THE RELATION OF STREPTOCOCCUS HEMOLYTICUS CARRIERS TO STREPTOCOCCUS EPIDEMICS IN THE ARMY.*

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Any consideration of the epidemiology of the widespread hemolytic streptococcus infections that have occurred in the army must of necessity be incomplete, since our knowledge is still in the formative stage, and there remain many gaps in the story that only further investigation can complete. It is merely necessary to state that no method for the immunologic classification of hemolytic streptococci has been available for us, nor has any method been devised to make certain whether a given streptococcus is virulent for man or not, to indicate two of the many difficulties that have confronted us. The relation that streptococcus carriers have borne to the prevalent streptococcus infections of the last two years is one of the most important phases of the problem.

Before entering upon a discussion of this subject it seems advisable to recall certain facts with respect to hemolytic streptococcus infections in general, since they serve to a considerable extent to orient us in the particular field to which this discussion is devoted. Two facts stand out preeminently above all others. Firstly, hemolytic streptococcus infections with but few exceptions are secondary in nature—that is, they occur in large part only in the presence of some preexisting disease or lesion which renders the individual susceptible to invasion by these organisms. This relation has been a matter of common knowledge for many years with respect to scarlet fever, puerperal sepsis, wound infection, erysipelas and other diseases. Certain exceptions, of course, exist as a conspicuous

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example of which may be mentioned epidemic septic sore throat. The second outstanding fact with respect to hemolytic streptococcus infections is that they occur mainly in epidemic form. We are all familiar with the history, at least of the old time hospital epidemics of puerperal fever, wound infection and erysipelas. We have all seen epidemics of streptococcus sore throat. Here, again, the rule is not absolute, and isolated cases of streptococcus infection not infrequently occur without relation to a streptococcus epidemic. By way of comparison, Theobald Smith has drawn attention to the fact that streptococcus infections in animals also occur as epidemics, mainly as secondary, not primary infections.

The direct application of these facts to conditions as they have existed in the army is quite apparent if one surveys the whole field. It is well known that the streptococcus infections that have occurred have in very large part affected the respiratory tract, producing a secondary bronchopneumonia with frequent empyema. Otitis media and mastoiditis also have been very prevalent. It seems unquestionable that this is because the antecedent infections that have prepared the soil for secondary streptococcus invasion have been almost exclusively respiratory diseases, rather than that the streptococci in themselves have had primarily any special predilection for the respiratory tract. Two diseases have been especially prominent in this respect—measles and influenza. During the winter of 1917-18, when streptococcus bronchopneumonia first became prevalent in the army camps, it almost exclusively followed measles. In the spring months of 1918, however, it began to occur in increasing amounts independently of measles, as the reports of Fox and Hamburger¹ and Lucke² from Camp Taylor, of MacCallum³ from Camp Dodge, and of the Empyema Commission⁴ at Camp Lee clearly show. Similar cases were very numerous at Camp Merritt during April and May, 1918, where measles played a negligible rôle as a predisposing cause. The theory was put forward that the hemolytic streptococcus had attained such virulence by this time that it was capable of producing a primary bronchopneumonia in the absence of an antecedent infection of the respiratory tract. This may have been so to a certain extent. Without wishing to be too positive on the subject, it is believed, in view of sub-

sequent experience, that this so-called primary streptococcus pneumonia was in reality in large part secondary to influenza, which was for the most part unrecognized at the time. It is impossible to go in detail into the reasons for this belief. It suffices to say that it has been clearly shown by Soper,⁵ by Opie and his collaborators,⁶ and by others, that epidemics of influenza, differing from the fall epidemic only in degree, occurred in many of the army camps during the months of March, April and May, 1918. Rereading of the clinical, pathologic and bacteriologic reports referred to above will only serve to strengthen this opinion. The relation of influenza to streptococcus infections during the fall of 1918 is too fresh in the minds of all to require further comment. One other disease has also predisposed to secondary streptococcus infections to an extent not generally recognized, namely, lobar pneumonia. The reports of Cole and MacCallum,⁷ Clendenning,⁸ and Opie⁹ have directed attention to this.

The epidemic character of the hemolytic streptococcus infections that have occurred in the army should be quite obvious to everyone, yet it is apparently often disregarded in discussions upon the relation of streptococcus carriers to secondary streptococcus infections. I wish particularly to emphasize the epidemic character of these infections, since it has a very important bearing on the rôle played by streptococcus carriers. That streptococcus bronchopneumonia has occurred in the form of epidemics rather than as an endemic disease such as pneumococcus lobar pneumonia, is clearly brought out by the fact that during the winter of 1917-18 it occurred very extensively in certain camps, particularly those in the south, while many of the northern and far western camps were almost entirely free from it. A similar selective incidence has occurred during the fall epidemic of influenza. In certain camps hemolytic streptococcus pneumonia has been conspicuous by its absence, while in others it has been exceedingly prevalent. The epidemic nature of these streptococcus infections was very evident at Camp Pike during the fall epidemic of influenza. Streptococcus pneumonia did not appear to any extent until the influenza had reached its height. It then gained very rapid headway and increasingly complicated or replaced secondary pneumococcus pneumonia as the influenza

epidemic declined. Similar observations have been reported by Goodpasture¹⁰ from the Naval Hospital in Chelsea, by Rackemann and Brock¹¹ at Camp Merritt, and by Blanton and his collaborators¹² at Camp Custer.

It is quite clear, then, that the hemolytic streptococcus bronchopneumonia, otitis media and mastoiditis that have been so prevalent in the army have not differed from hemolytic streptococcus infections in general in their two principal features—that is, they have been almost entirely secondary infections, and they have been truly epidemic in character. With these two facts clearly in mind we can much more intelligently approach the subject of streptococcus carriers in their relation to the streptococcus epidemics that have occurred in the army.

In speaking of streptococcus carriers it is necessary in order to avoid confusion to divide them into three groups: (a) chronic carriers, individuals who carry the hemolytic streptococcus over long periods of time; (b) contact or temporary carriers, those who acquire the hemolytic streptococcus and carry it for a relatively short time without its causing them any apparent injury; and (c) acute carriers, those who acquire the organism and in whom it produces disease. The first group is represented by individuals with more or less definitely pathologic tonsils, in the crypts of which hemolytic streptococci find a suitable place for continued existence. The reports of Nichols and Bryan¹³ and Pilot and David¹⁴ have dealt with this type of carrier. Undoubtedly opinion differs with respect to the incidence of these chronic carriers. It may be safely stated, however, that most observers who have had wide experience in the study of the bacterial flora of normal throats agree that hemolytic streptococci are found with rarity in the absence of streptococcus epidemics. Little data is available with respect to the incidence of temporary carriers of hemolytic streptococci under normal conditions, but with little doubt their number and importance are negligible, since, as has been stated, hemolytic streptococci are infrequently found in normal throats in the absence of a streptococcus epidemic. On the other hand, under the abnormal conditions that have existed during the past two years in the rapid assembling of large groups of men in our army camps, contact or temporary carriers of hemolytic streptococci have become very numerous

and probably have played a very important part in the development of the widespread streptococcus epidemics. It is only necessary to contrast the incidence of streptococcus carriers among new recruits before they have entered camp with that among men who have been in camp for varying periods of time to indicate the extent to which contact carriers may develop. In a group of 489 newly drafted men cultured as they arrived at camp, Levy and Alexander¹⁵ found 14.8 per cent to be carriers of hemolytic streptococci, while among men who had been in camp for a period of six months the incidence of carriers was 83.2 per cent. The third group of acute carriers is represented by the cases of streptococcus pneumonia, mastoiditis, tonsillitis, etc., and needs no further definition. It is of course obvious that the contact carrier may become an acute carrier if he develops measles or some other predisposing disease which renders him susceptible to invasion by the hemolytic streptococcus. Whether the chronic carrier may do so or not, is not so clear. Data which I will present would seem to indicate that he rarely does so, except possibly as a terminal event in chronic diseases.

Two points of view with respect to the relation of streptococcus carriers to streptococcus epidemics have been advanced. The first has been expressed in a recent editorial in *The Journal of the American Medical Association*,¹⁶ from which I quote in part: "As hemolytic streptococci commonly present in the crypts of the tonsils are probably the most important source of the streptococcic complications of various acute infectious diseases in persons innocently harboring the microorganisms, it is important to ascertain how the secondary infections from them arise. At any rate, it seems more reasonable, on the basis of knowledge available, to charge the responsibility to the tonsil borne bacteria rather than to an invasion of unusually virulent strains from outside the body. Outbreaks of disease due to the entrance of foreign virulent streptococci unquestionably do occur at times, as the epidemics of septic sore throat testify; but in general the streptococcic infections are presumably associated with preexistent foci, like the tonsils, which harbor the bacteria in the body." In brief, this is the theory of autogenous infection. The other point of view is indicated in the above quotation, namely, that

the secondary streptococcus complications are in large part due to invasion of virulent strains from outside the body—that is, to contact infection.

Although it is admitted that our knowledge is still far from complete, examination of all the available evidence would seem to indicate that the theory of contact infection is the only logical one with respect to the widespread streptococcus epidemics that have occurred in the army. In support of this opinion I wish to present briefly certain studies made at Camp Pike by the Pneumonia Commission headed by Colonel Opie.* This study covered the entire period of the 1918 fall epidemic of influenza from its beginning in early September until influenza had nearly disappeared in mid December. During the same period a considerable epidemic of measles occurred at Camp Pike. A particularly good opportunity to study the relation of streptococcus carriers to the development of streptococcus complications of measles, influenza and influenzal pneumonia was afforded, since the number of streptococcus carriers among normal men and among those entering the base hospital with measles, influenza and pneumonia at the beginning of the study was at a low ebb following the favorable conditions that had existed during the summer months when respiratory diseases were at a minimum and streptococcus infections were nearly absent.

Three groups of normal men were studied. The first consisted of 64 drafted men assembled at Hot Springs, Ark., preparatory to entraining for Camp Pike. These men were from isolated rural communities, were cultured as soon as they reported at the place of assembly, and therefore afford an excellent base line. Throat cultures in all were negative for hemolytic streptococci. The second group consisted of 337 men from various organizations at Camp Pike. They had entered camp in the June, July and August drafts. Twenty-five, or 7.4 per cent, were positive for hemolytic streptococci. The third group consisted of 65 normal individuals, compris-

*These studies are to be published in detail by members of the commission. The members of the commission were Lt. Col. Eugene L. Opie, M. M., Major Allen W. Freeman, M. C., Capt. Francis G. Blake, M. C., First Lieut. James C. Small, M. C., and First Lieut. Thomas M. Rivers, M. C.

ing the nursing and medical corps personnel of the measles wards during September. Six, or 9.2 per cent, were positive for hemolytic streptococci. For the purpose of argument it may be assumed that the positive cases represented chronic carriers, although it must be conceded that some may have been merely contact or temporary carriers. These figures are comparable with those of Levy and Alexander¹⁵ for men cultured upon arrival at Camp Taylor. The incidence of streptococcus carriers among men admitted to the base hospital with measles, influenza or pneumonia was quite similar. Eight hundred and sixty-seven cases of measles admitted between September 15 and December 15, showed only 37, or 4.3 per cent, positive for hemolytic streptococci on the first culture at time of admission. Eighty cases of pneumococcus pneumonia cultured during September showed only 1, or 1.3 per cent, positive for hemolytic streptococci. Throat cultures in 100 cases of influenza, made shortly after admission to the hospital on September 25 and 26 when the influenza epidemic was approaching its height, showed 6, or 6 per cent, to be positive for hemolytic streptococci. As with the normal men it may be assumed that the positive cases represented in the main chronic carriers of hemolytic streptococci. I wish to emphasize two points of particular interest with respect to these chronic carriers. The first is their relatively low incidence in the absence of a streptococcus epidemic. The second is that none of these chronic carriers admitted to the hospital with measles, influenza or pneumonia developed secondary streptococcus infections, although suffering from respiratory diseases preeminently leading to secondary invasion by the hemolytic streptococcus.

Simultaneous observations of the development of contact or temporary carriers yielded very interesting results. But one group of normals is available. Eighty-eight individuals of the medical corps personnel on the measles wards were cultured in November after streptococcus complications had become fairly prevalent among measles patients. Sixteen, or 18.2 per cent, were positive for hemolytic streptococci, an increase of 100 per cent over the figures for September. Cultures were made in 138 cases of influenza between November 27 and December 5 at time of admission to the hospital. Thir-

ty-nine, or 28.3 per cent, were positive, an increase of approximately 400 per cent over the figures for September. Not only was there a marked increase in the actual number of carriers but the much greater predominance of hemolytic streptococci over other bacteria on the plates was often very striking. It is believed that this increase in the number of streptococcus carriers was dependent upon the dissemination of hemolytic streptococci coincident with or following a considerable epidemic of streptococcus infections that started at the height of the influenza epidemic during the last week of September and that the majority of these cases represent temporary or contact carriers.

The development of contact carriers in the measles wards was studied by weekly throat cultures. Of the 830 cases of measles negative for hemolytic streptococci at the time of admission to the hospital 205, or 24.7 per cent, acquired the hemolytic streptococcus while in the hospital. The development of streptococcus complications among these contact carriers is in striking contrast with their absence among the chronic carriers. These complications were: Bronchopneumonia, 9; otitis media, 27; mastoiditis, 14; meningitis, 2; suppurative arthritis, 1; acute tonsillitis, 4. These cases, therefore, became acute carriers, while the rest remained simply contact carriers without developing streptococcus infections, possibly an indication that the streptococci which were becoming more and more prevalent had not attained that degree of virulence which they attained in the spring of 1918. It is noteworthy that among these cases of bronchopneumonia, otitis media, and mastoiditis the complication developed in all but five instances nearly coincidentally with the acquisition of the hemolytic streptococcus by the patient in so far as the limitations of weekly throat cultures could determine.

Even more striking evidence of the contact nature of these streptococcus infections was obtained in certain ward studies among patients suffering with influenzal pneumonia. These may be summarized briefly. In wards 3 and 8, between September 6th and October 5th, 163 cases of influenzal pneumonia were admitted, of whom 49, or 30.1 per cent, died. Cultures at autopsy showed that only two of these cases had streptococcus pneumonia. In striking contrast with this were the con-

ditions in wards 1 and 2. Between September 24th. and October 5th, 141 cases of influenzal pneumonia were admitted to these wards. Of these, 72, or 51.1 per cent, died. Cultures at autopsy showed that 43, or 59.7 per cent, of these 72 fatal cases had a secondary hemolytic streptococcus pneumonia. To appreciate the full significance of this striking difference between wards 3 and 8 on the one hand and wards 1 and 2 on the other, it is necessary to state that the patients admitted to these wards were in no sense selected. Sputum and throat cultures in cases admitted to wards 1 and 2 made prior to or shortly after admission to the ward showed that the majority of them, as in wards 3 and 8, were pneumococcus or mixed pneumococcus and bacillus influenzae pneumonias free from hemolytic streptococci at time of admission. The widespread and highly fatal secondary hemolytic streptococcus epidemic in wards 1 and 2 was shown to directly follow the introduction of a few cases of streptococcus pneumonia into these wards. Such a strikingly selective ward incidence of secondary streptococcus pneumonia can leave little doubt that these cases were due to invasion by highly virulent streptococci through contact infection from acute carriers. Even should it be granted that the majority of all these cases in both groups of wards were chronic carriers of hemolytic streptococci which the limitations of the throat culture method had failed to detect, the theory of autogenous infection can hardly be sustained in the presence of the almost complete selective incidence of secondary streptococcus infections between the two groups of wards.

In summary, our studies at Camp Pike showed that in the absence of a streptococcus epidemic the incidence of hemolytic streptococcus carriers among normal men and among patients admitted to the base hospital with measles, influenza or pneumonia was relatively low, not exceeding 10 per cent in any of the groups studied. It may be conceded that these represent chronic carriers. Following the outbreak of an epidemic of streptococcus infections the incidence of streptococcus carriers among normal men and among patients admitted to the base hospital with influenza showed an increase of from 100 per cent to nearly 400 per cent. It is believed that this increase represents a group of contact or temporary carriers

due to the dissemination of hemolytic streptococci coincident with the streptococcus epidemic. Contact carriers also developed to a considerable extent among patients with measles during their residence in the hospital wards. Secondary streptococcus complications occurred exclusively among these contact carriers, chronic carriers of hemolytic streptococci among patients with measles, influenza and pneumonia remaining free from streptococcus complications. In the majority of instances in which patients with measles developed a streptococcus complication, the onset of the complication was nearly coincident with the acquisition of the hemolytic streptococcus by the patient. Highly fatal ward epidemics of secondary streptococcus pneumonia among patients with influenzal pneumonia were shown to be due to contact infection and were directly traceable to acute carriers of hemolytic streptococci.

It remains to correlate these results with similar studies made by many observers during the spring of 1918, since there are certain noticeable differences, especially with respect to the incidence of streptococcus carriers and their relation to the development of secondary streptococcus complications. Only the report of Levy and Alexander¹⁵ from Camp Taylor will be considered, since this is fairly representative of conditions as they existed at that time and has been widely quoted in support of the theory of the wide prevalence of streptococcus carriers and of autogenous infection. It will be recalled that in a group of 95 normal men who had been in camp for approximately six months, 83.2 per cent were found to be carriers of *S. hemolyticus*. A similar high incidence of streptococcus carriers, 77.1 per cent, was found among 388 cases of measles at time of admission to the hospital. Streptococcus complications, which were fairly frequent, occurred almost exclusively among these men who were carriers at time of admission. In contrast with this high incidence of carriers among men resident in camp for six months, the incidence of carriers among 489 new recruits cultured upon arrival at camp was but 14.8 per cent. In analyzing these results it is necessary to point out that at the time the studies of Levy and Alexander were made a very extensive epidemic of secondary streptococcus infections had existed at Camp Taylor for some time and was still unabated. In view of this fact, it

would seem highly probable that a very large proportion of the carriers among normal men and measles patients were contact or temporary carriers who had acquired the carrier state coincident with the widespread dissemination of streptococci that must occur in the presence of an extensive streptococcus epidemic. This is very clearly so, in view of the relatively low incidence of carriers among recruits who had not been in contact with the epidemic. With these points in mind it will be seen that the results obtained by Levy and Alexander are not out of harmony with those found at Camp Pike.

SUMMARY.

In summary, it may be said that the available evidence would seem to indicate that the widespread streptococcus infections that have occurred in the army have in very large part been due to invasion of virulent streptococci in individuals rendered susceptible by predisposing diseases, chiefly measles, influenza, and pneumococcus pneumonia through contact infection, either direct or indirect, and that autogenous infection has played an insignificant rôle in the production of these streptococcus infections. Their truly epidemic character and their strikingly selective incidence would seem to admit of no other interpretation. Even should it be granted that a large proportion of the population innocently harbor hemolytic streptococci in their tonsils as chronic carriers it is difficult to maintain the theory of autogenous infection, since it predicates an equal incidence of streptococcus complications of measles and pneumonia at all times.

The relation of chronic carriers to the development of streptococcus epidemics is uncertain and must remain so until means are available for showing whether the hemolytic streptococci harbored by them are immunologically identical with those responsible for the epidemics. It is not impossible that they may be the initial source of these epidemics which arise when an opportunity for the dissemination of the streptococci which they carry is provided by the assembling of large groups of men in intimate association. From the point of view of prevention it would seem wise to consider this assumption as true until it is disproved or otherwise. It must not be over-

looked, however, that the starting point may equally well be found among a number of acute carriers represented by cases of streptococcus tonsillitis which are probably not infrequently present among large groups of drafted men at the time of their arrival in camp.

The rôle played by contact or temporary carriers in the development of a streptococcus epidemic, likewise, cannot be finally established until we are possessed of methods for the immunologic identification of hemolytic streptococci. Sufficient evidence is available, however, to show that they bear an intimate relation to the streptococcus epidemics of the army, even if only a time relation. It seems not improbable that they represent to a considerable extent the intermediate hosts, if we may use the term, which serve to widely disseminate the streptococci and assist in increasing the virulence of the organism by frequent passage. They should at least be regarded as a potential source of danger until negative evidence has been produced. It is possible, however, that contact carriers play only a passive rôle and occur merely coincidentally with the dissemination of streptococci that takes place during a streptococcus epidemic. That contact carriers may become acute carriers in the presence of a predisposing disease has been brought out.

The part played by the acute carrier in the spread of streptococcus infections cannot be too strongly emphasized. It has been clearly shown that he is an actual source of great danger. The introduction of an acute carrier into a ward devoted to the care of respiratory diseases may be followed by a rapidly spreading and highly fatal epidemic of streptococcus pneumonia which is comparable in all respects to the old time hospital epidemics of puerperal sepsis. Rigid isolation of every such case is the clear indication.

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