally discharged to duty. Only one died, and only one was invalided, stone deaf. Finally, after the completion of the carrier investigation in May, 1934, a sporadic case of C.S.M. was admitted in June. He recovered but was also invalided, deaf. No further cases have appeared up to October, 1934.

(2) The carrier rate for meningococci during the year preceding the experimental surveys

Before its revision in March, 1932, the technique for isolation of *N. meningitidis* in use at Chatham was not very reliable as indicated by the fact that only one culture of the organism was obtained from five cases and eighty-one contacts. After the introduction of the present technique, between March, 1932, and February, 1933, 211 contacts produced twenty-seven carriers of meningococci. As indicated in Table I, the carrier rates on the batches of contacts who were swabbed in this period did not differ significantly from 12·8 per cent.—the total rate for the period in question.

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These 211 contacts can also be subdivided as shown in Table II; from which it appears that the rates in the naval hospital itself were not significantly different from those prevailing in ships and other service establishments.

Table II. *Distribution of contact carriers between March,* 1932, *and February,* 1933.

Group	No. in group	C.S.M. carriers No.	C.S.M. carriers %	C.S.M. carriers S.E.
Ships	69	7	10·1	±3·6
R.N. Barracks	39	4	10·2	±4·8
Hospital patients	41	4	9·8	±4·6
Hospital staff	35	6	17·2	±6·4
Soldiers	27	6	22·2	±7·8
Total	211	27	12·8	±2·3

S.E. = standard error.

Although the groups are very small, yet the rates shown in Table I and Table II are all consistent with the supposition that, during the year preceding March, 1933, the meningococcus carrier rate was round about 13 per cent. throughout the Chatham area. In any event, as this rate was obtained on *selected* contacts to cases of C.S.M., it is not likely to have been smaller than the frequency of carriers which would have been found had *random* samples of the naval and military population been examined during the period in question.

(3) TECHNIQUE

No carriers were discovered among the contacts to the C.S.M. cases which were admitted to hospital before March, 1932, when the culture medium employed for isolating meningococci consisted of chilled beef agar sterilised in the autoclave with its surface smeared over with blood serum. In March, 1922, the medium at present in use was substituted. This medium, or slight modifications of it has given satisfaction in our hands for the last twenty years. Nutrient agar is made from freshly killed English beef, sterilised in the steamer, and standardised to pH 7·6. The medium is enriched by the addition of 15 per cent. of human ascitic, pleural, or hydrocele fluid, which has been sterilised by contact with chloroform. The plates were poured the day before use. The swabs were taken by touching the posterior wall of the nasopharynx with a piece of wool on the end of a stout bent wire. (In adults a bent wire can with a little practice be manipulated much more easily and rapidly, and with less risk of contamination with saliva, than the West's swab which is so often recommended.) The plates were kept at incubator temperature and were inoculated directly from the nasopharynx.

The addition of as much as 15 per cent. of human body fluid may appear extravagant, but in our experience it has been found that, if less than 10 per cent. is added, the growth of meningococci is generally less profuse, and the number of characteristic colonies is relatively and absolutely smaller. Enrichment to over 10 per cent. appears to make little or no difference. For routine use therefore, 15 per cent. was taken as a safe margin to cover any variations in the composition of the different batches of human body fluids which were used.

After inoculation, the plates were incubated at 37° C. and examined after 24 and 48 hours. Likely colonies were picked off and stained by Gram's method. They were subcultured on to slopes of the same medium as was used for the primary cultures, and planted into three tubes of peptone water, enriched with 10 per cent. human body fluid, and containing 1 per cent. of glucose, saccharose or maltose. (The technique employed for the agglutination reactions is described in Section 8.)

(4) The incidence of c.s.m. carriers after March, 1933

In March, 1933, by means of the same technique as had been in use throughout the previous year twenty-one carriers of meningococci were found among thirty-four sailors who were contacts to case 11 (see Table I). On agglutinating these cultures sixteen were read as Gordon's Type II, one as Type I, and four were inagglutinable. Case 11 itself was recorded as Type III. This phenomenal carrier rate of $62 \pm 8{\cdot}4$ per cent. (or 50 per cent. if the inagglutinable cultures are excluded) was largely responsible for the investigation with which this paper is chiefly concerned, because it was the largest naval c.s.m. carrier rate in our experience, which extends back to 1913.

At irregular intervals throughout the following year ten groups of naval ratings, mainly from the staff of R.N. Hospital, Chatham, were swabbed for meningococci. From these nasopharyngeal swabs 259 cultures of *N. meningitidis* were isolated. These organisms were all Gram-negative diplococci giving characteristic transparent, colourless colonies on human serum agar. All the strains formed acid without gas in glucose media, and did not effect saccharose and maltose media. About 90 per cent. agglutinated with one or more of Gordon's four types of anti-meningococcus sera.

On the primary plate cultures from the nasopharynx *N. meningitidis* was usually the predominant organism. Sometimes it was present in almost pure culture, colonies, other than those of meningococci, not being evident on the plate. Therefore the large number of positive results was not caused by the discovery of one or two colonies after a searching examination of the primary cultures, because the majority of the plates could be classed as "positive" or "negative" at a single glance.

Table III summarises the results of the ten carrier surveys which were made between March, 1933, and May, 1934.

It should be noted that:

(1) The total rate for the whole period was 54 per cent. (about 50 per cent. when inagglutinable strains of *N. meningitidis* are excluded).

(2) The rates of the subgroups did not differ significantly from the total

or "expected" rate; thus this series of carrier rates exhibited no seasonal variation.

(3) Probationers, who are the recruits to the naval nursing service, "staff," who are the trained men, and patients in hospital all produced similar high carrier rates.

(4) The group of patients, swabbed on November 21, were mostly gonorrhoea cases. In view of certain attempts to prove antigenic relationship between meningococci and gonococci (for example see Boor and Miller, 1934), it is of some interest to note that these gonorrhoea cases were as liable to latent infection with meningococci as other groups. Rake (1934), however, only found a meningococcus carrier rate of 1·7 per cent. in a group of female children suffering from gonorrheal vaginitis.

Table III. *R.N. Hospital, Chatham. Non-contact* C.S.M. *carrier rates between March,* 1933, *and May,* 1934.

Date swabbed	Group	No. in group	C.S.M. carriers No.	%	S.E.
23. iii. 33	P.S.B.A.	50	33	66	± 6·7
2. v. 33	,,	48	27	56	± 7·1
31. vi. 33	,,	50	31	62	± 6·8
15. viii. 33	,,	49	26	54	± 7·1
18. ix. 33	Staff	50	28	56	± 7·0
3. x. 33	,,	50	15	30	± 6·4
17. x. 33	P.S.B.A.	35	20	57	±11·2
21. xi. 33	Patients	50	24	48	± 7·1
7. ii. 34	Staff	49	30	61	± 7·0
16. v. 34	P.S.B.A. and staff	50	26	52	± 7·1
Mar. 1933–May, 1934	Totals	481	260	54	± 2·3
Mar. 1932–Feb. 1933	Contacts to C.S.M.	211	27	13	± 2·3
March, 1933	Cases	34	21	62	±10·1

P.S.B.A. = probationary sick berth attendants.

(5) At the bottom of Table III the carrier rate which was found among the contacts to the C.S.M. cases of the previous year (see Tables I and II) has been inserted for comparison with the present series. The difference in the percentages, 54 and 13, is 41, which is nearly eighteen times its standard error $\pm 2{\cdot}3$. The same media and isolation technique was used in each period, but the earlier "contact" groups consisted chiefly of sailors from outside the hospital. Nevertheless the rate $62 \pm 10{\cdot}1$ per cent. among the March contacts is significantly greater than $13 \pm 2{\cdot}3$, the rate among the earlier C.S.M. contacts, and suggests that the rates among the naval population outside the hospital were at this time as high as those within the hospital. It seems therefore to be a justifiable inference that early in 1933, for some unknown reason, an unprecedented and rather sudden increase in the prevalence of latent infection with *N. meningitidis* took place throughout the Chatham naval division, and was not confined solely to the inhabitants of the R.N. Hospital.

(5) Repeated examinations of the same group

The first four sets of swabbings shown in Table III were made on the same group of probationers. There were forty-seven men in this group, aged 18–23 years, who were present on all four occasions. The results of their examinations can be arranged as shown in Table IV. This shows that forty, no less than 85 per cent. of the group, were infected on one or more of four occasions within a period of 5 months. Hence very few people can be immune to latent infection with meningococci under the conditions in question.

Table IV. *Results of examining four times the same* 47 *probationers.*

12 or 26	per cent.	carried on	4 occasions
14 ,, 30	,,	,,	3 ,,
7 ,, 15	,,	,,	2 ,,
7 ,, 15	,,	,,	1 ,,
40 ,, 85	,,	,,	1 or more occasions
7 ,, 15	,,	,,	no occasions

Neisseria meningitidis was isolated from 111 of the 188 nasopharyngeal swabs. This is equivalent to a mean carrier rate of 59 per cent.

Among the thirty-three individuals, who were positive on more than two occasions, there were eight who gave a negative result between two positive ones, which may represent a real or pseudo-intermittency (*i.e.* the subject may have lost his infection only to be reinfected a month or so later, or the intermediate negative results were merely due to failure of the isolation technique). Most of this group of probationers completed their training in August, 1933, so that their subsequent bacteriological history is unknown.

(6) The c.s.m. carrier rate in association with service seniority

One hundred of the 150 trained men who formed the sick-berth staff of the hospital, were swabbed in September and October, 1933, in order to see if the heavy infection of the probationers was consistent with the theory that, being recruits, probationers were more prone than trained men to latent infection with meningococci. Further samples of staff and probationers were examined later, on the dates given in Table III. All the hospital staff who were swabbed during the period shown in Table III are rearranged according to their seniority in the navy in Table V. The probationers are recruits of less than a year's service; the attendants have all more than 1, but less than 5, years' service; the leading hands are men of 5–10 years' naval experience; while the most senior subgroups, petty officers and wardmasters, have all been over 10 years in the navy. Very nicely, in accordance with the theory that herd immunity to latent infection with meningococci increases with bacterial experience, the carrier frequency of the first three groups declines, but unfortunately for the theory, it rises again in the senior groups of petty officers and wardmasters who have rates which exceed those of the probationer recruits.

Table V. *R.N. Hospital, Chatham. Carrier rates according to seniority.*

Sick berth rating	No. in group	Meningococcus carriers No.	Rate % and s.e.	
Probationers	286	171	60 ± 2·9	untrained
Attendants	64	28	44 ± 6·3	38 ± 4·9 junior trained
Leading hands	35	10	29 ± 7·7	
Petty officers	21	16	76 ± 9·5	71 ± 7·8 senior trained
Wardmasters	13	8	62 ± 13·4	
Total ratings	419	233	56 ± 2·4	
Medical officers	12	3	25 ± 12·5	

The last column combines the four classes of trained men into two groups of junior and senior ratings for comparison with the probationers or recruits.

As indicated in Table V, the *trained* men can be divided into two groups (instead of four). The one "juniors" of less than, the other, "seniors" of more than, 10 years' seniority. The "juniors'" carrier rate of 38 per cent. is significantly less than the "seniors'" 71 per cent. (the difference 33 being over three times its standard error ± 9·2). At the same time the *untrained* recruits rate 60 ± 2·9 is significantly greater than that of the junior trained men (the difference 22 per cent. being nearly four times the standard error ± 5·7). The cause of these striking differences is obscure, but it does not appear possible to attribute them to a greater or less familiarity with the naval bacterial environment.

(7) The c.s.m. carrier rate in association with occupation and environment

With regard to the hospital duties of the groups shown in Table V, the wardmasters are chiefly employed in clerical and administrative work and have little direct contact with the patients. The probationers have less intimate and less frequent contact with the patients than the remaining three groups, whose duties are mainly general nursing. The nursing duties are such as would cause little difference between the risk of infection of these three latter groups, either from the patients, or from each other, during the daily round. Each subgroup has its own mess and recreation rooms, those of the petty officers and wardmasters being relatively the more spacious.

During the Great War much stress was laid on the sleeping quarters as a favourite site for the dissemination of meningococci; therefore the sleeping arrangements of the hospital staff will be given in some detail. The groups of trained men all sleep in beds and get roughly the standard 600 cu. ft. of space per man. The wardmasters and leading hands occupy separate cubicles and therefore, in hospital, their night environment is such as to preclude the spread of carrier infection. The petty officers (though senior to the leading hands) sleep in large dormitories, as do the attendants. There is, on the average, 6 ft. of wall space per bed (the Board of Education standard). However, the petty officers (and wardmasters), being nearly all married, generally sleep in their

35-2

own homes, except when on duty, while the attendants nearly all sleep in. This means that only about half a dozen of the beds in the petty officers dormitories are occupied on any one night. Thus, when sleeping in hospital, the petty officers have relatively much more space than the attendants. Yet in spite of their more spacious sleeping arrangements the petty officers had a meningococci carrier rate of 76 per cent. against the attendants 44. Again, the leading hands had the lowest rate, in harmony with their ideal sleeping accommodation (*i.e.* single rooms), while the wardmasters, the other group to have single rooms, had a rate which was double that of the leading hands. It seems impossible to attribute the high rates of the two most senior groups to the fact that they usually slept at home in a relatively airy bedroom occupied by only one other person.

Finally the probationer recruits, who were the only ratings who slung hammocks in hospital, had the least satisfactory night environment. The hammock hooks were 26 in. apart. The number of probationers under training, however, varies. Up to August, 1933, there were fifty-five. This number gave an average of 450 cu. ft. of space per man. In August, 1933, the number was reduced to thirty-two, which allowed the mean space per man to increase to 650 cu. ft. To-day, however, we do not worry about cubic space so much as the distance between beds or hammocks. When the number of probationers was reduced, it was possible to use alternate slinging billets, which almost doubled the average linear distance between the respiratory orifices of the sleeping probationers. Yet there was no fall in the meningococcus carrier rate which was 59 per cent. before, and 61 per cent. after, the event.

It is surprising that, in spite of being recruits and in spite of having the worst sleeping arrangements, the probationers were no more liable to latent infection with meningococci than were the most senior ratings who had the best sleeping accommodation.

The last subgroup given in Table V are the medical officers of the hospital. In general this group is far more sheltered from infection than the others. But they present an interesting carrier distribution in association with their occupations, in that the only three carriers to be found were the anaesthetist, the throat nose and ear specialist, and the ophthalmic surgeon—all officers whose duties bring their respiratory orifices in close approximation to those of their patients. The complete correlation of infection and occupation is however spoilt by the fact that the remaining member of the "face to face" officers, the dental surgeon, did not carry *N. meningitidis*.

(8) Agglutination reactions

No attempt was made to carry out an accurate antigenic analysis by means of absorption tests with specific anti-meningococcal sera. In fact, at first it was intended to do no more than divide the cultures of meningococci into agglutinable and not agglutinable strains, because some workers have insisted that flocculation with some sort of specific anti-serum is a necessary diagnostic criterion of *N. meningitidis*.

Before May, 1933, the agglutination technique is not considered to have been very reliable; but in this month the technique, which has been in use ever since, was introduced. A suspension of the strain to be tested was made to match a tube of a standard opacity which was equivalent to that of a thousand million cocci per c.c. The suspension was heated to 65° C. for 1 hour, and put up against each of Gordon's four type sera (as supplied by the Oxford laboratories). A control of the suspension in saline solution was always included for each culture. All the tubes were kept overnight in a water bath at 52° C., and read the next morning.

Between May and October, 1933 (the March, 1933, batch was not tested), the cultures were only put up in one dilution of 1 : 25 of Gordon's four types of anti-meningococcal sera, in order to see if they were agglutinable or not, and if possible to determine which serological type predominated. While most of the strains agglutinated with more than one type of anti-serum, it was evident that most of them flocculated more rapidly and completely with Type II serum. By the above rough-and-ready technique, 147 cultures were classified—121 as Type II, 13 as Type III, 12 as indistinguishable or inagglutinable, and a solitary culture agglutinated with Type I serum only. There is no pretence of suggesting that the above figures represent an accurate description of the frequency of serological types during the period in question. Nevertheless, from the experience gained with the more exact quantitative methods subsequently used, there is no doubt that Type II antigen (Gordon-Oxford) predominated at Chatham up to October, 1933, even though the predominance may have been somewhat exaggerated by the rough qualitative tests then in use.

When, however, the cultures isolated in November, 1933, were examined by the rough technique, in about half of them it was impossible, by the use of a 1 : 25 dilution only, to distinguish between Types II and III. From this time onwards, therefore, all cultures of meningococci were taken up to an agglutination end-point with each of Gordon's four types of anti-sera; and classed according to which type of serum flocculated them in highest dilution. This method of typing was shown to be reliable in the war period by Gordon and his co-workers (1920), in that, of 235 strains of meningococci typed in this way, there were only four in which the type was not confirmed by subsequent absorption of agglutinins. Therefore, at Chatham after November, 1933, the frequency distribution of serological types may be taken as representing a fairly accurate picture of the antigenic composition of the "meningococcal herd" (according to the Gordon-Oxford sera).

As stated above, until October, Type II cultures predominated over Type III, but Table VI shows that in November the number of cultures of Types II and III were equal; and that in February and May the Type III predominated over the Type II antigen. The more powerful flocculating action

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of Type III "Gordon-Oxford" anti-meningococcal serum on this series of cultures is better brought out in Table VII which gives the type of specific antiserum which agglutinated each culture in a higher dilution than any other serum, with the maximum dilution in which it did so. The phials in which the anti-meningococcus sera were supplied were all labelled, "titre 1 : 250."

Table VI. *R.N. Hospital, Chatham. Cultures of* N. meningitidis *isolated between November,* 1933, *and May,* 1934.

Maximum agglutination in Gordon-Oxford type sera	No. of strains isolated in November	February	May	Totals
II	11	6	5	22
III	11	16	13	40
II, III	—	3	1	4
I, II, III	—	2	2	4
IV	—	—	2	2
Inagglutinable	2	3	2	7
Control agglutinated	—	—	1	1
Totals	24	30	26	80

Table VII. N. meningitidis. *Maximum agglutination titre of the seventy-two agglutinable strains shown in Table VI.*

Gordon-Oxford type sera	Maximum agglutination titre 1/1000	1/500	1/250	1/125	1/50	1/25	No. of cultures
II	—	—	1	9	9	3	22
III	4	2	8	7	13	6	40
II, III	—	—	—	—	1	3	4
I, II, III	—	—	—	—	—	4	4
IV	—	—	—	—	—	2	2

Table VIII. N. meningitidis. *Amount of cross-agglutination.*

Type II cultures: Times diluted Gordon-Oxford type sera I	II	III	IV	Type III cultures: Times diluted Gordon-Oxford type sera I	II	III	IV
25	250	125	—	25	125	1000	25
25	125	50	50	25	50	1000	25
25	125	50	—	25	25	1000	25
—	125	50	—	25	—	1000	—
25	125	25	—	25	50	500	25
25	125	25	—	50	25	500	—
25	125	25	—	25	125	250	—
25	125	—	—	50	50	250	—
—	125	—	—	—	50	250	—
—	125	—	—	—	50	250	—
				25	25	250	—
				25	25	250	—
				—	25	250	—
				—	25	250	—

Table VII therefore indicates that the antiserum labelled Type III agglutinated fourteen cultures up to "full titre" of which six flocculated in still higher dilutions; whereas only one culture agglutinated in the serum labelled Type II up to 1 : 250, but nine up to a dilution of 1 : 125. An idea of the amount of cross agglutination is given in Table VIII in which is given the agglutination titre for each of the four types of Gordon-Oxford specific sera against the fourteen cultures which agglutinated to the greatest extent with Type III, and the ten which flocculated most readily with Type II Gordon-Oxford sera. Finally, the tendency to cross-agglutination is evident if the total seventy-two agglutinable cultures of *N. meningitidis* are tabulated thus:

43	agglutinated	in Type	I	serum
58	,,	,,	II	,,
70	,,	,,	III	,,
14	,,	,,	IV	,,

in a dilution of 1 : 25 or over.

Without knowledge of the data in Table VII this arrangement would suggest that the antigen corresponding to the Gordon-Oxford Type I antibody was not so very much less in evidence than the Types II and III, but, although forty-three strains of meningococcus flocculated to some extent in the 1 : 25 Type I tube, yet only four of them agglutinated in the 1 : 50 dilution. Similarly Type IV serum only agglutinated one culture in a 1 : 50 dilution.

All the saline control emulsions "stood up" well for over 24 hours, except in one instance (probably due to a technical error or contaminatory growth).

The results of the serological examinations can be summarised as follows:

(1) Ninety per cent. of these meningococci agglutinated with one or more of the Gordon-Oxford sera.

(2) Latterly, difficulty was experienced in distinguishing II and III culture types in contrast to the more commonly reported difficulty of separating Types I and III, and II and IV.

(3) Types I and IV appeared to form a very small fraction of the antigenic structure of the individual strains of meningococci, or of the whole collection considered as a "bacterial herd."

(4) In November, 1933, the antigen corresponding to the Gordon-Oxford Type III specific antiserum rather suddenly took predominance over the Gordon-Oxford Type II antigen.

After the completion of this serological investigation, The Standard Laboratory, Oxford, who supplied the specific type sera, issued a circular in which it was stated that Types II and IV meningococci belong to "a large heterogeneous group" of organisms having little or none of the characteristics of the original Gordon Types II and IV. Therefore they proposed in future to issue only two diagnostic meningococcus sera, Group I, equivalent to Gordon's Types I and III, and Group II, containing anti-bodies to several of the commoner antigens, not in Group I. In accordance with this classification of *N. meningitidis*, Group II was at first predominant at Chatham, but was later replaced largely by Group I—the carrier rate remaining constant throughout the substitution at the phenomenal level of 50 per cent.

The whole of this investigation affords one more example of the great complexity and variability of the antigenic composition of a specific bacterial herd. Not only do the so-called types of *N. meningitidis* vary in their frequency distribution in time and space, but each individual strain of meningococcus appears to be built up of several antigenic components, mixed in any proportions.

(9) Discussion

The earliest observations on meningococcus carriers, combined with the mass of observations which were made in the Great War, led to the belief that the incidence of c.s.m. cases depends on the magnitude of the carrier rate. From this hypothesis a practical generalisation has been perpetuated in text books on preventive medicine, and even in scientifically cautious reports, such as that of Murray (1929), where this "law" is laid down—"that a rise of this order (20 per cent.) in the non-contact carrier rate *is* a sure 'storm signal' of imminent trouble." But it would be better to replace the *is* (which we have put in italics) by "was"; because at Chatham, for more than a year, the carrier rate of agglutinable *N. meningitidis* was about 50 per cent., although at the time there was no case of c.s.m. among the 10,000 or so sailors, soldiers, and airmen, who garrisoned the Chatham area. It is a fair inference from the evidence in this paper that some 5000 carriers of meningococci were continually present among the service population of this important naval and military depôt and recruiting centre. A large fraction of these carriers slept in their own homes, in intimate family contact with susceptible young children, and mixed freely in the social life of the civilian community. Nevertheless, during 1933, only five cases of c.s.m. were notified from among the 140,000 civilians, which include the soldiers' and sailors' families, and comprise the population of Chatham, Rochester, and Gillingham. Before this period, although occasional cases of c.s.m. were being admitted to the naval hospital (which also receives all army and air force cases in the district) the meningococcus carrier rate was much smaller (12·8 per cent.). But the meningococcal situation at Portsmouth provides a still more striking antithesis to the present condition of affairs at Chatham. During the period of the Chatham investigation, March, 1933, to May, 1934, six cases of c.s.m. were admitted to the Portsmouth naval hospital, but only nine meningococcus carriers were found among 177 contacts to these cases, a carrier rate of $5{\cdot}1 \pm 1{\cdot}7$ per cent. In view of the Chatham findings we were at first cautious in accepting this great contrast in the carrier rates of the two naval ports as a real natural phenomenon, and suspected that it was really due to differences in bacteriological technique. We therefore communicated with Surgeon-Commander J. A. O'Flynn, the bacteriologist to R.N. Hospital, Portsmouth. O'Flynn was quite certain that the Portsmouth 5 per cent. blood-agar medium he was using was as good as ours. He had had no difficulty in isolating *N. meningitidis* from the spinal fluids of his six cases of c.s.m. At our request O'Flynn tried out the Chatham culture media and technique on fifty of the Portsmouth sick berth staff, half of them probationers. Only two cultures of meningococci, one Gordon Type II, one inagglutinable, were discovered in the nasopharyngeal swabs of this sample. This is equivalent to a carrier rate of $4 \pm 2{\cdot}3$ per cent. We have, therefore, no hesitation in believing that latent infection with *N. meningitidis* was in reality ten times as common in the Chatham area in the absence of meningitis, as in Portsmouth in its presence.

There has been little published on non-contact carriers of meningococci since the classical report of the Medical Research Council in 1920. In Manchester, however, during 1905–1927, meningococci could not have been common, because in the Ministry of Health's (1930) report on the nasopharyngeal flora it is stated: "Of 2455 nasopharyngeal swabs 60 (2·44 per cent.) yielded gram-negative cocci which...would be regarded as meningococci." The majority of such carrier rates as are reported, with the exception of those cited above in Rake's (1924) paper, refer to contact-carriers, and the reported rates, as a rule, vary round about 5 per cent. In the Royal Navy, even during the Great War, rates exceeding 10 per cent. were not common. The maximum naval meningococcus carrier rate, 27 per cent. (of 340 men), was found at Plymouth by Whiteside (1915), but he employed no agglutination tests, and was purposely using a very elastic definition of "meningococcus." Dudley (unpublished) during the same period at Chatham, found the contact carrier rate for *agglutinable* meningococci was 8·5 per cent.

In the army, however, during the war period, much higher rates were recorded. Glover (1920) found the maximum rate of 70 per cent. among recruits when C.S.M. outbreaks were present. Incidentally, in the absence of meningitis, Glover found that the large majority of carrier strains of meningococcus were not agglutinable—another antithesis to the recent findings at Chatham. In the Sudan C.S.M. epidemic, Davis (1931) found 43 per cent. of forty-seven contacts were carriers, but this carrier rate was accompanied by a C.S.M. morbidity of 10·5 per 1000, which must be the record C.S.M. attack rate.

The discovery therefore of a persistent C.S.M. carrier rate as large as 50 per cent., *unaccompanied by cases of* C.S.M., would appear to be a unique event. Rake (1934) in an investigation more analogous to the one at Chatham, took nasopharyngeal swabs at weekly intervals from two groups, the one, twenty-four laboratory workers, was under observation for an average of 65 weeks, during which period thirteen, or 41·6 per cent. of the *group*, were found infected one or many times with meningococci. The other group consisted of twenty-five young girls, in hospital with gonorrheal vaginitis, who were observed for an average of 14·5 weeks. Two individuals, or 8 per cent. of this *group*, were found to be carriers. Rake remarks that—"the difference in the carrier rate between the two groups—41·6 and 8·0 per cent.—is striking." But according to conventional usage the above percentages are not ordinary carrier rates, and, in any case, the above frequencies are not comparable between themselves, or with the carrier rates as estimated at Chatham and elsewhere. Other data in Rake's paper show that the first group must have supplied some 1560 swabs of which 221 were "positive," and the second 360, swabs of which six were "positive meningococcus." Therefore the comparable carrier rates were 14·2 and 1·7 per cent. Similarly in a third group of 569 forestry students the *comparable* C.S.M. carrier rate was 1·4 per cent. The tenfold difference between Rake's two adult carrier rates—$14{\cdot}2 \pm 0{\cdot}9$ and $1{\cdot}4 \pm 0{\cdot}4$ is however most striking. The ratio of these two rates to each other is the same as that of the 50 and 5 per cent. rates found at Chatham and Portsmouth. In this respect, therefore, Rake's work is further indirect confirmation of the validity of the Portsmouth carrier rate, in that, while employing an identical technique and personal equation, it was proved possible that the carrier rate in one set of adults could be tenfold that in another set, at times when there was no meningitis being notified.

Rake found that the meningococcus carrier rate is made up of chronic (if not permanent), intermittent, and transitory, infections. Permanent or chronic carriers were, however, responsible for by far the largest proportion of the total carrier rate. The data recently collected at Chatham is not suitable either to confirm or refute this conclusion. But the naval and military experience in the past definitely showed that the carrier rate was mainly made up of numerous transitory infections instead of a few chronic or permanent carriers. In fact, under the conditions existing at that time, chronic carriers were remarkably rare. Probably both conclusions are correct. The same unchanging group of adults, living under stable environmental conditions, would rather be expected to tend to a position of equilibrium consisting of permanent carriers and non-carriers. On the other hand the service units are in a continual state of flux, as drafts of men pass continually from port to port and garrison to garrison, and as they receive frequent additions of fresh susceptible recruits. Under such conditions carrier rates should be more liable to fluctuate, and to consist for the most part of temporary infections.

In view of the behaviour of most clinical infections, including C.S.M. itself, which all tend to attack recruits in preference to senior trained men, the fact that at Chatham recently (see Table V) the ratings of intermediate seniority (*i.e.* bacterial experience) had a meningococcus carrier rate which was significantly smaller than the rates of both the recruits and the most senior men, was perplexing. Still more paradoxical becomes this observation, when it is realised that the most senior trained men, who occupied the most spacious quarters, had appreciably the same carrier rate as the probationers whose day and night environment was considerably more cramped than that of any of the other groups.

The lack of evidence that the nature of the sleeping accommodation had any effect on the spread of latent meningococcal infection at Chatham, during recent times, is also disturbing, in view of Glover's (1920) convincing demonstration of the influence of the population density in sleeping quarters on the incidence of carriers and cases of C.S.M. The sleeping quarters in the naval hospital were however far more spacious than those of the war-time recruits, among whom Glover found carrier rates as high as those at Chatham. We can assume, therefore, that the strains of meningococci at Chatham had a high infectivity (power of spreading from host to host), as indicated by the 50 per cent. carrier rate, in combination with a low invasiveness (power of spreading within the host itself), as indicated by the absence of C.S.M. cases.

In certain very infectious diseases, for example influenza, which convey little protection against subsequent attack, it is often (but not always) impossible to obtain any evidence that infection spreads more easily in the dormitories than elsewhere. Indeed it is probable that under such circumstances the briefer, but frequently closer, daytime contacts offer better opportunities for the passage of parasites from host to host than the more prolonged "contacts" in the dormitory; which "contacts" may be wholly ineffective if the beds are spaced far enough apart. Thus an exceptionally high infectivity could account for there being no evidence of the usual association of the meningococcal carrier rate with differences and changes in the sleeping accommodation of otherwise similar groups.

Specific bacteria of low invasiveness ("virulence") are less likely to cause as much reaction in their host as those of greater invasive power, and they are therefore unlikely to cause as much, or as durable, specific active-immunity as more virulent strains. It is true that Topley, Greenwood and Wilson (1931) found a strain of *B. aertrycke* of high infectivity and low virulence, to mice, as judged by intraperitoneal inoculation, but possessing as good immunising powers as strains of much greater virulence. This was, however, admittedly an exceptional strain. On the other hand, Perry, Findlay and Bensted (1934) found that, in *B. typhosus* cultures of human origin, invasiveness ("virulence") ran parallel with their capacity for protecting mice. It would therefore seem a reasonable inference, that the meningococci inhabiting Chatham during recent times, by reason of a lower invasiveness than usual, conveyed little lasting specific acquired immunity to re-infection; an hypothesis which may explain why the recruits and the most senior ratings were attacked equally. It must be added, however, that there is little evidence from the war-time records that seniority (*i.e.* acquired immunity) was a factor of much weight in determining the liability to latent infection with *N. meningitidis*, although it was a factor of paramount importance in determining the liability to patent attack by C.S.M. We know in the analogous case of diphtheria that a high resistance to clinical attack can be acquired by latent infection; an immunity which is accompanied by no apparent decline in the liability to reinfection as a carrier (Dudley, May and O'Flynn, 1934).

To summarise—during recent times at Chatham, the high carrier rate, representing a high parasitic infectivity, insured that every susceptible, sooner or later, had an opportunity of being infected with the meningococcus, while the low invasiveness, as represented by the absence of meningitis, prevented any appreciable rise in the specific *acquired herd immunity* to carrier infection. Therefore *natural hereditary herd immunity*, which should be practically the

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same in all groups of naval ratings, was left as the decisive factor in determining the magnitude of the meningococcus carrier rate.

Carrier surveys, such as that at Chatham, confirm the opinion that the segregation and treatment of meningococcus carriers can have little or no effect on the incidence of C.S.M. When the carrier rate is high it is obviously impracticable and absurd to attempt to isolate perhaps a quarter or more of the population. Again, Rake's observations show that in such circumstances many meningococcal carriers are chronically, if not permanently, infected. These subjects are usually irresponsive to any treatment; and it is illegal, impossible, and undesirable, to incarcerate them in an isolation hospital for life. When the carrier rates are small, and the duration of infection generally brief, things are no better; because it was shown experimentally at Chatham that during the Great War, if the three or four carriers, which were discovered on first swabbing a batch of recruits, or contacts to a C.S.M. case, were segregated, that, by the time these first three or four subjects had cleared themselves of meningococci, they had been replaced by three or more fresh infections from among the originally uninfected remainder of the batch. Moreover, in Chatham at this time treated and untreated meningococcus carriers cleared themselves of infection with equal rapidity. There are really no satisfactorily controlled experiments which demonstrate that treatment, apart from the fact that a hospital is usually a more salubrious environment than a ship or barracks, has any appreciable effect on latent infection with meningococci. Indeed, such observations as those of Bull and Bailey (1927) who were able to transform harmless carrier infections of *B. leptisepticum* in rabbits into symptomatic infections by the intranasal injection of common antiseptics of ordinary therapeutic strength, and even fatal pneumonia when brilliant green was used, make it appear that douching, spraying, and gargling, are just as likely to damage, as to improve, the bacterial resistance of a *healthy* mucous membrane. Hence the attempts to prevent meningococcal and other infections by mass spraying, or other local treatment, are better abandoned. Rolleston (1925) remarks that the incidence of C.S.M. in the sea-going ships of the navy increased after the introduction of massed nasopharyngeal swabbing of recruits and naval drafts, and the isolation of the meningococcal carriers thus found. We have, however, no intention of suggesting this increased morbidity was the result of these alleged preventive measures, but merely to point out that the measures apparently had no effect, one way or the other, on the incidence of meningitis.

Finally it is even possible that a high carrier rate, such as that prevailing recently at Chatham where the strains of meningococcus were obviously of low pathogenicity, may actually prevent meningitis by raising the herd resistance to meningococci in general. So that should subsequently a more pathogenic strain of *N. meningitidis* appear in the environment, it will be unable to invade the meninges of the already latently immunised herd.

SUMMARY

1. In Chatham naval hospital a carrier rate for agglutinable meningococci of 50 per cent. persisted for over a year, during which period there were no cases of cerebro-spinal meningitis among the naval and military population of the port.

2. During the same period the carrier rate at Portsmouth among the contacts to six cases of meningitis was 5 per cent.

3. During the year previous to the present Chatham investigation the carrier rate at Chatham was 13 per cent. among the contacts to five cases of C.S.M.

4. There was no association of the meningococcus carrier rate with density of population or season of the year.

5. The most senior ratings, with the most spacious accommodation, had as high a carrier rate (60 per cent.) as the recruits with the worst sleeping quarters. Ratings of intermediate seniority had an intermediate rate (38 per cent.).

6. Agglutination tests indicated that the antigenic composition of the bacterial herd of *N. meningitidis* changed rather suddenly, while the total meningococcal carrier rate remained constant.

7. Many of the above recent observations are at variance to what was seen at Chatham, and elsewhere, during the Great War. An attempt is made therefore to reconcile the past with the present experiences.

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