MENINGOCOCCUS CARRIER RATES AND MENINGITIS INCIDENCE[1]

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The purpose of this paper is to review certain general features of the epidemiology of meningococcus meningitis in the light of a survey of meningococcus carriage which was carried on continuously from December, 1941, to May, 1945, with a final carrier test in December, 1946. This was part of a survey including hemolytic streptococci, *Corynibacterium diphtheriae* and *Hemophilus influenzae*, which was conducted by the Commission on Pre-epidemic Survey in the First Service Command under the Board for the Investigation and Control of Influenza and Other Epidemic Diseases in the Army, Preventive Medicine Division, Office of the Surgeon General, United States Army.

Of the group of diseases on which carrier studies were done, meningitis was the only one that presented an epidemic situation during the period of the study which made worthwhile a more extensive study of the relationship of findings in the carrier studies to the occurrence of meningitis during the same period, and as well to the epidemiology of meningitis in general. As it happened, the carrier study embraced the whole period of one of the cyclic increases and decreases in the occurrence of meningitis to be pointed out, and extended through four seasonal waves of the disease. Thus, the data available for analysis are unique in that carrier rates for the several types of meningococci are now known both for epidemic and interepidemic periods, as well as for epidemic and interepidemic seasons. This should not only provide a better understanding of the role of the carrier rate in the epidemiology of meningitis but at the same time should clarify certain questions concerning the mechanisms which influence the carrier rate—chiefly that of "overcrowding", long held to be a major determinant first in an increase in carrier rates and, in turn, in an increase in the disease, particularly under conditions of mobilization.

Meningitis is extraordinary in the wide extent to which its infectious agent is distributed in the population and the comparative infrequency of disease in those harboring the organism. Furthermore, there is no reliable evidence that immunity from previous exposure is a determinant in restricting the occurrence of the disease, nor that population immunity, as is clearly the case with a number of virus diseases, stands in the way of repeated harborage and transmission of the organism by the same individual. Nonetheless, it has become clear that the extent of the occurrence of the disease is by no means wholly a simple function of the prevalence of meningococcus carriers. Epidemics may occur in certain

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groups while other groups with the same carrier rate remain free of the disease, or the disease may change from sporadic to epidemic with no corresponding increase in the prevalence of the meningococcus in the same group. Again it appears that attack rates may vary markedly in different groups, notably recruits and seasoned troops, though the carrier rates may be the same.

In the period during which emphasis has been on the infectious agent and its mode of spread, the point of view in the epidemiology of infectious disease has been qualitative to a large extent, dealing more with the unusual—the epidemic—as a thing apart. Attempts have been directed more toward a search for some specific and single cause of localized epidemics, though these may be little more than reflections of the more general prevalence of the disease. Search for the introduction of a virulent strain of the organism or one to which the population affected has no immunity from previous exposure or else some circumstance, some "accident of hygiene" which simply brings about a more rapid passage of the organism, one accompaniment of which has been supposed to be an increase in virulence of the organism, has frequently been the main objective in carrier studies. Epidemiology is now coming more to the quantitative point of view envisioned by Theobald Smith (1). Attempts are made to measure "all the possible factors . . . and to evaluate their relative importance" (2). Numbers of factors known to play a part are measured during interepidemic periods, as well as in epidemic periods, and brought together into trends toward that concatenation of numbers of circumstances which determine disease either in smaller or in larger numbers. This point of view is removing the epidemic in many diseases from the category of "accidents of hygiene" and making them understandable as imbalances—sometimes exceptional upsets—in what we call disease, but in what in the broader sense may be a remarkable host-parasite equilibrium (3). It was in accordance with this broadened view of epidemiology and bacteriology that the purpose of this study was to follow the trends of carriage in both inter-epidemic and epidemic periods with the hope of earlier detection and localization of indications of impending disease prevalence and the discovery of any conditions in miliatry establishments which might influence carriage. The objective was the possible application of more timely, more suitable, or more effectively localized precautionary measures than had been possible previously.

Although these more immediate objectives may not have been attained, the results of the carrier study in the case of meningococcus, when analyzed in the light of the occurrence of meningitis in the establishments where the studies were carried out, in the area in which the establishments are located, and in the country at large, make possible certain inferences which do have a bearing on the epidemiology of the disease in general. As Russell has said, the losses from war are so enormous that it would be illogical to refer to war produced scientific advances as dividends or to point to them with thoughtless pride. Rather, such progress constitutes salvage which sometimes may be of considerable value because the urgency of the war conditions demands more elaborate studies than are ordinarily undertaken and hence sometimes affords answers to difficult problems. New lessons are learned even if painfully and at great expense (4). Both the urgency of

the questions presented by the war and their magnitude, as well as the formation of large units of people for military purposes which sometimes are "convenient" for certain types of studies, brought about in many instances far more comprehensive studies through team work than those which have been customary in peacetime—too frequently limited to the single handed efforts of individual investigators in normally dispersed populations.

In many ways, the results of these studies are in keeping with already existing conceptions of the epidemiology of meningococcus meningitis; in certain respects, essential differences between the epidemiologic behavior of meningitis and the epidemiologic patterns of other diseases generally considered as of the same type are brought out; and finally, it is believed that some of the findings call for some revision of conceptions which had previously evolved in large part from studies carried out under similar conditions but on a smaller scale and with less improved techniques. Notable amongst the differences between this and previous studies is the advance made between World War I and World War II in distinguishing serologic types of meningococci.

The carrier study was planned and carried out as a "routine" check on carriers with a view toward the collection of information which would enable the prompt institution of preventive measures in military establishments. Frequent reports were made to the Office of the Surgeon General concerning the prospective occurrence of meningitis over shorter or longer periods as indicated by carrier rates, but as the study turned out, it is believed that the results will be of more value if they are now reported more as if they represented an orderly study aimed primarily at the clarification of a number of propositions which had been basic to what had been the "prevailing view" of the epidemiology of meningitis. In the course of the study, it became increasingly apparent that both the occurrence of meningitis and the carrier rates in the military establishments studied were essentially the same as those prevailing at the same time throughout the country. For this reason and for the additional reason that the extraordinary disproportion between the number of carriers and the number of cases rendered it unlikely that any meaningful result could come from any attempt to establish local carrier-case relationships, the results of the carrier study will be analyzed as they relate to certain broader epidemiologic features of the disease. Features of the epidemiology of the disease which will be considered are: *a*, the type composition of meningococcus carriage; *b*, the occurrence of the disease in epidemic cycles; *c*, the seasonal prevalence of the disease; and *d*, higher attack rates in the military than in the civilian population, with a higher attack rate in recruits than in seasoned troops.

A question was still confronting students of epidemiology which had already been raised and well expressed by Hirsch before the discovery of the meningococcus: "In a certain number of the epidemics that have been confined to the military . . . the earliest cases, and the majority of the cases throughout, occurred *among recruits*. It was natural to seek for an explanation of the fact in their altered mode of life, and more especially in the unwonted *bodily strain of their drill* or other duties of the service. Some . . . have gone so far as to make that

factor the true and only cause of the disease. It is clear that the significance to be assigned to that factor in the etiology is only that of a predisposing cause . . . It is much more reasonable, in my view, to connect the prevalence of meningitis epidemics among bodies of troops with their lodgment in more or less *crowded, badly kept, and insufficiently ventilated* tenements, or, in other words, with the same conditions that afford a peculiarly favorable soil for the development of this and many other infective diseases . . ." (5). (In more modern terms, increased opportunity for transmission of an infectious agent results from the 'urbanization' through mobilization of non-immunes, as in measles.)

The organism, *Neisseria intracellularis*, had been described by Marchiafava and Celli in 1884, but the significant study was that of Weichselbaum, who, three years later, described it in detail as the organism found in 6 cases of cerebrospinal fever. The substitution of actual laboratory tools and the experimental method for the older method of observation which was so largely relegated to the realm of speculation gave great emphasis to the role of the infectious agent. As with many other infectious diseases, the discovery of a microbial etiologic agent "revolutionized our entire conception of epidemiology by displacing the then dominant and paralyzing theories of predisposition by the more hopeful infective theory". The trend in research took the direction of the newer techniques. The central idea in epidemiology became the infectious agent and its mode of spread. But the sporadic distribution of cases even in epidemics and especially the finding of meningococci in the nasopharynx of normal people as well as in those with the disease soon pushed the bacteriologic study of meningitis beyond the mere question of exposure to the infectious agent. With the new techniques available, the explanation came to be sought in variations or differences in the infective agent.

Differences in strains of meningococci were first recognized in the course of the preparation of therapeutic antimeningococcus serum. Several or many strains of the organism were employed for the inoculation of animals on the supposition that biologic variations in strains would be covered. The observation that strains of the organism isolated from the nasopharynx of healthy persons frequently were not agglutinated by sera prepared with strains from cases led to attempts at classification into serologic types, first with a view to the manufacture of more inclusive therapeutic sera, and only later with a view to a better understanding of epidemiologic relationships. That the earlier classifications represented only an imperfect separation of distinct types of the organism and that they had little to do with pathogenicity is indicated by cross reactions between strains of different types, by a lack of agreement between the classifications set up by different workers, and by the fact that all types could be found both in the clinical disease and in the healthy carrier.

The combined force of the "new" type classifications and the pressing needs of the military situation in World War I brought about carrier studies which led to the quick elaboration of a formula to explain the epidemic occurrence of the disease and to meet the pressure for preventive measures. It was perhaps in part its plausibility and in part its preciseness which caused it to be so widely adopted.

Observations made even in the course of these studies which, under ordinary circumstances, would have raised doubts on many points passed unnoticed. It is furthermore curious that even though serologic typing so largely gave impetus to the epidemiologic studies concerning carrier rates, the epidemiologic deductions did not for the most part take into consideration the various serologic types. They were based rather on the overall carrier rate. This was natural since the type classifications of the time failed to distinguish any one type which was predominantly pathogenic.

The World War I concept had it that previous to an outbreak of meningitis "carriers of the meningococcus increased steadily" from a "normal" rate of 2 to 4% to 20 or 30%, and that soon after it had passed the "danger point" of 20%, cases would begin to appear. The very large literature of the time does not clearly bring out any facts, or theory, for that matter, upon which the 20% "danger point" was based. There are statements concerning individual situations which, even if not of any particular significance from a statistical point of view, were so vivid that they were readily incorporated into the conception of the epidemiology of meningitis. "The carrier rate, which was 19.25% . . . reached what is usually considered the danger point of 20% (see War Office Memorandum on Cerebrospinal Fever, p. 2) just 6 days before the first case occurred" (6). Again, the carrier rate "which had been kept beautifully low during November (5% on November 29) now commenced to rise in ominous fashion; on December 6, it was nearly 17%; on the 21st, 19%, just under the 20% danger line as laid down in the War Office memorandum". The idea was not in the least impeded by such lines as ". . . sporadic cases may admittedly arise with any carrier rate . . ." (7), and that 22% of civilians examined in an outpatient infirmary "although they had no relation to cerebrospinal fever" harbored in their nasopharynx organisms indistinguishable from the meningococci (8), a result confirming previous studies which showed that "meningococci are to be found in a considerable percentage of persons in whom no relation to cases of cerebrospinal meningitis is discoverable".

Having fixed a cause of epidemics with such a high degree of precision as the "warning rise" and "20% danger point", it was natural to hurry on to an explanation for these "sure storm signals of imminent danger". Investigating the cause of this "warning rise" in the carrier rate, Glover was led to suspect a relationship between it and overcrowding in the sleeping huts. These huts were "at the best, poorly ventilated", and during the stress of war, "the mobilization standard had been overstepped" so that beds instead of being separated were practically touching each other. Glover noticed that the carriers in a given hut tended to be aggregated together. This pointed strongly to the direct transmission of the meningococcus from one man to another sleeping in the next bed. He tried the effect of spacing out the beds in the hope that the infection would be diminished. The results obtained "seemed to be in accordance with expectation". The effect of the distance between the beds was not confined to the carrier rate. At Caterham depot, "where there was severe overcrowding", an outbreak of cerebrospinal fever had occurred during each winter of the war, but subsequent to

the adoption of the spacing-out policy in 1917–18 "not a single case occurred". It is sometimes difficult in these studies to determine whether a high carrier rate was associated with actual overcrowding, or to what extent a high carrier rate was in itself interpreted as evidence of overcrowding. A sharp rise in the non-contact carrier rate "is a sure a storm signal of imminent danger of an outbreak as it is a sign of overcrowding or of dangerously deficient ventilation" (7). (The latter was sometimes invoked in instances of otherwise unsatisfactory evidence of "overcrowding".)

The far-reaching and hopeful implications regarding the relation between overcrowding and the carrier rate and that between the carrier rate and the disease, as well as the importance of the "warning rise," seem to have been in large part the cause of the wide acceptance of the whole doctrine, but there has been a noteworthy absence of confirmation of the main theses. In the Detroit epidemic of 1928–29, Norton and Gordon found no correlation between the degree of overcrowding in the home and the contact carrier rate (9). During the outbreak of 1931 at Aldershot, Armstrong and his colleagues were unable to obtain any evidence from a study of the position of carriers in dormitory barracks rooms that infection occurred mainly at night (10). The carriers were scattered quite irregularly without any particular relation to the position of the beds. Other nasopharyngeal surveys of the civilian population, like that of Rake (11), have shown that the carrier rate in institutions may be as high as 20% and over without any outbreak of cerebrospinal fever occurring. Perhaps the most striking figures, however, are afforded by Dudley and Brennan. Working at the Chatham Naval Hospital, they found that between January, 1932, and March, 1933, there were 11 cases of cerebrospinal meningitis with a carrier rate of about 13%. During the period March, 1933, to May, 1934, the carrier rate was 54%, yet no case of meningitis occurred. During the same period at the Royal Naval Hospital, Portsmouth, there were 6 cases of meningitis with a carrier rate of only 5%. Analysis of the distribution of carriers at Chatham showed no constant relationship between the density of the population and the carrier rate. The senior ratings with the most spacious sleeping accomodation had as high a carrier rate—60%—as the recruits with the worst sleeping quarters (12).

That all was not well with the World War I concept of meningitis and its prevention—that "when the carrier rate rises, it is direct evidence . . . of overcrowding; when that is remedied, the carrier rate automatically falls" (13)—is further indicated by frequent reports that "measures employed to prevent meningitis . . . cannot be considered as altogether successful. In spite of the great care exercised in the isolation of cases, wholesale examinations made to detect and eliminate carriers of meningococci, and the various other methods employed in the military to limit the spread of the disease, the incidence of meningitis in troops was still much greater than in the civilian population".

After the extensive researches of the World War I period, the status of serologic typing of meningococci, insofar as it provided any epidemiologic explanation of the occurrence of the disease or indicated methods of control, was much the same as that of other groups of organisms where the most exquisite type differen-

tiations have failed to distinguish the pathogen. It has been through a long process of careful selection of strains rather than the introduction of any new principle that the present day classification of serologic types of meningococci has evolved. After World War I, it was generally considered that serum therapy in meningitis was on a satisfactory basis. This attitude may have been to no little extent due to the absence over a period of years of extensive epidemics, rather than to any adequate appraisal of the validity of the typing methods used as the basis of serum production. It was not until the striking failure of serum therapy in the next epidemic wave which began in 1927 and reached its height in 1929 that the typing of meningococci again became the subject of intensive study. From 1700 reported cases in 1926, the number of cases tripled by 1929. This full fledged recurrence of what we now recognize as one of the cyclic waves of meningitis in the absence of war, the association with which meningitis epidemicity had been so emphasized by World War I studies, called forth much speculation as to some exogenous origin. Arguments were more or less successfully built up to the effect that new strains from the Orient introduced to the West Coast were spreading eastward. Serum therapy was failing—all the more reason for suspecting new strains which had not been included in the preparation of serum. Again meningococcus typing became the subject of extensive investigation, and again these studies were undertaken primarily in the interest of serum therapy.

In this new work—from 1928 to 1930—when the old standard type cultures of the Gordon classification were used for preparing type sera, it was found that they had "spread" antigenically. The previously supposed fixed specificity of types could well have been brought into question when it was found that typing should be done soon after isolation, before spread in antigenicity or the tendency to cross-agglutination had taken place. About two-thirds of Type I and III strains appeared by simple agglutination to be identical. In others, absorption of "mixed" agglutinins was necessary for type identification, and this of course made the standard for type designation an arbitrary one. The point of view seems to have been that type specificity was actually as fixed as species specificity, and that the varying degrees of interrelationships between types found were not actual characteristics of the organism but represented faults in procedure such as in the selection of strains for the preparation of typing sera. The effort in the laboratory was in the direction of refinement in procedure in the attempt to "narrow" the antigenicity of strains, sometimes so broad as to cross with nearly all other strains. At the same time, in the laboratory the relationship was so close that it was not possible to determine whether an organism was Type I or III.

It was the combined force of serologic, epidemiologic, clinical and chemical evidence which finally gave rise to the conviction that at least as far as "practical" pathogenicity is concerned Types I and III were the same. This not only marked a return to the point of view going as far back as 1915, but was a decided advance in the direction of correlation between meningococcus meningitis and a definitive pathogen amongst the several types, all of which had been—according to previous typing criteria—more or less equally pathogenic.

As Branham has pointed out, in most of the four epidemic periods since 1915 the majority of strains isolated (apparently from cases) have been Types I and III, now Type I, in 1931 as high as 96%. In such figures, an indication was seen that there is an epidemic meningococcus (Type I) and another Type (or group) II, responsible for sporadic or interepidemic cases; also that group II organisms are the carrier or nasopharyngeal strains. In addition, "nasopharyngeal" strains have often been so non-specific that they cannot be assigned to any specific type, though they not only are agglutinated by polyvalent serum but as well have the typical cultural and fermentative reactions of meningococci. It would seem that such an epidemic-sporadic correlation with different types was probably oversimplified. It rather implies that there are two entities caused by two types of meningococci but types which are as unrelated to each other as are different species in general, and that the two entities are as different in respect to their epidemiologic patterns as unrelated epidemiologic entities might be. The result of these studies which have been reviewed by Branham (14) is the present type classification of meningococci, under which meningococci from cases of the disease largely fall into a single type—the pathogen.

That this classification has meaning is shown by the fact that clinical meningitis is now associated in the vast majority of cases with a single serologic type, and that, as shown in the present study, the incidence of the disease runs parallel to the prevalence of this type of organism rather than that of any or all the other three types which are distinguished. This does not mean, however, that the other serologic types are wholly unrelated to the epidemiological picture, for, as will be seen, when there is a change in type composition an increase in the frequency of one type may be accompanied by a more or less corresponding decrease in one or more of the other types. Thus the relative increase in frequency of one type—for example, the increase in frequency of Type I meningococci which correlated with increase in the incidence of meningitis—does not appear to represent simply the "introduction of a new strain" but rather some interaction between the different types of the organism.

At about the time typing of meningococci reached the point of refinement which made it a differential procedure of precision, the advent of the newer chemotherapeutic agents went far, as with pneumococcus, to make typing no longer necessary from the point of view of the purpose for which it was originally undertaken (production of therapeutic serum). Typing of the meningococcus has nonetheless turned out to be the only instance of serologic typing which constitutes a method of epidemiologic importance in sharply differentiating organisms that produce disease—the pathogenic Type I— from those that do not. The present day understanding of the relationship between the prevalence of a single type meningococcus and meningitis not only brings into question some of the sweeping and laborious measures which had earlier been advocated as the *sine qua non* for the control of meningitis, particularly in the mobilization of armies, but calls for revision of some of the basic conceptions of the epidemiology of the disease.

The question whether meningitis is determined by "predisposing factors" or

by "contagion", raised before the discovery of the meningococcus, can now be restated in a somewhat modified form: To what extent is the incidence of meningitis determined by each of the two necessary factors for causing the disease, the dissemination of the organism and predisposing factors in those who harbor a particular type of the organism? In other words, the strictly microbic point of view of a straight contest between host and infectious agent begins to yield to the conceptions of a state of remarkable equilibrium between the host and parasite, in which the disease occurs only exceptionally, when this equilibrium is thrown out of balance by factors which, although not yet clearly understood, do not necessarily reside entirely in the parasite.

It was both the advance which had been made in the typing of meningococci and the advent of new drugs with the possibility of their prophylactic use which called for a restudy of meningococcus carriage when meningitis again became epidemic during mobilization of World War II.

TECHNIQUE OF MENINGOCOCCUS CARRIER DETECTION

Since the methods used in carrying out the bacteriological study which is the basis of this report have never been described in detail, it seems worthwhile at this time to present them in complete form. A preliminary description of the culture medium used was published in 1941 (15) and has received minor modifications here described for the first time. Allusion has also been made to the manner of transporting the nasopharyngeal cultures (16), but with no consideration for the reasons for its use or the experimental data by which it was shown to be satisfactory.

Collection of Cultures. Swabs are prepared on aluminum alloy wires, 0.0625″ gauge, 8 inches long. One end of the wire is turned back on itself about 3/16″ to form an attachment for the absorbent cotton. The swabs are dry sterilized in packages with the wires straight, and when used each one is bent about an inch from the end to form an angle which enables the operator easily to reach the nasopharynx. After taking the culture, the swab is inserted into a Wassermann tube containing about 1.0 ml of sterile horse blood, and the cotton plug replaced around the wire. Under these conditions, the meningococci have been shown to survive for several hours through a wide range of temperature (0 to 37C), and may be transported to the laboratory for culturing. If cultures can be taken in the laboratory, plates may be inoculated directly and no blood tube is required.

Preparation of Starch-Agar. Add 17 to 20 g dry, shredded agar to 500 ml tap water in a two-liter flask. Autoclave at 15 lbs for 15 minutes to dissolve. While still hot, the following solution is added. It may be prepared while the agar is being autoclaved:

Beef heart or meat infusion	300 ml (*a*)
"Casamino Acids, Tech."	17.5 g (*b*)
Starch paste	100 ml (*c*)
Para-amino benzoic acid, 1.0%	1 ml (*d*)
Phenol red, 0.2%	2 ml (*e*)

Tap water—bring total volume to 500 ml. Adjust pH to 7.6

Mix and distribute at once either into test tubes (about 20 ml each for pours, 5 ml for slants) or flasks of 250–500 ml. Autoclave *not more than 10 minutes at 10 lbs.* Over-autoclaving spoils the medium.

The flasks can be used to pour plates at once (about 20 ml per plate).

The tubes may be melted in boiling water and used as needed.

(*a*) Meat Infusion: 1 lb meat (chopped lean beef or beef heart), 500 ml water. Suspend meat in water, bring to active boiling, strain through cheese cloth and filter through paper. This may be used at once or stored in ice box, in glass stoppered bottles with a few ml of chloroform.

(*b*) A complete hydrochloric acid hydrolysate of casein, neutralized with NaOH (17). Supplied in dry form by Difco Laboratories, Inc., Detroit, Michigan.

(*c*) Starch Paste: Suspend 1.5 g ordinary starch (corn starch or laundry starch, *NOT* "soluble starch") in 10 ml cold water. Pour slowly into 90 ml boiling water, while stirring and bring to active boil.

(*d*) Para-Amino Benzoic Acid: Suspend 1 g in 75 ml water. Add strong sodium hydroxide drop by drop, with shaking, until dissolved (about 0.3 g NaOH required). Dilute to 100 ml. The solution keeps well.

(*e*) Dissolve 0.2 g phenol red by grinding in a mortar with 5–10 ml water and adding approximately normal NaOH a few drops at a time until a clear, deep red solution is obtained. Make up to 100 ml with distilled water.

Procedure. When thoroughly cool, the plates are inoculated with the nasopharyngeal swabs. Two swabs may be cultured on each plate. The material from the swab is rubbed over a circular area about 1.5 cm in diameter, and then, with a sterile loop, radial streaks are made over half the plate. The plates are placed in a tin can having a well-fitting cover. A short piece of candle is lighted and set into the can, and the cover put on. Incubation is at 36 to 37C for 18 to 20 hours.

With very little experience, it is possible to recognize colonies of meningococcus which on this medium are fairly large (2 mm), convex, and transparent or slightly opalescent. In order to insure freedom from contaminants, it is wise to restreak from a well isolated colony to a fresh plate, two colonies to a plate, incubating the fishings in the candle jar. The following day transplants are made from the fishings either to slants or to small segments of plates (10 to a plate) of starch agar. On the third day, the growth so obtained is used for agglutination.

With a loop sufficient growth is transferred to 2.0 ml saline to give a suitable suspension, and ten drops from a capillary of the suspension are added to agglutination tubes containing 10 drops of dilute (usually 1:50) polyvalent antimeningococcus serum and sera of Types I, II, and II alpha. The tubes are shaken for 10 minutes either on a Kahn shaker or by hand, at room temperature, and read at once with naked eye or a hand lens. No control with saline or normal serum is required. Agglutination should occur with polyvalent and one of the type sera, the other two remaining negative.

If the polyvalent serum gives a positive result but no typing occurs, the strain should be examined for its fermentative ability, and depending on the result is either rejected or classed as "non-typable" or "X".

Fermentation may be carried out on starch agar slants. These are made by adding 1% glucose, maltose or sucrose and either phenol red or brom thymol blue to the starch agar medium, tubing, and autoclaving at 5 lbs for 15 minutes.

The slants are inoculated heavily on the surface and incubated in a candle jar for 18 to 20 hours. The color change is quite distinct but confined to the surface layer of the medium.

Transportation of Nasopharyngeal Swabs. Experience has shown that the meningococcus tends to die out rather quickly in material taken from the nasopharynx on cotton swabs. It has long been the custom, therefore, to transport the plates which are to be inoculated with such material to the site of culturing, except when it is possible to have the individuals to be examined come directly to the laboratory. Special containers have been used in which, by means of a warm water jacket, the petri dishes containing the material can be maintained at approximately body temperature from the time of inoculation to the actual moment when they could be returned to the laboratory and placed in an incubator. For a survey of the sort which is here reported, this is a cumbersome and laborious matter which it seemed desirable to make some effort to avoid. Experiments were undertaken therefore to determine whether or not the meningococcus could remain viable for several hours if the swabs were immersed in a small amount of sterile horse blood. The procedure followed was to inoculate warm plates at the time of taking the cultures and then to place the swab with the remaining material in a Wassermann tube containing 1 ml of sterile horse blood, replacing the cotton stopper around the aluminum wire. These tubes and the original plates were then transported to the laboratory, which required usually from 2 to 4 hours. The plates were carried in warm water jacketed boxes, while the tubes were placed in racks without regard to outside temperature except to avoid freezing in winter. On reaching the laboratory, the plates were transferred to an incubator and a fresh set of plates was inoculated from the swabs. The latter were returned to the blood and the tubes kept under a variety of conditions, i.e., in the ice box, at room temperature and in the incubator for varying periods of time. Further inoculations were then made, and finally the results from all sets of cultures were compared.

The result of these tests indicated clearly that as high a proportion of positive cultures and approximately the same numerical distribution of colonies on the plates could be expected from the blood tubes as from plates inoculated directly from the patient and kept warm. The meningococci appeared to survive for periods of 10 to 12 hours and even longer, more or less regardless of temperature between 0 and 37C. A very considerable number of positive cultures have even been obtained from blood tubes which were delayed in transit during a period of exceptionally cold weather and were frozen solid and not cultured until 48 hours after being taken. In this case, the number of positives obtained was distinctly lower than would have been expected, but a remarkable degree of survival occurred even under these unfavorable conditions.

The mechanism by which the horse blood maintains viability of the meningococcus is not clear. Broth and saline are ineffective as is the starch medium

made up with the omission of agar. Attempts to use horse serum have shown that it is not as good as the whole blood. There are rather marked differences among individual sera in their ability to keep the organisms alive, but the whole blood from which even the poorer sera are obtained seems to be satisfactory. It appears that the cellular elements of the blood are involved in some way, and actually, if washed cells suspended in saline are used, the effect is almost as good as that of the original whole blood. This mechanism has not yet been analyzed further.

Preparation of Agglutinating Sera. In the early period of this work, sera were obtained at various times from Dr. Sara Branham of the National Institutes of Health and from Dr. John J. Phair of the Meningitis Division of the Commission for the Control of Influenza and Other Epidemic Diseases in the Army. The greater part of the sera, however, have been produced in this laboratory by the immunization of rabbits with type strains obtained from Dr. Branham. A certain amount of chicken serum has also been prepared following the procedure described by Phair (18). No great difficulty has been experienced in obtaining suitable rabbit agglutination sera, and in one experiment in which 6 rabbits and 6 chickens were immunized with Type IIα, 2 rabbits and 1 chicken died during immunization and perfectly satisfactory sera were obtained from all the other animals, with the titers of the rabbit sera averaging about twice those of the chickens (1:400 as against 1:200). The Type IIα, however, is known to be a fairly effective antigen and possibly the comparison on the basis of this type alone would not hold with other strains.

Reliability of the Method. Schoenbach and Phair (19) have examined in detail a number of variables inherent in the technique of surveys aimed to depict the prevalence of the organism in a population. For example, when two adequate media, or prompt or delayed inoculation of plates with swabs kept in defibrinated horse blood were compared, the results were not adversely affected. When different criteria for identification of meningococci were compared on the same individuals cultured repeatedly, the prevalence rates at each diagnostic threshold were relatively constant. Of the diagnostic criteria studied, colonial appearance, fermentation, agglutination with polyvalent serum and with type specific sera seemed to be the method of choice, but, as will appear later, the prevalence of carriers of organisms agglutinating only with polyvalent serum appears to be not an unimportant component of the meningococcus carrier rate.

The technique employed in this work, consisting of the fishing of no more than 1 or 2 colonies from each plate and the carrying through the agglutination of only a single culture, does not provide information on the frequency with which mixed infection occurs. Since it has long been known that in the case of other organisms, such as hemolytic streptococci and pneumococci, more than one type may be present in the throat of the same individual, there would appear to be no reason to doubt that the same thing may occur with the meningococcus. To examine each culture exhaustively in this regard would be an extremely cumbersome matter and for most purposes, at least in this study, would appear to be an added refinement. For example, if, in any particular group of men, a relatively small percent were harboring one type of meningococcus and a relatively small

percent were harboring a second type, it would be expected that an insignificantly small proportion would by chance harbor both types of organisms. In a comparatively small group of carriers, we have been able to show the coexistence of two or more types of meningococcus in certain individuals. The same finding has recently been reported somewhat more extensively by Phair. On the other hand, there are certain observations which would suggest that the type or types of meningococci carried by a given individual are not entirely chance, dependent upon the frequency of different types in the group and the rate of "turnover" in carriers in a group, but tend to be one type—at least for significant periods of time. As many as 10 colonies typed from the same swab have all turned out to be the same. And again, in a group of carriers followed for 16 days, by daily swabbing and then by biweekly swabbing for 4 weeks (medical students), the same individual was found to harbor the same type of meningococci with remarkable constancy. Repeated cultures on the same individuals at weekly intervals over a period of months showed more frequent changes in type which, however, were within range of the carrier rates for different types at the time and the rate of turnover in carriers. To what extent multiple carriage (or "cross infection" as between the several types) may occur on the one hand, or to what extent the carriage of one type may in the "interference" sense prevent "cross infection" with other types is not known. A third theoretical possibility suggested by certain changes in type composition in meningococcus carriage, to be discussed later, is that factors in the individual harboring the organism may determine the transition in types of meningococci.

Since, as it turns out, the chief interest throughout this study is the carrier rate for the different types of meningococci in the group and not the carrier status of the individual, we do not feel that the existence of a certain number of multiple carriers, or the existence of the reverse situation (where harborage of one type is antagonistic to harborage of another type) vitiates the overall percentages of carriers of the various types which form the basis of the epidemiologic inferences which are set forth.

In any event, correlations between the trends in carrier rates for Type I meningococci, as found in this study, and the occurrence of meningitis to be referred to later afford evidence that the procedure employed revealed a carrier status which actually existed.

DISTRIBUTION OF MENINGITIS AND OTHER DISEASES

It is felt that some consideration of certain marked differences between the patterns of distribution of meningitis and certain other "crowd" diseases will be helpful in the interpretation of the probably broader significance of the results of this local carrier study, as well as the relation of the carrier rate to the features of the distribution of meningitis which will be considered. One reason is that the prevailing conception of meningitis, particularly in respect to higher attack rates in recruits, has been based to a considerable extent not so much upon direct evidence as upon analogy with the behavior of such immunizing infections as measles and mumps under circumstances of mobilization. The principle which

has been applied as the explanation for high attack rates in recruits is to the effect that mobilization or "urbanization" brings together a population group containing a higher proportion of non-immunes from rural sections, with a resulting increase in the rate of spread of the infectious agent.

Measles, chickenpox, scarlet fever, mumps, diphtheria and poliomyelitis in a given locality show a tendency to periodicity, but in large areas like the registration area of the United States no trends in the direction of cycles or periodicity can be discerned. In general, the more or less uniform incidence from year to year in the United States as a whole tends to be made up of a preponderant incidence in certain sections of the country each year which have not recently been affected, and a correspondingly diminished incidence in other sections. Broadly speaking, this pattern of varying geographic prevalence is probably the result of the operation of the epidemiologic principle of exhaustion of susceptibles by immunization, either clinical or subclinical. In contrast to the widespread immunizing infections, the incidence of typhoid fever shows no tendency toward geographic movement or periodicity. The areas of prevalence have remained the same from year to year. These areas have doubtless been determined initially by environmental conditions favoring transmission, and have been maintained in more recent years to a large extent by the persistence of chronic carriers resident in these areas. There has been a consistent downward trend throughout the country during the period of modern sanitation. The overall continuous diminution in incidence can be attributed to diminution in the number of chronic carriers, through natural causes, and to modern sanitary conditions which is steadily diminishing the recruitment of new carriers.

Meningococcal meningitis follows a pattern that is indicative of neither the immunization of population groups or areas during years of prevalence, as in the immunizing infections of childhood, nor of any overall restriction of epidemic areas by persistence of chronic carriage, as in typhoid. In general, the distribution of meningitis is relatively uniform throughout the country, both in years of lower and in years of higher prevalence. Reported cases for the whole of the registration area over a period of years (1915–1948) plot into an undulating curve made up of a series of waves of increases and decreases, each extending over periods of from six to eleven years. The peaks of occurrence have been reached in 1918, 1929, 1936 and 1943. Because of less systematic reporting, it would not be worthwhile to attempt to trace this periodic behavior of meningitis back to earlier years. However, the 3,429 deaths in greater New York in the winter of 1904–05 (20) and reports of epidemics in other parts of the country at about that time indicate a fifth wave, doubtless similar to those which have been more closely recorded in later years. Hirsch, in reviewing the occurrence of meningitis in the early part of the 19th century, called attention to what seemed to be a more or less periodic recrudescence of the disease at intervals of about ten years.

That this periodicity in meningitis represents a continuing phenomenon and is not made up of independent seasonal epidemics in larger or smaller areas in successive years is at first suggested by the regularity of the undulating periodic curve, with the incidence in the whole of the registration area in any one year

always in direct relation to that for the year before and the year after. That the epidemic of meningitis is not primarily a seasonal phenomenon is perhaps even more strikingly suggested by the same periodicity in incidence both for the epidemic season and for the interepidemic summer months of the year. Finally, the periodicity in meningitis is of a distinctly different character from that seen in the immunizing infections of childhood, where with an epidemic in one year the "exhaustion of susceptibles" reaches a point which will usually be followed immediately by a period of low incidence pending the recruitment of a proportion of non-immunes in the population sufficient to again make possible an epidemic.

That periodicity in meningitis is caused by some general rather than by local circumstances is borne out by a study by Gover and Jackson (21), in which separate compilations for each of nine areas of the United States and in part for individual states all showed a closely corresponding periodicity. Peak years, as well as the length of the periods and severity of epidemics, were essentially the same in all areas.

In table 1 and chart 1, are shown the annual incidence in the registration area of the United States of a number of the infectious diseases, as reported in Public Health Reports during the period 1915–1947. In diphtheria and typhoid, the steady and marked downward trends in the last 25 years are not only so great as compared with other diseases of the group, but are so nearly identical that one almost must guard against a too hasty conclusion that they are of the same epidemiologic pattern and that the declines are the result of the same cause. But of course, the different reasons for these two public health successes are well known.

In the other diseases of the group, the slight upward trends probably represent only improved reporting. This is clearly the case in poliomyelitis. Before 1927 or 1928, reporting was largely restricted to paralytic cases, but with the impetus given to "preparalytic" diagnosis at that time, there are indications that early diagnosis has uncovered the occurrence of nonparalytic poliomyelitis formerly missed but now comprising upwards of one-half of all cases reported (22). It is noteworthy that there has not been a corresponding increase in deaths from poliomyelitis in the same period (23).

The curve for meningitis is the only one which presents a distinct periodicity. The only other curve which is at all suggestive is that of mumps, where there are two slight undulations which incidentally pretty much coincide in time with those of meningitis; however, it is doubtful whether any importance should be attached to them. The geographic distribution of mumps throughout the period has not been examined, but it would seem likely that the slight undulations in the mumps curve could easily be the result of chance occurrence at one or another period of more or few areas of prevalence in the same years. It is known that the geographic movement of mumps from year to year is of the same general order of the movement of the other immunizing infections (24).

At an earlier period, it was natural to assume that the distribution of disease was always a direct reflection of the dissemination of its infectious agent and that variations in disease, as for example, seasonal fluctuation, were always

due to corresponding variations in the dissemination of the infectious agent. It is now known through epidemiologic, immunologic and bacteriologic studies that the patterns of distribution of many infectious agents may greatly exceed or greatly differ from those of the clinically recognizable diseases which they cause.

TABLE 1

Morbidity—certain notifiable diseases

United States Registration Area, 1915–1947 (from Public Health Reports)

YEAR	MEASLES	SCARLET FEVER	MUMPS	CHICKEN POX	DIPHTHERIA	TYPHOID AND PARA-TYPHOID	POLIOMY-ELITIS	MENINGO-COCCUS MENINGITIS
1915	144,116	61,966	—	—	76,477	43,022	1,636	1,306
1916	417,445	76,795	—	—	86,864	53,623	27,363	1,576
1917	527,394	119,937	—	—	114,822	53,417	4,214	4,946
1918	428,018	85,193	—	—	91,631	44,248	2,514	6,253
1919	180,264	105,358	—	—	128,076	37,263	1,898	2,603
1920	465,048	157,547	—	—	80,914	36,129	2,293	2,630
1921	282,074	189,856	—	—	204,133	45,673	6,253	2,165
1922	265,905	158,975	46,253	131,018	166,038	34,400	2,232	1,634
1923	755,506	175,540	52,267	153,195	147,599	34,617	3,245	1,916
1924	511,305	184,738	125,354	202,081	119,831	34,825	5,271	1,417
1925	225,027	184,521	113,755	170,500	95,109	48,990	5,926	1,573
1926	677,395	192,625	75,596	186,822	93,425	41,377	2,520	1,964
1927	441,349	208,893	122,474	217,316	106,191	34,411	10,151	2,996
1928	561,721	174,692	137,671	205,858	91,156	26,951	5,069	5,477
1929	366,056	182,634	103,269	216,635	85,365	23,289	2,837	10,551
1930	419,465	175,221	124,259	228,354	66,576	27,201	9,188	8,384
1931	474,549	200,607	129,012	232,328	70,671	26,459	15,925	5,426
1932	403,294	210,014	106,748	227,200	59,784	26,618	3,811	3,102
1933	400,894	212,395	91,467	253,532	50,462	23,349	5,072	2,913
1934	799,455	220,050	104,789	258,306	43,156	22,217	7,517	2,500
1935	743,856	260,962	141,134	273,863	39,266	18,355	10,839	5,736
1936	299,493	244,332	207,013	226,120	30,018	15,898	4,523	7,320
1937	321,510	228,887	153,380	281,107	28,536	16,033	9,511	5,484
1938	822,811	189,631	152,749	286,848	30,508	14,903	1,705	2,919
1939	403,317	162,897	131,826	258,746	24,053	13,069	7,343	1,993
1940	291,162	155,464	118,374	280,300	15,536	9,809	9,826	1,665
1941	894,134	128,928	199,609	299,580	17,987	8,601	9,086	2,032
1942	547,393	128,194	287,150	303,107	16,260	6,678	4,033	3,826
1943	633,627	142,622	203,046	304,203	14,811	5,540	12,449	18,221
1944	630,291	191,220	177,526	319,902	14,122	5,529	19,029	16,315
1945	146,002	175,398	198,026	286,507	18,669	4,860	13,619	8,190
1946	695,843	116,042	161,735	229,863	16,354	3,993	25,698	5,693
1947	221,115	84,379	155,852	317,565	12,405	4,068	10,734	3,399

One of the greatest discrepancies to be found between parasite prevalence and disease prevalence is that which is seen in meningitis. Here, the carrier rate may comprise even the majority of a population group, and at the same time the clinical disease may still be comparatively rare. Indeed, this high degree of dissociation between microbe and its disease was formulated by the studies in

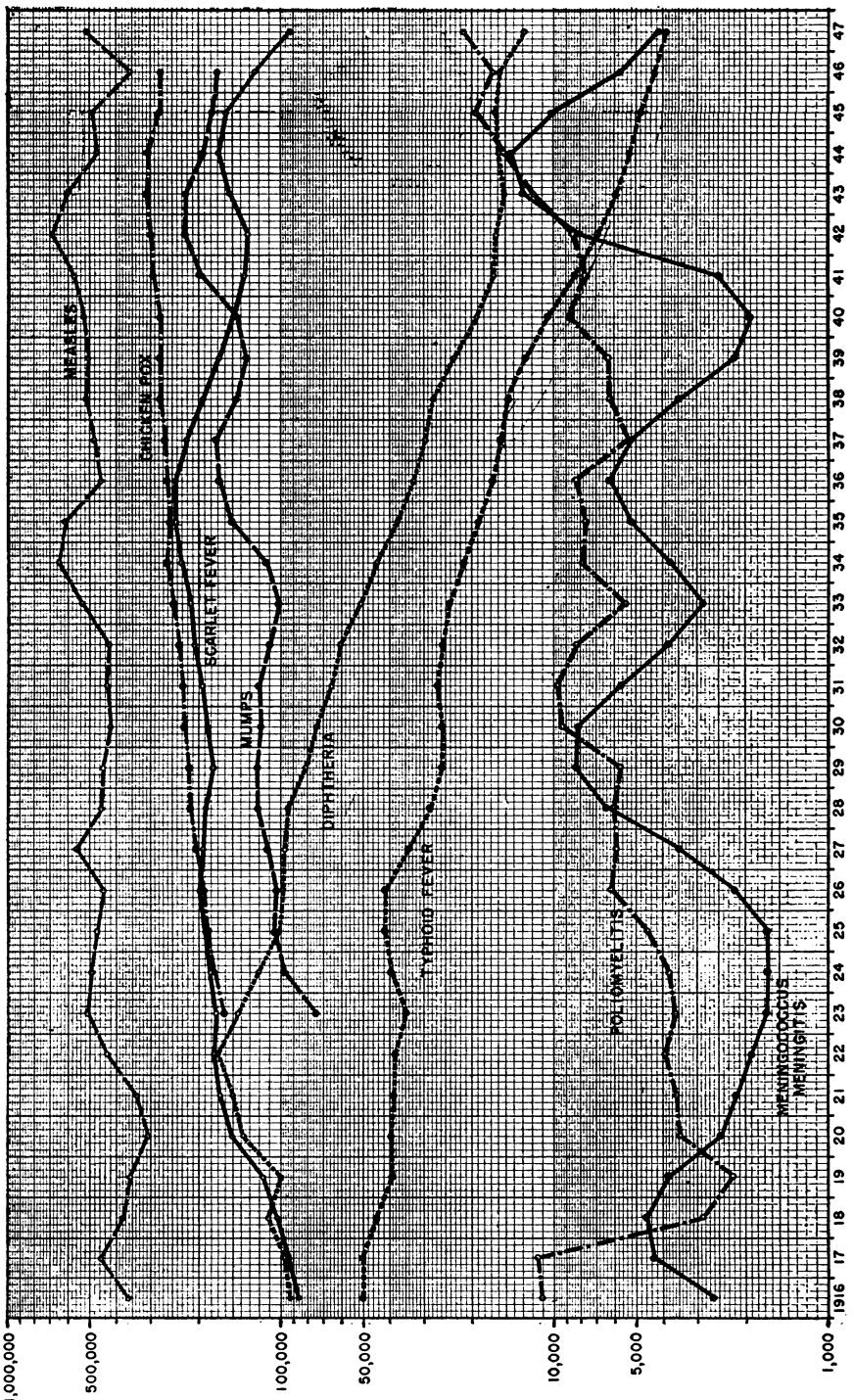

CHART 1. Morbidity: Certain Notifiable Diseases. United States Registration Area, 1915–1947. 3-way moving averages are plotted to smooth the curves so that they will show trends over periods of years rather than variations from year to year.

World War I into the doctrine that the carrier rate constituted a warning of impending disease only when it had gained a foothold on as many as a fifth of a population.

Nonetheless, the older generalization that parasite and disease must go hand in hand still seems to have been in large part responsible for many of the epidemiologic conceptions in meningitis, where the winter occurrence of the disease was attributed to a winter rise in the prevalence of meningococci which, in turn, had resulted from increased chances of transmission through crowding, poor ventilation, and so forth. That seasonal fluctuation of meningitis is not a manifestation of the major determinant in the epidemiology of meningitis is well shown when the reported occurrence of the disease in the registration area is plotted by months. It has been shown that meningitis occurs in distinct epidemic periods, extending over a period of years, and that all parts of the country participate in this "cyclic" occurrence of the disease. That season itself is responsible for only a secondary fluctuation which is superimposed upon the longer cyclic fluctuation is strikingly apparent (table 2, chart 2), when it is seen that the incidence of the disease at any given season throughout the period and, notably, the incidence in the season of lowest incidence is subject to the same longer cyclic fluctuation. That the closer aggregation of people resulting in increased transmission of the organism in winter may have been assigned too large a role as a basic requirement for the occurrence of meningitis is at once suggested when it is seen that the incidence of the disease in the lowest month of the year during periods of higher prevalence frequently greatly exceeds that for the months of highest incidence in those intervening periods of low prevalence. It seems clear that the more basic factor in meningitis epidemicity follows the longer cycle and that the factor responsible for seasonal fluctuation is secondary.

It is not improbable that the failure in the past to recognize this distinction between the "true epidemic curve" (extending over a period of years) and the superimposed but secondary seasonal fluctuation has been responsible for certain erroneous hypotheses in the epidemiology of meningitis, particularly with reference to the spread of the organism as the determinant of incidence of the disease. Attention has doubtless been restricted too largely to studies of the more immediately presenting "seasonal rise" in meningitis in the search for the epidemiologic determinant, rather than to what is in reality the "epidemic" extending over a period of several years.

From this analysis of the geographic, chronologic and seasonal distribution of meningitis, it may be anticipated that no single cause for both the epidemic cycle and the seasonal cycle will be found. If, for example, the epidemic cycle can be associated with prevalence of the meningococcus, it is expected that the reason for seasonal fluctuation might have to be sought either in some seasonal variation in the infective *quality* of the meningococcus or in some seasonal variation in susceptibility of the host.

As already stated, the original purpose of the study was to follow the general trends of meningoccoccus carriage in the two military establishments, as they might afford indications of impending disease occurrence or point to more

effective control measures. To this end, the method of sampling decided upon was to take nasopharyngeal swabs twice a week from 100 men of all those coming to the infirmaries of each of two establishments. This method was chosen for two

TABLE 2

Meningococcal meningitis, seasonal variation in incidence

United States Registration Area, 1915–1948

YEAR	CASES												
	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Total
1915–16	85	80	58	95	115	126	157	166	152	160	149	142	1485
1916–17	94	108	101	106	190	294	632	831	733	559	344	229	4221
1917–18	202	205	242	485	897	983	1016	844	616	337	312	286	6425
1918–19	229	269	210	254	254	288	313	270	244	166	200	160	2857
1919–20	149	186	173	200	302	270	282	250	247	195	173	176	2603
1920–21	187	163	187	198	199	235	243	179	160	152	180	201	2284
1921–22	158	153	152	153	163	190	179	158	148	118	94	132	1798
1922–23	112	97	127	116	160	158	241	175	175	154	138	142	1795
1923–24	114	145	182	132	151	119	140	154	123	114	110	104	1588
1924–25	114	109	101	78	163	123	190	158	133	109	106	119	1503
1925–26	126	97	81	168	170	212	251	198	182	151	146	110	1892
1926–27	124	120	132	168	282	261	318	328	268	259	205	199	2664
1927–28	197	206	208	265	370	379	627	583	635	465	325	392	4652
1928–29	340	355	367	641	1079	1082	1434	1366	1286	862	620	497	9929
1929–30	446	499	572	808	1110	1181	1319	1209	765	476	375	427	9187
1930–31	325	353	388	456	697	672	754	719	533	359	259	311	5826
1931–32	255	255	283	329	367	334	389	354	258	197	168	190	3379
1932–33	159	170	221	295	392	318	430	323	251	175	163	176	3073
1933–34	127	121	178	239	222	232	301	251	235	216	137	158	2417
1934–35	143	153	138	241	362	562	740	722	725	549	362	314	5011
1935–36	242	296	348	511	773	931	1228	1116	772	435	344	259	7255
1936–37	249	285	385	475	681	679	874	712	530	329	322	263	5784
1937–38	206	262	283	341	403	384	366	312	250	216	160	162	3345
1938–39	140	170	146	210	234	227	229	192	171	129	127	100	2075
1939–40	116	138	146	140	151	189	190	161	152	117	114	121	1735
1940–41	109	108	113	140	214	177	202	266	169	150	149	108	1905
1941–42	133	133	145	189	230	273	339	486	337	319	275	212	3071
1942–43	217	240	285	573	1267	1677	2867	2385	2052	1754	971	712	15000
1943–44	829	853	876	1663	2274	2214	2699	1905	1794	959	770	761	17597
1944–45	472	619	815	761	1172	1082	968	777	866	542	462	448	8984
1945–46	350	424	397	498	1120	724	703	526	531	357	365	237	6232
1946–47	231	331	250	248	415	340	355	479	282	229	269	176	3605
1947–48	164	250	207	283	332	354	433	267	278	251	205	194	3218
Total Cases.....	7144	7953	8497	11459	16911	17270	21409	18822	16053	11560	9099	8218	154395

reasons; it insured a cross section of the camps, and it was thought that any impending epidemic might be detected in its incipiency. In addition to this procedure which was the routine throughout the study for the determination of

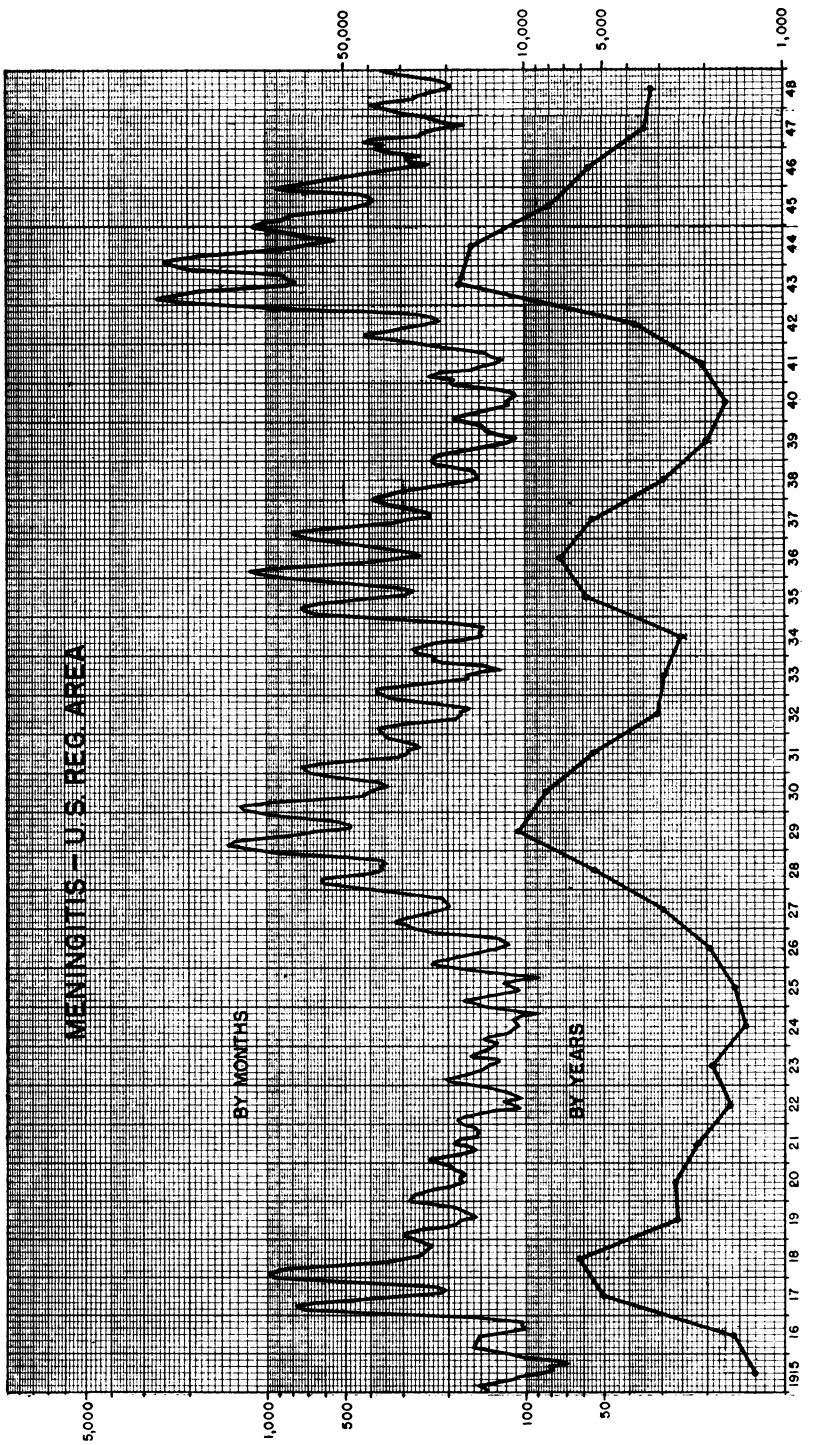

CHART 2. Meningitis. United States Registration Area, 1915–1948. Plotted by years to show cyclic variation, and by months to show secondary seasonal fluctuations. 2-way moving averages are used in plotting the distribution by months.

the trends in carrier rates, many special groups were cultured from time to time for special or comparative purposes. That the carrier rates as ascertained for the camps as a whole were the significant ones in relation to the epidemiology of meningitis is indicated by the close similarity in carrier rates in the special groups such as recruits and seasoned troops, in outfits or barracks with high case rates as compared with those with low case rates, and in civilian as compared with the military population.

In table 3, the results of a carrier study extending over a period of six months in inductees as compared with the carrier rates prevailing in the two military establishments are shown. The cultures on inductees were taken on the day of their arrival at the Reception Center at Fort Devens, in the main from all parts of New England, New York State and Pennsylvania. The carrier rates in inductees is therefore considered as probably representative of the rates prevailing in the

TABLE 3

Meningococcus carrier rates in seasoned troops and recruits*

Camp Edwards and Fort Devens Combined; and Reception Center, Fort Devens

	TOTAL		TYPE I		TYPE II		TYPE IIα		TYPE X	
	Edw. and Dev.	Recep. Center	Edw. and Dev.	Recep. Center	Edw. and Dev.	Recep. Center	Edw. and Dev.	Recep. Center	Edw. and Dev.	Recep. Center
Jan. 1944	29.2	30.0	15.2	15.5	6.1	6.9	7.7	7.2	0.2	0.3
Feb. 1944	29.8	27.0	13.7	13.9	9.4	9.8	6.6	2.8	0.1	0.5
Mar. 1944	26.3	32.0	12.0	11.8	6.7	10.7	6.5	7.5	1.2	2.0
Apr. 1944	25.2	31.6	9.1	11.3	7.7	8.6	8.1	11.3	0.4	0.3
May 1944	24.1	33.4	10.6	13.6	5.9	8.1	7.2	10.1	0.3	1.6
June 1944	25.8	38.3	7.9	16.6	10.2	12.4	6.4	7.8	1.3	1.5

* Per 100.

civilian population of this section of the country. As in the two military establishments, cultures were taken on samples of 100 men twice a week. There was considerable variation in the results (as in the establishments themselves) in the carrier rates found in the individual groups of 100 men, but no greater than those observed in the establishments. In the table, the carrier rates shown for both are based on the total cultures taken within the month. Not only were the total carrier rates essentially the same for the two groups throughout the six months of this study, but the type composition of carriage was likewise essentially identical in the two groups. It may be noted further that there is no suggestion of seasonal variation in carriage (within the period covered) as there is in meningitis, both in the military and in the civilian population.

In table 4 are shown the results of carrier tests which were done at intervals on a much smaller civilian group in Boston (Harvard Medical School students). On three occasions, cultures on 100 students were done. The results are shown with carrier rates which prevailed in the military establishments at the same time. In October, 1943 both the carrier rate and the type composition of carriage were

essentially the same in the two groups. In February, 1944, the carrier rate (a single sampling) on medical students revealed a carrier rate which was only about half that for the same month in the military establishments, but the type composition of carriage was not significantly different. In 1945, the carrier rate in the medical students was about twice that of the military establishment with, however, essentially the same type composition.

A carrier test done on medical students in December, 1946, (over a year after the study in military establishments had terminated) again showed a high carrier rate, but with a significant shift in type composition from that which had been found during the epidemic period covered by the main part of the study both in the military and in civilians. Type I had practically disappeared and Type X had returned to a rate of 8.3% out of a total rate of 26.7%. Thus, the type composition of carriers was again much the same as it had been at the beginning of the carrier study and in the incipiency of the epidemic period. During the entire period

TABLE 4

*Meningococcus carrier rates**

Fort Devens and Camp Edwards Combined, and Harvard Medical School Students

	TOTAL		TYPE I		TYPE II		TYPE IIα		TYPE X	
	Edw. and Dev.	HMS	Edw. and Dev.	HMS	Edw. and Dev.	HMS	Edw. and Dev.	HMS	Edw. and Dev.	HMS
Oct. 1943	23.7	25.4	11.8	13.6	8.2	7.3	2.8	0	0.9	4.5
Feb. 1944	29.8	15.2	13.7	5.1	9.4	.8	6.6	3.4	0.1	5.9
Jan. 1945	10.0	25.2	4.7	10.1	3.5	7.6	1.5	5.9	.4	1.7
Dec. 1946	—	26.7	—	0.7	—	16.2	—	1.5	—	8.3

* Per 100.

covered by the study, no case of meningitis had occurred in this civilian group.

In table 5 are shown carrier rates in a number of battalions, as well as in batteries or barracks of these battalions, in which cases were occurring at the time they were cultured. In general, the carrier rates in these units were not greatly different from the carrier rates for the camp in general as shown by the routine survey, regardless of whether the unit had a low or high case rate. As a matter of fact, cultures taken in August, 1943, on all the men in one barrack in which 6 of the 10 cases for the whole battalion occurred showed a carrier rate (total 44.4%, Type I 27.3%) the same as that obtained only a week later in a battalion housed on the opposite side of the camp, and in which no cases occurred (total 41.3%, Type I 27.3%).

Only one instance was encountered where there was a difference in carrier rates which was accompanied by a corresponding difference in meningitis attack rates. As shown in the section to follow on the carrier rate, both the trends in carrier rates and the shifts in type composition in the two establishments were so nearly identical that there could be little doubt that the factors determining carriage were not local but were of a more general nature. The single exception

was what is described as an independent increase in Type I carriers in Camp Edwards in the winter and spring of 1942–43 which was accompanied by correspondingly increased attack rates in meningitis at Camp Edwards at that time. Both from the method of sampling employed (individuals from all parts of the Camp) and from the failure to find higher carrier rates in units within the Camp

TABLE 5

Meningococcus carriers in battalions with higher and lower case rates

DATE	BATTERY	NO. CASES	TOTAL CULT.	POSITIVE CULT.		TYPE I		TYPE II		TYPE IIα		TYPE X	
				No.	%	No.	%	No.	%	No.	%	No.	%
	359th C.A.S.L. Bn.	10											
8/23/43	C—Barrack 2530	6	95	42	44.4	30	27.3						
8/23/43	C	7	233	108	46.3	68	29.2	12	5.1	25	10.7	3	1.3
4/ 1/43	A, B, C & Hdq.	9	259	91	35.1	38	14.7	23	8.9	20	7.7	10	3.9
4/ 5/43	A, B, C	8	179	80	44.7	39	21.8	10	5.6	24	13.4	7	3.9
	386th C.A.(A.A.) Bn.	7											
3/18/43	Hdq.	0	181	107	59.1	77	42.5						
3/15/43	386 C.A.(A.A.) Bn. & 738 C.A.(A.A.) Bn.	10	295	190	64.3	155	52.5						
	551st C.A.(A.A.) Bn.	5											
3/31/43	A, B, C & Hdq.	5	264	162	61.4	110	41.7	7	2.7	32	12.1	13	4.9
	387th C.A.(A.A.)	4											
3/ 8/43			290	93	32.1	64	22.0						
4/ 8/43	B & Hdq.	3	215	110	51.2	75	34.9	9	4.2	21	9.8	5	2.3
3/22/43	A, B, C	1	298	88	29.5	40	13.4						
	738th C.A.(A.A.)	3											
3/ 1/43	B, D	1	220	128	58.2	73	33.2						
3/ 4/43	B, D	1	296	97	32.7	74	25.0						
	550th C.A.(A.A.)	2											
3/24/43			142	57	40.1	27	19.0	11	7.7	14	9.9	5	3.5
3/25/43	A, B, C, D	2	253	159	62.8	122	48.2	8	3.2	14	5.5	15	5.9
3/29/43	A, B, C, D & Hdq.	2	225	149	66.2	109	48.4	7	3.1	13	5.8	20	8.9
	231st A.A.S.L.												
8/30/43		0	242	100	41.3	66	27.3	11	4.5	23	9.5	0	0

with higher attack rates, it seemed evident that the Type I carrier rate was only the broad base upon which meningitis occurred but not the factor which determines the highly selective location of cases in a population with a given carrier rate, as, for example, in recruits as compared with seasoned troops or in one barrack or outfit and not in another.

It was for these reasons that no further attempts were made to establish local

TABLE 6

Meningococcus carrier rates

Fort Devens and Camp Edwards combined

DATE	TOTAL CULT.	TYPE I		TYPE II		TYPE IIα		TYPE X		ALL TYPES	
		No.	%	No.	%	No.	%	No.	%	No.	%
12/41	684	11	1.61	3	0.44	3	0.44	62	9.06	79	11.55
1/42	1413	46	3.26	14	0.99	9	0.64	207	14.65	276	19.53
2/42	1372	34	2.48	52	3.79	21	1.53	177	12.90	284	20.70
3/42	1445	52	3.60	71	4.91	55	3.81	222	15.37	400	27.40
4/42	1457	62	4.26	83	5.70	58	3.98	219	15.03	422	28.96
5/42	1434	44	3.07	74	5.16	51	3.56	144	10.04	313	21.83
6/42	1348	53	3.93	94	6.97	65	4.82	110	8.16	322	23.89
7/42	1387	90	6.49	134	9.66	79	5.70	132	9.52	435	31.36
8/42	1307	51	3.90	98	7.50	55	4.21	68	5.20	272	20.81
9/42	1242	34	2.74	152	12.24	39	3.14	53	4.27	278	22.38
10/42	1281	35	2.73	170	13.27	72	5.62	121	9.45	398	31.07
11/42	1187	48	4.04	161	13.56	60	5.05	94	7.92	363	30.58
12/42	1243	110	8.85	196	15.77	55	4.42	55	4.42	416	33.47
1/43	1218	135	11.08	85	6.98	43	3.53	43	3.53	306	25.12
2/43	1269	193	15.21	74	5.83	42	3.31	83	6.54	392	30.89
3/43	1996	645	32.31	110	5.51	112	5.61	122	6.11	989	49.55
4/43	1844	254	13.77	107	5.80	153	8.30	60	3.25	574	31.13
5/43	1361	226	16.61	76	5.58	130	9.55	25	1.84	457	33.58
6/43	1452	255	17.56	79	5.44	121	8.33	12	0.83	467	32.16
7/43	1231	155	12.59	76	6.17	115	9.34	15	1.22	361	29.33
8/43	1051	121	11.51	46	4.38	86	8.18	2	0.19	255	24.26
9/43	862	164	19.03	70	8.12	45	5.22	1	0.12	280	32.48
10/43	757	89	11.76	62	8.19	21	2.77	7	0.92	179	23.65
11/43	1030	135	13.11	61	5.92	54	5.24	2	0.19	252	24.47
12/43	1025	144	14.05	93	9.07	48	4.68	0	0	285	27.80
1/44	1043	158	15.15	64	6.14	80	7.67	2	0.19	304	29.15
2/44	870	119	13.68	82	9.43	57	6.55	1	0.11	259	29.77
3/44	1044	125	11.97	70	6.70	68	6.51	12	1.15	275	26.34
4/44	1058	96	9.07	81	7.66	86	8.13	4	0.38	267	25.24
5/44	1175	125	10.64	69	5.87	85	7.23	4	0.34	283	24.08
6/44	993	78	7.86	101	10.17	64	6.45	13	1.31	256	25.78
7/44	1198	53	4.42	57	4.75	57	4.75	50	4.17	217	18.11
8/44	1776	92	5.18	83	4.67	64	3.61	45	2.53	284	15.99
9/44	1457	82	5.63	101	6.93	61	4.19	18	1.23	262	17.98
10/44	1464	38	2.60	115	7.85	43	2.84	1	0.07	197	13.46
11/44	1400	67	4.71	94	6.71	30	2.14	3	0.21	194	13.86
12/44	1300	58	4.46	26	2.00	36	2.77	2	0.15	122	9.38
1/45	1600	75	4.69	56	3.50	24	1.50	6	0.38	161	10.06
2/45	1100	37	3.36	44	4.00	19	1.73	1	0.09	101	9.18
3/45	1800	37	2.06	88	4.89	24	1.33	0	0	149	8.28
4/45	1300	9	.69	54	4.15	17	1.31	0	0	80	6.15
5/45	1600	19	1.19	39	2.44	23	1.43	0	0	81	5.06

carrier-case relationships and that the remainder of this study will deal with the carrier rate as it relates to certain of the more general features of the distribution of meningitis. First, the carrier rates for the different types of meningococci and

certain clearly marked changes or shifts in the type composition of carriage will be considered, and later, some consideration will be given to the relation of the carrier rate for Type I meningococcus to such general features of meningitis as its preponderance in the military and in recruits and its seasonal prevalence.

THE CARRIER RATE

From the beginning of the study in January, 1942, to April, 1943, there was an irregular but general increase in the total carrier rate from 15% to 40%, and from May, 1943, to May, 1945, a decrease to 6%. As indicated by a test survey in December, 1946, on a civilian population which had been found at several times during the study to have a carrier rate closely coinciding with that in the military

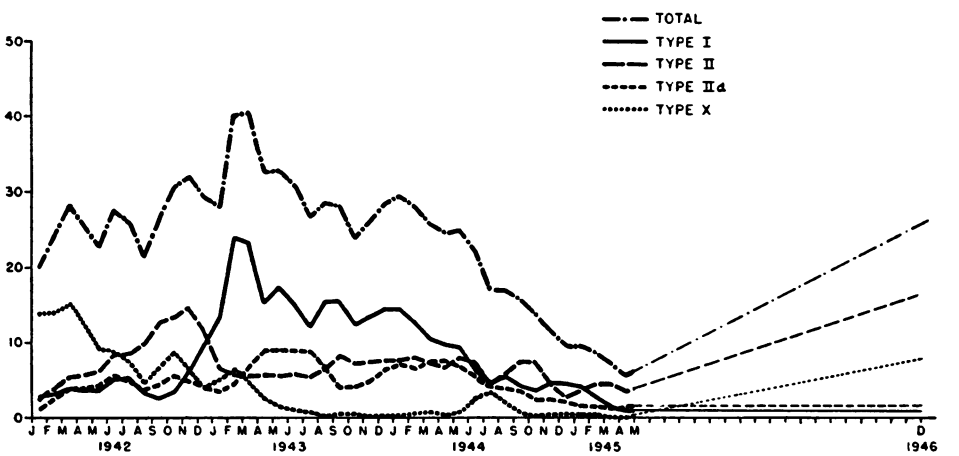

CHART 3. Meningococcus Carrier Rates. Fort Devens and Camp Edwards combined, 1942–1945. 2-way moving averages of the army carrier rates are plotted by months to May, 1945. These curves are joined arbitrarily by straight lines to corresponding points found in a single civilian carrier test in December, 1946 to indicate that the total carrier rates had again returned to the levels found in the beginning of the study, but with Type I remaining minimal.

establishments, the total meningococcus rate had again risen to 26%. The type composition of the carrier rate, however, showed marked differences at different periods in the study. Throughout 1942, the carrier rate involved predominantly Types II and X. During 1943 and the first half of 1944, Type I predominated, and during the last half of 1944 and the first five months of 1945, the four types were approximately equal and all diminishing. In December, 1946, the distribution of types in the civilian group was similar to that at the beginning of 1942 in the military establishments,—predominantly Types II and X.

Beyond the somewhat general observation that Type I is the "epidemic" and other types are the "carrier" or "endemic" strains, no special study of the type composition of meningococcus carriage over any considerable period of time seems to have been made previously. In table 6 and chart 3, the composite carrier rates for the two military establishments are shown. It can be seen from chart 3 that the rise in the total carrier rate in 1942 and 1943 is not a simple

matter of increase in the number of carriers of all types of meningococci, nor for that matter an absolute increase in carriers of any type. The carrier rate for one type may be increasing, while the rates for one or more of the other types are stationary or are actually declining. Indeed, it is seen that with an increase in the number of carriers of one type, and sometimes lasting over a considerable period of time, there may be a decrease in the number of carriers of another type, so closely corresponding in time and extent as to suggest some kind of interaction between the two types of meningococci. It can be seen that the first part of the increase in the number of Type I carriers is accompanied by a corresponding decrease in carriers of Type II and perhaps of Type X. However, the increase in the number of Type I carriers continued in such a manner through the spring of 1943 that it was clearly a wholly independent increase in the number of carriers of this one type. It will be shown later than this independent increase in Type I carriage took place in only one of the military establishments. In view of the many changes which have been made in the past in type classification of meningococci, a question might be raised whether such changes as the almost exact reversal in type composition might be "laboratory produced" through some change in procedure of typing. On the other hand, the frequency with which spontaneous transformation of a given culture from one type to another are observed under laboratory conditions suggests the possibility that type transformation may likewise occur in the course of natural dissemination of the organism. That the latter may be the case is suggested by a number of circumstances attending the occurrence of the phenomenon in this study.

A. The reversals in type composition are not abrupt as would be expected if they were the result of any change in the procedures used in type determination, but take place over considerable periods of time.

B. The Type I carrier rate which in a sense is largely the product of changes in type composition correlates with the occurrence of meningitis (due preponderantly to Type I) sufficiently well to indicate that the Type I carrier rate, as shown by the study, reflects a carrier rate of meningococci which actually existed.

C. Finally, certain differences in type composition and changes in type composition in the two military establishments as were found in the carrier studies done in the same laboratory, with no differences in procedure, is further reason for believing that the changes in type composition were not laboratory produced but were actually occurring.

The carrier rates for the different types in Fort Devens and Camp Edwards are given in tables 7 and 8 and shown in chart 4. It will be seen that, in general, the carrier rates for the different types tend to run parallel in the two camps and that the shifts in type composition which have already been referred to are of the same order in the two camps, with the exception of the independent increase in carriers of Type I meningococcus occurring in the early months of 1943 in Camp Edwards. At Fort Devens, the increase in Type I carriage at this time was accompanied by a corresponding decrease in the frequency of carriage of the other types, while in Camp Edwards only part of the increase in Type I was accompanied by a decrease in other types. That the type composition of

meningococcus carriage may be complex, made up in part of independent changes in the carrier rate for one type and in part of reciprocal interactions

TABLE 7

Meningococcus carrier rates, Fort Devens

DATE	TOTAL CULT.	TYPE I		TYPE II		TYPE IIα		TYPE X		ALL TYPES	
		No.	%	No.	%	No.	%	No.	%	No.	%
1/42	731	4	.5	8	1.1	3	.4	89	12.2	104	14.2
2/42	704	6	.9	19	2.7	10	1.4	78	11.1	113	16.1
3/42	762	9	1.2	34	4.5	21	2.8	120	15.7	184	24.1
4/42	693	25	3.6	32	4.6	17	2.5	101	14.6	175	25.3
5/42	752	13	1.7	36	4.8	20	2.7	95	12.6	164	21.8
6/42	726	19	2.6	52	7.2	29	4.0	64	8.8	164	22.6
7/42	720	36	5.0	63	8.8	41	5.7	65	9.0	205	28.5
8/42	631	23	3.6	37	5.9	29	4.6	32	5.1	121	19.2
9/42	739	17	2.3	91	12.3	26	3.5	33	4.5	167	22.6
10/42	753	19	2.5	93	12.4	41	5.4	54	7.2	207	27.5
11/42	592	20	3.4	67	11.3	27	4.6	37	6.2	151	25.5
12/42	575	31	5.4	79	13.7	13	2.3	29	5.0	152	26.4
1/43	802	75	9.4	57	7.1	23	2.9	24	3.0	179	22.3
2/43	701	68	9.7	42	6.0	9	1.3	44	6.3	163	23.3
3/43	809	103	12.7	63	7.8	39	4.8	48	5.9	253	31.3
4/43	887	108	12.2	42	4.7	62	7.0	23	2.6	235	26.5
5/43	686	93	13.6	45	6.6	50	7.3	8	1.2	196	28.6
6/43	751	96	12.8	35	4.7	55	7.3	3	0.4	189	25.2
7/43	731	69	9.4	43	5.9	69	9.4	8	1.1	189	25.8
8/43	751	77	10.3	23	3.1	51	6.8	2	0.3	153	20.4
9/43	662	122	18.4	57	8.6	36	5.4	0	0	215	32.5
10/43	657	78	11.9	55	8.4	20	3.0	5	0.8	158	24.0
11/43	630	76	12.1	41	6.5	30	4.8	1	0.2	148	23.5
12/43	625	95	15.2	69	11.0	27	4.3	0	0	191	30.6
1/44	443	77	17.4	27	6.1	28	6.3	1	0.2	133	30.0
2/44	370	52	14.1	32	8.6	28	7.6	1	0.3	113	30.6
3/44	344	36	10.5	25	7.3	22	6.4	2	0.6	85	24.7
4/44	358	46	12.8	27	7.5	28	7.8	0	0	101	28.2
5/44	375	34	9.1	25	6.7	32	8.5	0	0	91	24.3
6/44	293	40	13.7	32	10.9	21	7.2	3	1.0	96	32.8
7/44	498	21	4.2	26	5.2	33	6.6	25	5.0	105	21.1
8/44	876	66	7.5	32	3.7	40	4.6	28	3.2	166	19.0
9/44	757	53	7.0	68	9.0	40	5.3	9	1.2	170	22.5
10/44	764	23	3.0	69	9.0	21	2.7	0	0	113	14.8
11/44	600	25	4.2	26	4.3	12	2.0	0	0	63	10.5
12/44	700	30	4.3	14	2.0	21	3.0	1	0.1	66	9.4
1/45	900	35	3.9	25	2.8	10	1.1	4	0.4	74	8.2
2/45	600	17	2.8	12	2.0	10	1.7	1	0.2	40	6.7
3/45	900	4	0.4	34	3.8	4	0.4	0	0	42	4.7
4/45	600	3	0.5	18	3.0	7	1.2	0	0	28	4.7
5/45	800	6	0.8	13	1.6	7	0.9	0	0	26	3.3

between carriers of different types, is again indicated in chart 5. This chart is designed to examine further the possible mechanisms through which Type I

carriage increases, it being the significant type in respect to the immediate causation of meningitis. In chart 5, the Type I carrier rates for the two military

TABLE 8

Meningococcus carrier rates, Camp Edwards

DATE	TOTAL CULT.	TYPE I		TYPE II		TYPE IIα		TYPE X		ALL TYPES	
		No.	%	No.	%	No.	%	No.	%	No.	%
1/42	682	42	6.2	6	0.9	6	0.9	118	17.3	172	25.2
2/42	668	28	4.2	33	4.9	11	1.6	99	14.8	171	25.6
3/42	683	43	6.3	37	5.4	34	5.0	102	14.9	216	31.6
4/42	764	37	4.8	51	6.7	41	5.4	118	15.4	247	32.3
5/42	682	31	4.5	38	5.6	31	4.5	49	7.2	149	21.8
6/42	622	34	5.5	42	6.8	36	5.8	46	7.4	158	25.4
7/42	667	54	8.1	71	10.6	38	5.7	67	10.0	230	34.5
8/42	676	28	4.1	61	9.0	26	3.8	36	5.3	151	22.3
9/42	503	17	3.4	61	12.1	13	2.6	20	4.0	111	22.1
10.42	528	16	3.0	77	14.6	31	5.9	67	12.7	191	36.2
11/42	595	28	4.7	94	15.8	33	5.5	57	9.6	212	35.6
12/42	668	79	11.8	117	17.5	42	6.3	26	3.9	264	39.5
1/43	416	60	14.4	28	6.7	20	4.8	19	4.6	127	30.5
2/43	568	125	22.0	32	5.6	33	5.8	39	6.9	229	40.3
3/43	1187	542	45.7	47	4.0	73	6.1	74	6.2	736	62.0
4/43	957	146	15.3	65	6.8	91	9.5	37	3.9	339	35.4
5/43	675	133	19.7	31	4.6	80	11.9	17	2.5	261	38.7
6/43	701	159	22.7	44	6.3	66	9.4	9	1.3	278	39.7
7/43	500	86	17.2	33	6.6	46	9.2	7	1.4	172	34.4
8/43	300	44	14.7	23	7.7	35	11.7	0	0	102	34.0
9/43	200	42	21.0	13	6.5	9	4.5	1	0.5	65	32.5
10/43	100	11	11.0	7	7.0	1	1.0	2	2.0	21	21.0
11/43	400	59	14.8	20	5.0	24	6.0	1	0.2	104	36.0
12/43	400	49	12.2	24	6.0	21	5.3	0	0	94	23.5
1/44	600	81	13.5	37	6.2	52	8.7	1	0.2	171	28.5
2/44	500	67	13.4	50	10.0	29	5.8	0	0	146	29.2
3/44	700	89	12.7	45	6.4	46	6.6	10	1.4	190	27.1
4/44	700	50	7.1	54	7.7	58	8.3	4	0.6	166	23.7
5/44	800	91	11.4	44	5.5	53	6.6	4	0.5	192	24.0
6/44	700	38	5.4	69	9.9	43	6.1	10	1.4	160	22.8
7/44	700	32	4.6	31	4.4	24	3.4	25	3.6	112	16.0
8/44	900	26	2.9	51	5.7	24	2.7	17	1.9	118	13.1
9/44	700	29	4.1	33	4.7	21	3.0	9	1.3	92	13.1
10/44	700	15	2.1	46	6.6	22	3.1	1	0.1	84	12.0
11/44	800	42	5.2	68	8.5	18	2.3	3	0.4	131	16.4
12/44	600	28	4.7	12	2.0	15	2.5	1	0.2	56	9.3
1/45	700	40	5.7	31	4.4	14	2.0	2	0.3	87	12.4
2/45	500	20	4.0	32	6.4	9	1.8	0	0	61	12.2
3/45	900	33	3.7	54	6.0	20	2.2	0	0	107	11.9
4/45	700	6	0.9	36	5.1	10	1.4	0	0	52	7.4
5/45	800	13	1.6	26	3.3	16	2.0	0	0	55	6.9

establishments are shown, together with the carrier rates for all other types combined. It can be seen that at Fort Devens the increase in Type I carriage in

1943 is accompanied by a closely corresponding decrease in carriage of other types. At Camp Edwards, the increase in Type I carriage of 1943 can only in

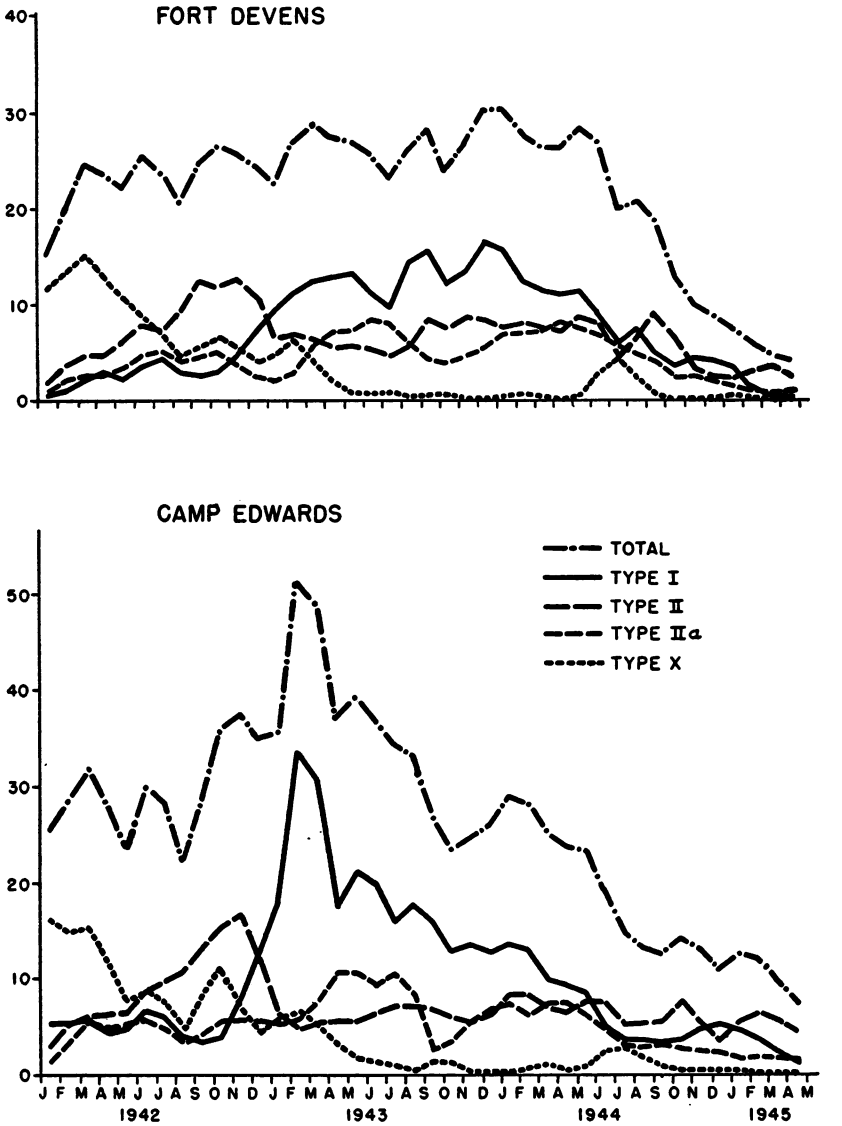

CHART 4. Meningococcus Carrier Rates. Fort Devens and Camp Edwards, 1942–1945. Illustrating a similar carrier phenomenon in the two military establishments with the exception of excessive increase in Type I carriage in the early months of 1943 at Camp Edwards.

part be accounted for by a corresponding decrease in other types, and evidently is in part due to an absolute increase in Type I carriage.

From this analysis of the type composition of meningococcus carriage, it would

appear that the carrier rate of Type I meningococcus does not represent the simple introduction and spread of this "pathogen", with consequent occurrence of this disease, in a population already with a high carrier rate of other types

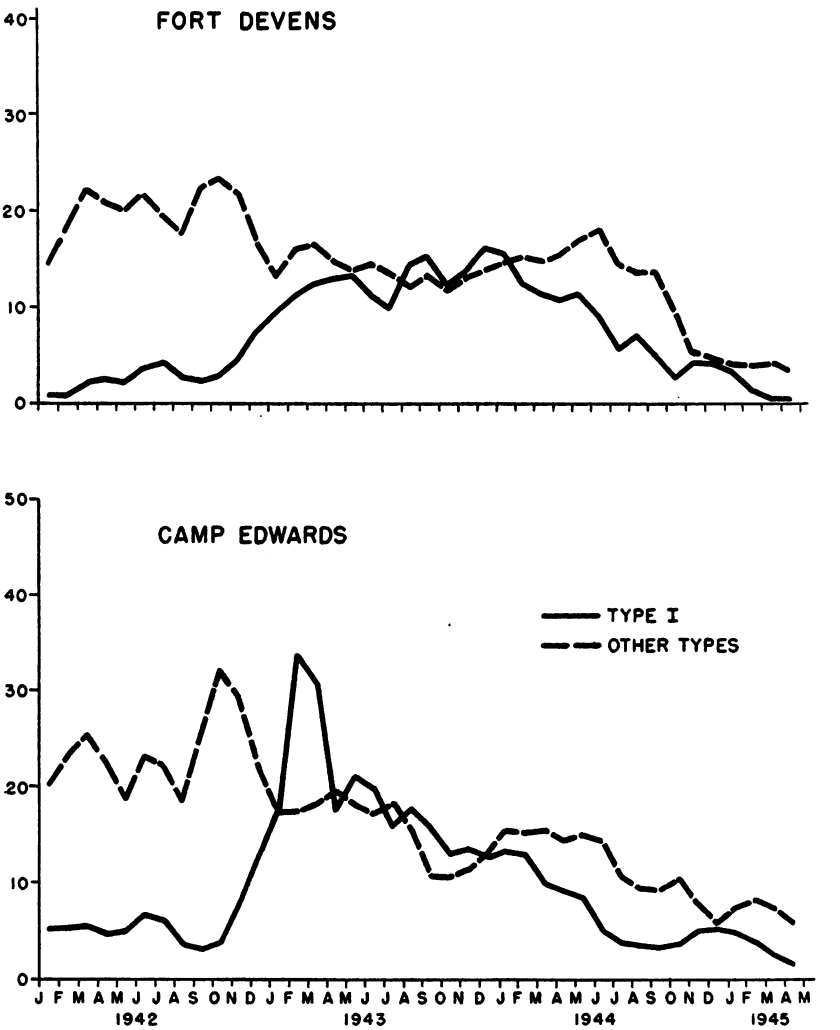

CHART 5. Meningococcus Carrier Rates. Fort Devens and Camp Edwards, 1942–1945. Type I carriers and Types II, IIα and X combined are plotted to show that the major increase in Type I carriers was accompanied by a corresponding decrease in the carrier rate for other types. The independent increase in Type I carriers in 1943 at Camp Edwards is also shown.

of the organism. The finding that an increase in Type I carriers, or of any type for that matter, is accompanied by a corresponding decrease in carriers of other types suggests that the carrier rate for the pathogen is more largely of "internal" origin, the result of some interaction of types in the course of their dissemination.

The mechanism through which such a type transformation could take place is not known, but the persistence with which a given individual is found to carry a single type over a considerable period of time when, according to the carrier rates for other types in the group, there were equal chances of exposure to other types suggests that the factor which determines the type which an individual carries may reside in conditions which occur in general in the human host.

Relation of the Carrier Rate to Meningitis

The failure to find differences in carrier rates in different categories of troops in the same camps to which could be attributed variation in meningitis attack rates, and the finding of essentially the same carrier phenomenon in two military establishments, in civilians in the same state and in inductees coming from a much wider area, are all considered as reasons for believing that meningococcus carrier rates as shown by the present study doubtless were a close reflection of carrier rates which were prevailing throughout the country during the same period. This belief is supported by the fact that the prevalence of meningitis in the area where the study was made was a close parallel of meningitis as it was occurring throughout the country. For these reasons, it is felt that a consideration of certain general features of the occurrence of meningitis in relation to the carrier rates in this study is justifiable.

The reasons for thus broadening the base of comparison between the trends in carrier rates and in meningitis may be summarized as follows:

1. The restriction of comparison to cases which occurred within the establishments where the carrier studies were done would, because of the relatively small number of cases with fluctuations in incidence which were either too momentary for close analysis, or not of statistical significance, render difficult any meaningful conclusions.

2. As shown in the section on distribution of meningitis and other disease, the trends in meningitis over the period were taking place with such uniformity in all parts of the country that the same underlying cause must have been prevailing throughout the country.

3. That the base upon which meningitis was occurring was the Type I meningococcus carrier rate is indicated both by the fact that this was the organism found with regularity in clinical cases and that the overall trends in meningitis in the camps, in the area in which the camps were located, in the larger area from which inductees came, as well as in the country at large, all followed the trend in the Type I carrier rate in the camps, in the area in which the camps were located and in the larger area from which the inductees came.

4. Finally, the results of the comparison are in themselves an indication that it was a valid one. As will be shown when the incidence of meningitis in this epidemic period, both in the army and in the civilian populations, are reduced to attack rates in carriers (the local carrier rates), a seasonal fluctuation is found which coincides with the average seasonal fluctuation in the disease over a long period of years—in epidemic and non-epidemic times.

This comparison with particular reference to higher attack rates in the military

and seasonal fluctuation—the two features of the disease which give it its special military importance—clearly bring to the surface the proposition that these two regularly observed variations in the disease are not due, as long believed, to corresponding variations in the carrier rate.

TABLE 9

Meningococcal meningitis, army and civilian attack rates and ratio of army attack rates to civilian attack rates

MONTH	1942			1943			1944		
	Army R/10,000	Civilian R/10,000	Army / Civilian	Army R/10,000	Civilian R/10,000	Army / Civilian	Army R/10,000	Civilian R/10,000	Army / Civilian
Jan.....	2.0	0.2	10.00	19.0	1.3	14.62	10.0	2.1	4.76
Feb.....	5.0	0.3	16.67	24.0	1.7	14.12	11.0	2.2	5.00
Mar.....	4.0	0.3	13.33	29.0	2.3	12.61	11.0	2.1	5.24
Apr.....	3.0	0.4	7.50	24.0	2.3	10.43	10.0	1.9	5.26
May.....	4.0	0.3	13.33	14.0	2.0	7.00	8.0	1.4	5.71
June.....	3.0	0.3	10.00	9.0	1.4	6.43	6.0	0.9	6.67
July.....	2.0	0.2	10.00	6.0	1.0	6.00	5.0	0.7	7.14
Aug.....	2.0	0.2	10.00	6.0	0.6	10.00	3.0	0.6	5.00
Sept.....	2.0	0.2	10.00	3.0	0.7	4.29	3.0	0.5	6.00
Oct.....	2.0	0.2	10.00	3.0	0.8	3.75	3.0	0.6	5.00
Nov.....	3.0	0.3	10.00	3.0	0.9	3.33	3.0	0.6	5.00
Dec.....	9.0	0.4	22.50	6.0	1.4	4.29			

TABLE 10

Meningococcal meningitis, army in the continental United States: Per cent of men under six months service

MONTH	1942	1943	1944	1945
January.....		53.6	17.7	14.2
February.....		51.2	15.3	14.5
March.....		48.2	15.8	15.9
April.....	47.8	43.0	16.6	
May.....	51.4	38.4	16.0	
June.....	55.0	35.0	15.4	
July.....	56.0	31.9	15.0	
August.....	57.8	28.6	16.7	
September.....	57.5	24.1	15.4	
October.....	58.5	22.0	14.0	
November.....	58.2	20.5	14.0	
December.....	56.4	19.1	13.8	

In table 9 are given the meningitis attack rates by months from January, 1942, to November, 1944, for the army in the continental United States and for the civilian population. The ratios of the attack rates in the army to those in the civilian population are also shown. During 1942 and the first four months of 1943, the army attack rates were on the average about 12 times those in the civilian population. From May to December, 1943, the ratio of the army attack

rates to those in the civilian population decreased steadily to a ratio of about 5 to 1 where they remained throughout the period of the study. The circumstance with which this marked shift in the ratio of the two attack rates can be correlated is the varying proportion of the army which consisted of recruits (men under six months service). In table 10, the proportion of the army which consisted of men under 6 months of service is shown for this period, and in chart 6, these figures are shown in comparison with the ratio of the army attack rates to civilian attack rates.

The close parallel between the curve depicting the ratio of the attack rate in the army to the attack rate in the civilian population and that showing the

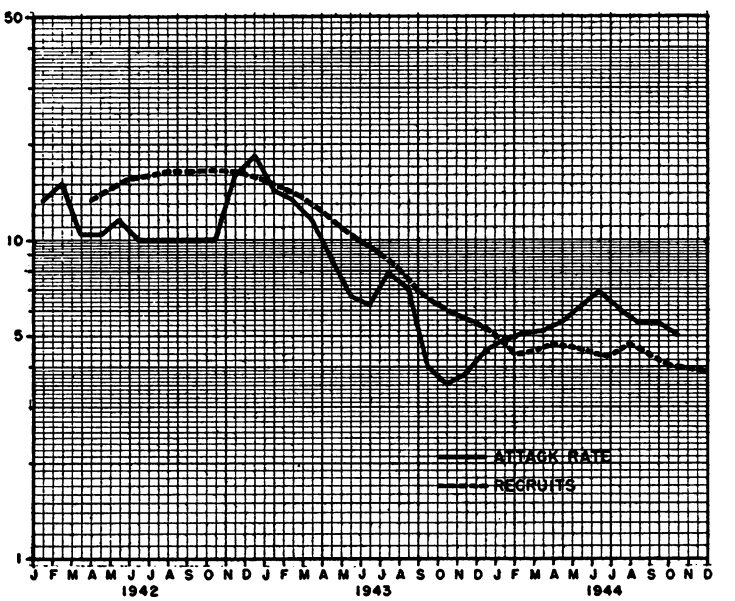

CHART 6. Meningococcal Meningitis. Ratio of army attack rates to civilian attack rates compared with variation in ratio of recruits in the army.

ratio of recruits to seasoned troops in the army is in itself an indication that, as is already well known, the excessive occurrence of meningitis in the army is largely to be accounted for by the composition of the army as between recruits and seasoned troops. Evidence was not found that carrier rates in recruits with high attack rates differed from those in seasoned troops or in civilian populations. Indeed, when the height of the carrier rate in seasoned troops or in the civilian population is considered, it is obvious that the higher attack rate in recruits could not be attributed even theoretically to correspondingly higher carrier rates in recruits. Thus, the present carrier study raises a question as to the validity of the conventional explanation for higher attack rates in armies and in recruits, long held to be the result of crowding of non-immunes with a resulting higher carrier rate incident to mobilization. When allowance is made for the proportion

of the army which was made up of recruits, it can be seen that the trend in attack rates in the army closely parallel those in the civilian population, with both showing a general parallel with the Type I carrier rate in the military establishments. It perhaps should be mentioned that recruits were included in the

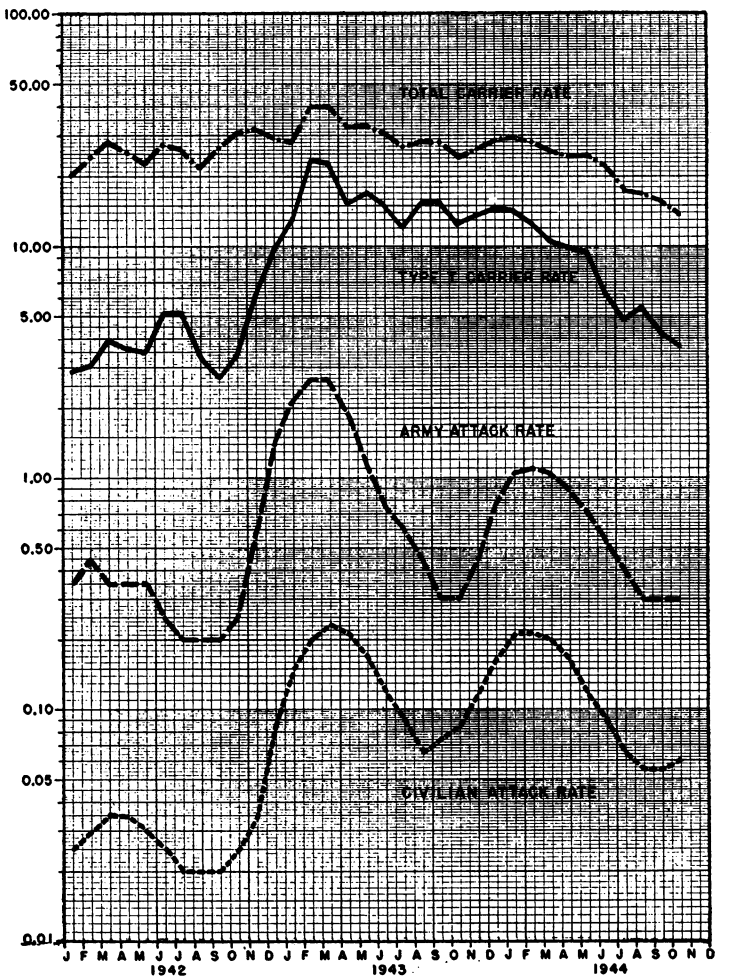

CHART 7. Meningococcus carrier rates for all types and for Type I in comparison with meningitis attack rates in the army and in the civilian population.

carrier study in the proportion in which they comprised the groups on which the study was made.

Chart 7 shows the total meningococcus carrier rates and the Type I carrier rates from January, 1942, to November, 1944. On this chart are also shown meningitis attack rates in the army and in the civilian population. It is at once clear that the trend in the total carrier rate for the period bears little resemblance to the trends in meningitis either in the army or civilian population. On the

other hand, the trend in the Type I carrier rate is in general similar to that seen in the occurrence of meningitis both in the army and in the civilian popula-

TABLE 11

Meningococcal meningitis, ratio of army and civilian attack rates to the army type I carrier rate

DATE	TYPE I CARRIER RATE, %	CIVILIAN R/10,000	CIVILIAN R/10,000 ÷ TYPE I CARRIER RATE	ARMY R/10,000	ARMY R/10,000 ÷ TYPE I CARRIER RATE
1942					
Jan-Feb	2.87	0.25	.0871	3.5	1.2195
Feb-Mar	3.04	0.30	.0987	4.5	1.4802
Mar-Apr	3.93	0.35	.0891	3.5	.8906
Apr-May	3.67	0.35	.0954	3.5	.9537
May-June	3.50	0.30	.0857	3.5	1.0000
June-July	5.21	0.25	.0480	2.5	.4798
July-Aug	5.20	0.20	.0384	2.0	.3846
Aug-Sept	3.32	0.20	.0602	2.0	.6024
Sept-Oct	2.74	0.20	.0730	2.0	.7299
Oct-Nov	3.39	0.25	.0737	2.5	.7375
Nov-Dec	6.45	0.35	.0543	6.0	.9302
Dec-Jan	9.97	0.85	.0853	14.0	1.4042
1943					
Jan-Feb	13.15	1.50	.1140	21.5	1.6350
Feb-Mar	23.76	2.00	.0842	26.5	1.1553
Mar-Apr	23.04	2.30	.0998	26.5	1.1502
Apr-May	15.19	2.15	.1415	19.0	1.2508
May-June	17.09	1.70	.0995	11.5	.4974
June-July	15.08	1.20	.0796	7.5	.4973
July-Aug	12.05	0.80	.0664	6.0	.4970
Aug-Sept	15.47	0.65	.0420	4.5	.2909
Sept-Oct	15.40	0.75	.0487	3.0	.1948
Oct-Nov	12.44	0.85	.0683	3.0	.2412
Nov-Dec	13.58	1.15	.0847	4.5	.3314
Dec-Jan	14.60	1.75	.1199	8.0	.5479
1944					
Jan-Feb	14.42	2.15	.1491	10.5	.7281
Feb-Mar	12.83	2.15	.1676	11.5	.8963
Mar-Apr	10.52	2.00	.1901	11.0	1.0456
Apr-May	9.86	1.65	.1673	9.0	.9128
May-June	9.69	1.15	.1187	7.0	.7224
June-July	6.78	0.80	.1180	5.5	.8112
July-Aug	5.00	0.65	.1300	4.0	.8000
Aug-Sept	5.41	0.55	.1017	3.0	.5545
Sept-Oct	4.12	0.55	.1335	3.0	.7282
Oct-Nov	3.66	0.60	.1639	3.0	.8197

tion during the same period. From these considerations, it is inferred that differences in army and civilian attack rates may be due not so much to differ-

ences in carrier rates, but to differences in attack rates in carriers which result from some circumstance incident to mobilization and particularly the first months of military life.

Seasonal Variation in the Ratio of Attack Rates to the Type I Carrier Rate

That variation in attack rates in meningitis under different circumstances may not be a simple function of corresponding variation in the carrier rate is

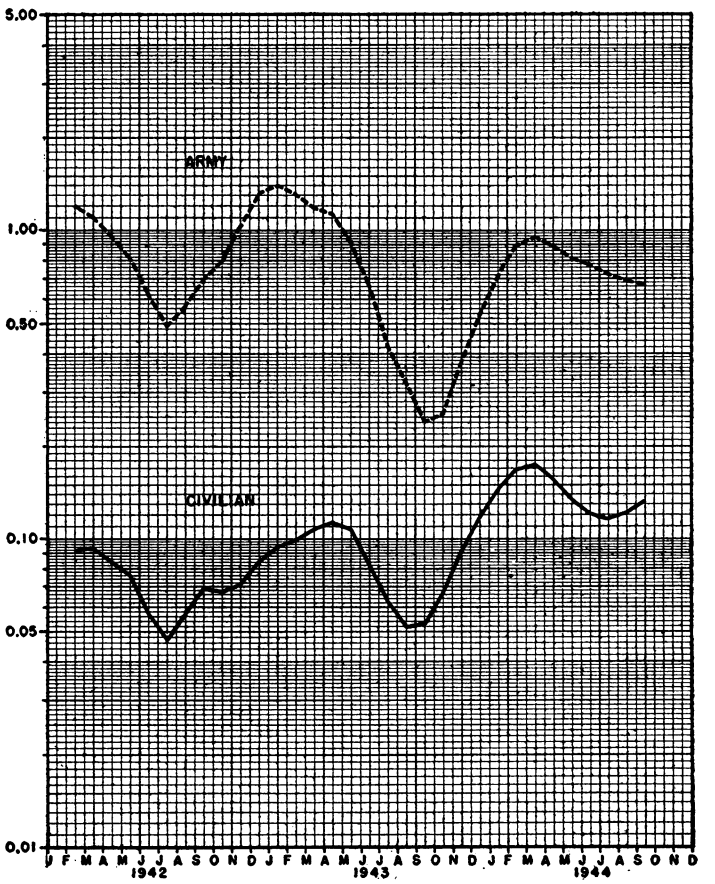

CHART 8. Ratio of army and civilian attack rates to the army Type I carrier rate.

perhaps most strikingly shown by the seasonal variation in the ratio of meningitis attack rates, both in the army and in the civilian population, to the Type I carrier rate. Although in the first part of the period covered by this study, the attack rate in the army was over 10 times that in the civilian population, and in the last part of the study only 5 times as high, insofar as season was concerned, both attack rates showed a similarly fluctuating ratio to the Type I carrier rate in the army. Furthermore, the seasonal variation in the ratio of the attack rates both in the army and in the civilian population to the Type I carrier rate corres-

ponds closely with seasonal variation in the incidence of meningitis in the United States over a period of years.

Although there was little relationship between the total carrier rate found in this study and the occurrence of meningitis either in the army or in the civilian

TABLE 12

Meningococcal meningitis, percentage seasonal variation in incidence by epidemic years, September—August

United States Registration Area, 1915–1948

YEAR	SEPT.	OCT.	NOV.	DEC.	JAN.	FEB.	MAR.	APR.	MAY	JUNE	JULY	AUG.
1915–16	5.7	5.4	3.9	6.4	7.7	8.5	10.6	11.2	10.2	10.8	10.0	9.6
1916–17	2.2	2.6	2.4	2.5	4.5	7.0	15.0	19.7	17.4	13.2	8.1	5.4
1917–18	3.1	3.2	3.8	7.5	14.0	15.3	15.8	13.1	9.6	5.2	4.9	4.5
1918–19	8.0	9.4	7.4	8.9	8.9	10.1	10.9	9.5	8.5	5.8	7.0	5.6
1919–20	5.7	7.1	6.6	7.7	11.6	10.4	10.8	9.6	9.5	7.5	6.6	6.8
1920–21	8.2	7.1	8.2	8.7	8.7	10.3	10.6	7.8	7.0	6.7	7.9	8.8
1921–22	8.8	8.5	8.4	8.5	9.1	10.6	10.0	8.8	8.2	6.6	5.2	7.3
1922–23	6.2	5.4	7.1	6.5	8.9	8.8	13.4	9.7	9.7	8.6	7.7	7.9
1923–24	7.2	9.1	11.5	8.3	9.5	7.5	8.8	9.7	7.7	7.2	6.9	6.5
1924–25	7.6	7.3	6.7	5.2	10.8	8.2	12.6	10.5	8.8	7.3	7.1	7.9
1925–26	6.7	5.1	4.3	8.9	9.0	11.2	13.3	10.5	9.6	8.0	7.7	5.8
1926–27	4.7	4.5	5.0	6.3	10.6	9.8	11.9	12.3	10.1	9.7	7.7	7.5
1927–28	4.2	4.4	4.5	5.7	8.0	8.1	13.5	12.5	13.6	10.0	7.0	8.4
1928–29	3.4	3.6	3.7	6.5	10.9	10.9	14.5	13.8	12.9	8.7	6.2	5.0
1929–30	4.9	5.4	6.2	8.8	12.1	12.9	14.4	13.2	8.3	5.2	4.1	4.6
1930–31	5.6	6.1	6.7	7.8	12.0	11.5	12.9	12.3	9.1	6.2	4.4	5.3
1931–32	7.5	7.5	8.4	9.7	10.9	9.9	11.5	10.5	7.6	5.8	5.0	5.6
1932–33	5.2	5.5	7.2	9.6	12.7	10.3	14.0	10.5	8.2	5.7	5.3	5.7
1933–34	5.3	5.0	7.4	9.9	9.2	9.6	12.5	10.4	9.7	8.9	5.7	6.5
1934–35	2.9	3.1	2.8	4.8	7.2	11.2	14.8	14.4	14.5	11.0	7.2	6.3
1935–36	3.3	4.1	4.8	7.0	10.7	12.8	16.9	15.4	10.6	6.0	4.7	3.6
1936–37	4.3	4.9	6.7	8.2	11.8	11.7	15.1	12.3	9.2	5.7	5.6	4.5
1937–38	6.2	7.8	8.5	10.2	12.0	11.5	10.9	9.3	7.5	6.5	4.8	4.8
1938–39	6.7	8.2	7.0	10.1	11.3	10.9	11.0	9.3	8.2	6.2	6.1	4.8
1939–40	6.7	7.9	8.4	8.1	8.7	10.9	11.0	9.3	8.8	6.7	6.6	7.0
1940–41	5.7	5.7	5.9	7.3	11.2	9.3	10.6	14.0	8.9	7.9	7.8	5.7
1941–42	4.3	4.3	4.7	6.2	7.5	8.9	11.0	15.8	11.0	10.4	9.0	6.9
1942–43	1.4	1.6	1.9	3.8	8.4	11.2	19.1	15.9	13.7	11.7	6.5	4.7
1943–44	4.7	4.8	5.0	9.5	12.9	12.6	15.3	10.8	10.2	5.4	4.4	4.3
1944–45	5.3	6.9	9.1	8.5	13.0	12.1	10.8	8.7	9.6	6.0	5.1	5.0
1945–46	5.6	6.8	6.4	8.0	18.0	11.6	11.3	8.4	8.5	5.7	5.9	3.8
1946–47	6.4	9.2	6.9	6.9	11.5	9.4	9.8	13.3	7.8	6.4	7.5	4.9
1947–48	5.1	7.8	6.4	8.8	10.3	11.0	13.5	8.3	8.6	7.8	6.4	6.0
Average....	5.4	5.9	6.2	7.6	10.4	10.5	12.7	11.5	9.8	7.6	6.4	6.0

population, the Type I carrier rate as shown in chart 7 can be definitely related to the increase in meningitis in both population groups. The increase in the Type I carrier rate from October, 1942, to March, 1943, as well as the decrease from March to September, 1944, coinciding in time with seasonal increases and

decreases in meningitis suggests that there is a seasonal fluctuation in Type I carriers which may be associated with seasonal prevalence of meningitis. It can be seen, however, that in the months of lower incidence of meningitis in the summer of 1943, between the two seasonal peaks of meningitis, there was no accompanying decrease in the Type I carrier rate. When the meningitis attack rates both in the army and in the civilian population are divided by the Type I carrier rate as shown by the carrier study (giving a calculated attack rate in Type I carriers), table 11, a definite seasonal fluctuation is seen (chart 8). This

TABLE 13

Seasonal variation in ratio of civilian and army attack rates to army type I carrier rate

		JAN. FEB.	FEB. MAR.	MAR. APR.	APR. MAY	MAY JUNE	JUNE JULY	JULY AUG.	AUG. SEPT.	SEPT. OCT.	OCT. NOV.	NOV. DEC.	DEC. JAN.
Civilian Attack R/10,000 ÷ Type I Carrier Rate	1942	.087	.099	.089	.095	.086	.048	.038	.060	.073	.074	.054	.085
	1943	.114	.084	.100	.141	.100	.080	.065	.042	.049	.068	.085	.120
	1944	.149	.168	.190	.167	.119	.118	.130	.102	.134	.164	.200	.250
Total		.350	.351	.379	.403	.303	.246	.233	.204	.256	.306	.339	.455
Average		.117	.117	.126	.134	.101	.082	.078	.068	.085	.102	.113	.152
Per Cent		9.18	9.18	9.88	10.51	7.92	6.43	6.12	5.33	6.67	8.00	8.86	11.92
Army Attack R/10,000 ÷ Type I Carrier Rate	1942	1.220	1.480	.891	.954	1.000	.480	.385	.602	.730	.738	.930	1.404
	1943	1.635	1.155	1.150	1.251	.995	.497	.490	.291	.195	.241	.331	.548
	1944	.728	.896	1.046	.913	.722	.811	.800	.555	.728	.820	.763	.983
Total		3.583	3.531	3.087	3.118	2.717	1.788	1.675	1.448	1.653	1.799	2.024	2.935
Average		1.194	1.177	1.029	1.039	.906	.596	.558	.483	.551	.600	.675	.978
Per Cent		12.20	12.03	10.52	10.62	9.26	6.09	5.70	4.94	5.63	6.13	6.90	9.99

seasonal fluctuation in attack rate in carriers both in the army and in the civilian population, although the attack rate was much higher in the army and underwent a marked change (associated with the recruit composition of the army), are both in close agreement with seasonal prevalence of meningitis in general. The average seasonal prevalence of meningitis for the registration area of the United States, 1915–19, (table 12) in comparison with the average seasonal variation in the attack rate in carriers in the army and in the civilian population (table 13) for the years 1942, 1943 and 1944 are shown in chart 9. It thus appears that although the epidemic prevalence of meningitis (lasting over a period of several

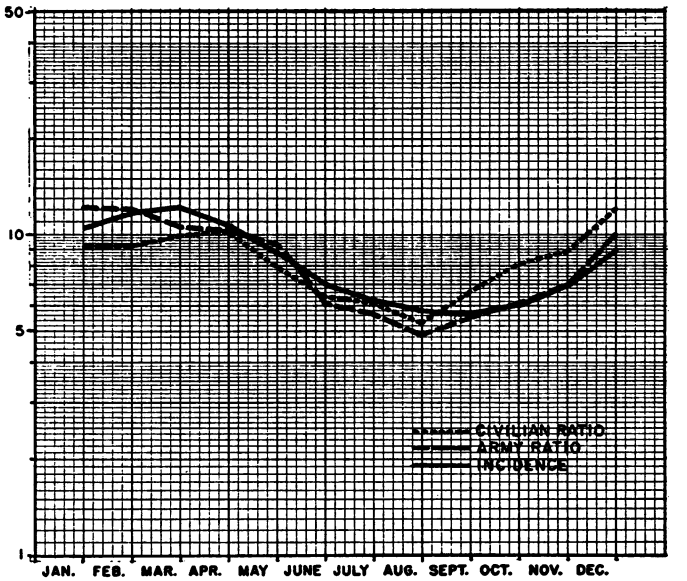

CHART 9. Seasonal variation in ratio of army and civilian attack rates to army Type I carrier rate compared with seasonal variation in meningitis. United States Registration Area, 1915–1943.

TABLE 14

Meningococcal meningitis, incidence by length of service

MONTHS OF SERVICE	TOTAL	
	No.	%
Less than 1	527	15.0
1	993	28.3
2	501	14.3
3	349	9.9
4	230	6.5
5	164	4.6
6	125	3.5
7–9	246	7.0
10–12	144	4.1
13–18	86	2.5
19–24	68	1.9
25 & over	74	2.1
Total Known	3507	
Unknown	582	
Grand Total	4089	

years) is determined primarily by an increase in Type I carriers, seasonal fluctuation in the occurrence of meningitis is not determined by a corresponding seasonal variation in Type I carriers but by some other seasonal influence which affects

the attack rate in carriers. This seasonal variation affects alike military populations where attack rates are higher and civilian populations where they are lower.

CONTROL OF MENINGOCOCCUS CARRIAGE

As pointed out in the first part of this paper, no local carrier rate or case incidence differentials were found which could serve as a basis for the application of preventive measures restricted to barracks, outfits, or areas within military establishments. There are indications that there are likewise no localized signs of impending meningitis in civilian populations. The preponderant occurrence

TABLE 15

Meningococcus carrier rates before and after sulfadiazine

	572ND AAA BN. 1½ GRAMS			572ND AAA BN. 2 GRAMS			572ND AAA BN. 4 GRAMS			133RD AAA BN. 6 GRAMS			359TH AAA BN. 8 GRAMS		
	No. Cult.	All Types	Type I	No. Cult.	All Types	Type I	No. Cult.	All Types	Type I	No. Cult.	All Types	Type I	No. Cult.	All Types	Type I
Before Sulfadiazine	70	25.7	15.7	70	31.4	20.0	60	33.3	18.3	110	35.4	12.7	233	46.4	29.2
After Sulfadiazine															
2 weeks	60	16.7	11.7	57	12.3	12.3	57	7.2	1.8	100	1.0	1.0	214	1.9	1.4
4 weeks	48	29.2	27.1	52	17.3	11.5	49	14.3	14.3	77	6.5	5.2			
5 weeks													100	2.0	1.0
6 weeks										87	6.9	4.6			
7 weeks	27	33.3	18.5	31	51.6	32.2	28	32.1	25.0				192	3.6	1.6
8 weeks										100	14.0	9.0			
9 weeks	45	24.4	20.0	37	18.9	18.9	36	18.2	15.1						
10 weeks										70	32.8	14.3			
12 weeks										89	21.4	15.7			
14 weeks													156	14.1	6.4
15 weeks										98	23.5	14.3			
16 weeks													148	8.1	3.4

of the disease in recruits, in the face of what appears to be a relatively uniform carrier rate in both the military and in the civilian populations, does constitute a selectivity which could be utilized with practical serviceability in the prevention of meningitis in the military.

From table 14 it is seen that 78.6% of 3,507 cases of meningitis in the army (1942 and 1943) occurred in men of less than 6 months service and that 57.6% of cases occurred in men of under 3 months service. It thus appears that the prompt administration of an effective prophylactic to inductees and the maintenance of a refractory state for the first 4 months of their military training would be both desirable and practical. The serviceability of such a plan resides in the fact that administration could be directed to the group at greatest risk and nicely timed

to the period of this risk. Furthermore, the relatively short period of higher risk in recruits is clearly demarcated.

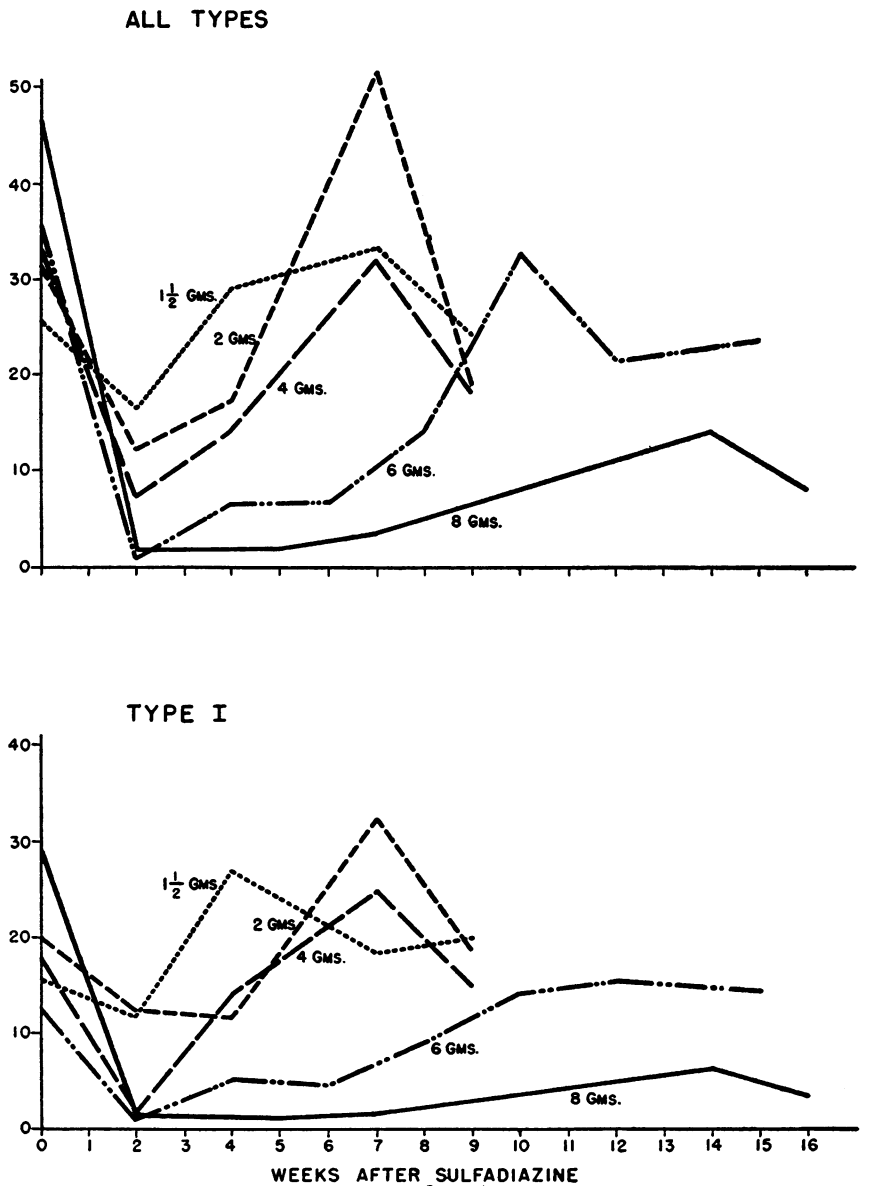

CHART 10. Top: Meningococcus carrier rates for Types I, II, IIα and X combined, before and after graded doses of sulfadiazine, 2 to 8 grams. Bottom: Type I meningococcus carriers before and after graded doses of sulfadiazine.

A number of studies made in military establishments during the epidemic prevalence of meningitis between the years 1942–1945 have shown that the

administration of sulfadiazine not only acts as a prophylactic against meningitis, but results in a prompt clearing of carriage of the organism for varying periods of time, apparently dependent upon the dosage employed (25, 26, 27, 28).

With these considerations in mind, tests were done to determine the effect of graded doses of sulfadiazine on the clearing of meningococcus carriage as well as the duration of its protective effect against subsequent harborage of the organism. For this purpose, five groups of men were cultured, and then the carriers were given doses of 1.5, 2, 4, 6 and 8 grams of sulfadiazine respectively. The men were recultured at intervals up to 16 weeks, as shown in table 15.

In this study, tests were not done to demonstrate the immediate clearing of carriage following even small doses of the drug as in some of the previous pub-

TABLE 16

Meningococcus carriage before and after sulfadiazine

BEFORE SULFADIAZINE		AFTER 1.5 TO 4 GRAMS SULFADIAZINE				
Type	No.	I	II	IIα	X	Total
I	36	30	1	1	0	32
II	20	3	3	0	0	6
IIα	4	2	0	2	0	4
X	0	0	0	0	0	0
Total.....	60	35	4	3	0	42

BEFORE SULFADIAZINE		AFTER 4 TO 8 GRAMS SULFADIAZINE				
Type	No.	I	II	IIα	X	Total
I	82	2	3	1	0	6
II	34	8	2	0	0	10
IIα	28	4	0	0	0	4
X	3	0	0	0	0	0
Total.....	147	14	5	1	0	20

lished studies, but cultures taken two weeks after administration of the drug indicated that the freedom from carriage at this time varied with the amount of drug given. Subsequent cultures revealed that within 4 to 6 weeks the carrier rate in men receiving doses up to 4 grams of the drug was again as high as it had been previous to administration of the drug. In contrast, those men receiving 6 and 8 grams remained at a lower level of carriage and for a longer period. The carrier rate in men receiving 8 grams was still minimal at the end of 16 weeks. It is altogether unlikely that the changes in carrier rates following sulfadiazine, correlating as they do with graded doses, could have resulted from chance variation in carriage in these groups of men. It thus would appear that the administration of 8 grams of sulfadiazine to recruits upon induction would serve to maintain a refractory state throughout the period during which the risk of meningitis in the military is highest (chart 10).

It was found, as shown in table 16, that with smaller doses (4 grams and under) the individuals who again became positive carried in general the same type of organisms that they had carried before administration of the drug, while the relatively few individuals who again became positive after 6 or 8 grams tended to harbor other types. This suggests that the smaller doses only suppressed carriage while the larger doses actually eradicated the organism which the individual was carrying.

DISCUSSION

Chapin said, in 1910, "Probably the most important discovery bearing on preventive medicine since the demonstration of the bacterial origin of disease is that disease germs frequently invade the body without causing disease". This principle of mild, missed cases, latent or subclinical infection, or healthy carriage is strikingly seen in meningococccus meningitis where large numbers, even the majority, of a population may be harboring the organism, and yet only one in several thousand develops the disease.

Studies during World War I brought the carrier aspects of meningitis especially into prominence. To say nothing of preponderant numbers of carriers over cases, it was said that, "The case is generally too sick to spread the germs extensively, while the carrier is free to do so". Thus, the carrier was seen as the important factor in the continued existence of the disease, and the aim in prevention was the detection and isolation of carriers. "The object of the carrier program [was] to prevent a virulent organism from reaching a susceptible person". However, the complete control of carriers by isolation alone was generally recognized as impracticable, and control measures tended to be confined to convalescents and immediate contacts with cases, combined with such general measures as increasing air space or space between beds in sleeping quarters on the grounds that the "crowding of mobilization" was a major factor in the spread of the microörganism.

The association between meningitis and carriage reached its height in the doctrine originating in the studies of Glover (during World War I) to the effect that cases of meningitis could be expected to occur only when the carrier rate exceeded what was supposed to be an innocuous minimum threshold.

From the experience in World War II, we now see that the incidence of the disease is greater in recruits than in seasoned troops, greater in the military than in civilian populations and greater in winter than in summer, despite the fact that the carrier rate appears to be the same in all. (And this applies to Type I meningococcus, the preponderant cause of meningitis.)

It now becomes clear, therefore, that although the prevalence of meningitis in general may be attributed to the prevailing carrier rate, variations in incidence of the disease in military and civilian populations, in recruits and seasoned troops, and in winter and summer can no longer be ascribed to corresponding variations in either the prevalence or rate of spread of the organism, but rather, to variations in the frequency with which the disease is caused in those who harbor the microörganism of the pathogenic type, possibly by factors in the exposed rather than in exposure. The magnitude of any attempt to eradicate carriers of meningococci would be so great that studies looking toward a prac-

ticable method of control of the disease should include studies of factors which determine susceptibility in the few of the many who are exposed to the infection.

The sudden heightening of liability to disease with mobilization would easily appear on the surface to be the result of the operation of the well known epidemiologic principle of "urbanization" of non-immunes. In the immunizing infections of childhood—measles, mumps, scarlet fever and diphtheria—the acceptance of the idea of increased opportunity for contact through herding of non-immunes is entirely in keeping with many of the epidemiologic features of these diseases. On the other hand, many epidemiologic features of meningitis as well as other evidence or sometimes "absence of proof", in addition to certain features of carrier rates shown by this study, suggest that meningitis in the first place is not one of the "immunizing infections of childhood", almost a necessary requirement for a mobilization epidemic due to "crowding" *per se* of any disease the infectious agent of which is widespread. In the second place, the close parallelism between the occurrence of meningitis in all parts of the country in both military and civilian populations afford reasons for believing that the underlying requirement for the occurrence of the disease (prevalence of Type I meningococci) is a general one and is not influenced to any great extent in one locality or other by such factors as variation in carrier rates, variation in immunity in population groups, and so forth. In other words, many of those epidemiologic factors which are so clearly responsible for variation in the common infections such as measles appear to be lacking in meningitis. In short, meningococcus carriage is evidently so frequent and general in the population that it seems altogether unlikely that any mobilized groups of adults could contain any significant proportion of individuals who had never before harbored the meningococcus, or for that matter Type I, and who therefore would constitute the non-immunes who upon mobilization exposure account so largely for military meningitis.

That the behavior of meningitis in the military (high incidence in recruits) is not the result of abetting exposure by mobilization of non-immunes is again suggested by some further comparison with the group of diseases where mobilization epidemics in the past have been so clearly the result of the workings of this principle.

The health record of the army (29) during World War II was remarkably good in respect to this type of disease. In general, it compared favorably with that of the peacetime armies made up largely of seasoned troops, or with that of the civilian population. This might have been anticipated from the disappearance to a large extent in more recent years of the major difference in rates of immunization in urban and rural populations, which is attributed to a general trend toward "urbanization" of the rural population.

The fact that meningitis is the one disease in the group formerly promoted by mobilization which has shown no evidence of a similar effect of urbanization is still another reason for suspecting that mobilization of non-immunes may not be the reason for its "epidemicity" in recruits.

From this study, it is concluded that meningitis is not, as previously thought, primarily a "disease of mobilization" but that military meningitis is a direct

reflection of the prevalence of the disease in the area from which mobilization is drawn. The disease, both in the civilian and military populations, is based in all probability on the same generally prevailing Type I carrier rate. Seasonal fluctuation in meningitis, as judged from this carrier study, is likewise due to factors other than seasonal fluctuation in the carrier rate or, in other words, seasonal variation in the transmission of the organism.

It is clear that without the participation of many individuals it would have been physically impossible to carry out a survey of the sort which is here discussed. The collection and transportation of cultures, together with their subsequent handling in the laboratory, represent a major outlay of time and effort over a period of four years. The writers gratefully acknowledge the important part played by many assistants and associates in carrying out this work. The active participation of Dr. Emanuel B. Schoenbach in organizing the laboratory study was of the utmost value. Particular acknowledgment is made to Miss K. Hendrie for much of the laborious tabulation and organization of the voluminous data.

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