

THE BACTERIOLOGY OF THROAT CARRIERS OF
STREPTOCOCCUS HEMOLYTICUS.*

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In controlling the spread of infectious diseases, the detection of healthy carriers of the specific organisms is a recognized part of the laboratory program along with the diagnosis of actual cases and vaccination when available. In diseases spread from the mouth and nose, diphtheria offers the best example of what can be done by this method of attack. Diphtheria bacilli can be found in the throats of healthy carriers by suitable cultures; the virulence or significance of the organisms found can be determined; chronic carriers of virulent organisms, who are usually immune themselves, can be isolated or cured by tonsillectomy; acute carriers of virulent organisms can be examined for immunity by a skin reaction, and if not immune can be immunized by antitoxin and isolated. In passing, it may be said that this program is rarely ever completely realized in practice on account of the amount of work involved, but parts of it are of practical value. In the prevention of epidemic meningitis, carrier work also has its place, which has been made more definite by the recent differentiation of types of meningococci. In lobar pneumonia, too, the differentiation of types of pneumococci has made the carrier problem more definite and practicable by excluding certain less important but prevalent groups from consideration.

In hemolytic streptococcus infections, however, the carrier problem is difficult. No virulence test or differentiation of groups is available, and the number of apparent carriers may be very large. In a recent survey of attendants and patients

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at the Walter Reed Hospital, Simmons¹ found the weekly carrier rate in March and April to be between 50 and 90 per cent with no cases of streptococcus pneumonia.

Judged by the evidence available at present, these streptococci are as good streptococci as those isolated from exudates in fatal cases of streptococcus empyema or meningitis. By analogy and experience we are forced to believe that some of these organisms found in carriers are pathogenic and that others are practically saprophytes, but until we know which are which we are equally forced to consider them all as potentially dangerous.

A word may be said here about nomenclature. The term streptococcus hemolyticus has been recently coined and in itself does not stand for a definite biologic species. It means simply hemolyzing streptococci, of which there are at least two kinds, human and bovine. For clinical purposes, however, it is synonymous with the older term, "streptococcus pyogenes," which culturally forms a single species. Using Holman's classification based on sugar reactions, different species may occasionally be found among the hemolyzing streptococci of the throat, but, as has been said, the great majority of these organisms are culturally identical.

A word may also be said about the hemolyzing enzyme. This is apparently not of clinical significance in the way of producing anemia. At least, in a series of ten cases of severe streptococcus infection, compared with ten cases of severe pneumococcus infections at the Walter Reed Hospital, no difference could be seen in the hemoglobin estimations; both series showed a secondary anemia averaging about 70 per cent. Like pigment formation in certain bacteria, the property of hemolysis in streptococci seems to be a metabolic activity that has no clinical equivalent.

The detection of carriers of streptococcus hemolyticus is fairly simple and resolves itself into a question of obtaining suitable material from the patient and of making a suitable examination in the laboratory.

The specimen of the flora of the throat is usually obtained as in examinations for the diphtheria bacillus by passing a sterile cotton swab over the fauces and posterior wall of the pharynx. In strongly positive cases material collected in this

way is satisfactory. It is known, however, the crypts of the tonsils are the most frequent habitat of hemolytic streptococci.² The evidence for this conception is as follows: 1. Cultures from the surfaces of the tonsils are positive more frequently and more strongly than cultures from any other area of the nasopharynx. 2. Crypt cultures in vivo are positive in a higher percentage of cases than surface cultures. 3. Crypt cultures of excised tonsils are positive in a high percentage. 4. Excision of the tonsil is the surest way of curing carriers. Under these circumstances it is evident that cultures of the tonsils are the most reliable source of material. In a series of fifty normal cases examined at the Walter Reed Hospital 28 per cent were positive with the ordinary throat cultures, while 50 per cent were positive by crypt cultures, an error of 22 per cent in the ordinary examination. A proper tonsil culture can be taken only with due care as to exposure and instruments, and is preferably made with the help of a laryngologist, although a light massage of the tonsil with the end of the swab suffices to bring out crypt contents in most cases.

Streptococci in such material are not very delicate and withstand some drying and change of temperature, but of course should be cultured with reasonable promptness. The standard culture media for the first inoculation is blood agar. As originally introduced by Shotmüller in 1903, this consisted of 40 per cent blood, but the percentage used at present is 5 to 10 per cent defibrinated human, rabbit or sheep blood. The various technical steps in working out a positive culture are fully stated in the methods for identification of streptococcus hemolyticus adopted by the Medical Department, U. S. Army, June 1, 1918.³ The method consists in subculture of the original hemolyzing colonies into plain broth for further identification by means of morphology, bile solubility and a second hemolysis test. This requires 48 hours. In large surveys by experienced workers, the original surface culture answers the purpose in most cases, and the result can be given in twenty-four hours. A prompt report is of course desirable in case of patients admitted to hospital or of recruits under quarantine.

The streptococci thus isolated seem to form a strikingly similar group of organisms, as judged by many of the usual procedures in bacteriology. Slight differences in morphology

of certain cultures as to size of organisms, length of chains or appearance of colonies, etc., have been noted, but when due allowance is made for cultural conditions, these differences do not appear significant. The degree of hemolysis is also an uncertain criterion for differentiation. Virulence tests are made by injecting different quantities of broth culture intravenously in rabbits or intraperitoneally in mice or rats. The striking feature about these tests is the absence of difference in cultures from clinically virulent infections and from healthy carriers. From both kinds of cases a comparatively large amount of cultures is necessary to kill an animal on first inoculation, but the virulence can be raised somewhat by animal passage.

Differences in ability of different organisms to break up various sugars has long been used in bacteriology as a means of differentiation, as is illustrated by the typhoid colon group, but on various sugars these streptococci behave in much the same way. The following table gives the results of a careful examination of 100 strains; over half of these were from carriers, while the others came from definite streptococcus infections. During the course of this work several differences appeared at first, but as each tube was examined for purity and for growth and the examination repeated when necessary all differences disappeared and the results were uniform.

Sugar reactions of 100 strains of hemolytic streptococci:

Source of Strain	Num- ber	Glu- cose	Lac- tose	Saccha- rose	Man- nitol	Mal- tose	Dex- trin	Inu- lin	Sal- icin
Tonsils excised	43	+	+	+	—	+	+	—	+
Throat carriers	26	+	+	+	—	+	+	—	+
Empyema	18	+	+	+	—	+	+	—	+
Miscellaneous (middle ear, etc.)	11	+	+	+	—	+	+	—	+

One advance, however, has already been recorded in the simple differentiation of bovine and human types worked out by Avery and Cullen.⁵ These workers have shown that the end reaction of bovine and human strains have a sharply defined range in the hydrogen ion concentration scale and that the simple addition of an indicator such as methyl red serves to distinguish the acid bovine strains with a range from 4.3

to 4.5 from the less acid human strains with a range of 4.8 to 5.3. This advance seems to dispose of one false lead proposed to explain the recent epidemics of streptococcus infections in the army—namely, that they came from milk, butter and cheese. Milk can, of course, spread hemolytic streptococci, but the bovine types are of no clinical significance, and milk is dangerous only if it has been contaminated by human strains. This differentiation may rule out a few cases of bovine strain carriers.

Immunologic Differentiation.—By analogy, with the pneumococci the most promising field is that of differentiation by agglutination. As is well known in the case of pneumococci, the separation of types has been of great value in diagnosis, prognosis, prevention and treatment by focusing attention on certain groups which are more important than the ordinary pneumococci found in the mouth. Some preliminary work of this kind has already been reported by Havens,⁶ although the possible clinical significance of a separation of this kind is not yet known. On the other hand, according to Kinsella and Swift,⁷ the method of complement fixation again shows that these streptococci are alike.

It is evident that practical measures for the control of streptococcus infections through the carrier point of attack must depend on the result of bacteriologic studies. If streptococci can be differentiated into more or less important groups attention can be directed to carriers of the most important group. On the other hand, if the streptococci are all equally dangerous, measures must be based on this fact, but if this is the case frankness demands the statement that the problem will be very difficult on account of the large number of the carriers which exist at present. It is to be hoped that bacteriology may also contribute some specific answer to the following questions:

Is the chronic carrier the reservoir of streptococcus infections or is the disease spread chiefly by cases and by acute contact carriers? Is the chronic carrier dangerous to himself or is he immune? So far the answer to these questions must be attempted on epidemiologic evidence, as no reliable test for virulence or immunity is available in the way of skin reactions or serum reactions.

SUMMARY.

1. Satisfactory carrier work in the effort to control the spread of hemolytic streptococcus infections is difficult for the following reasons:

(a) The carriers may be very numerous, including over one-half of the population.

(b) The streptococci found are nearly all identical culturally with each other and with streptococci isolated from streptococcus lesions.

2. The problem will be made easier if progress is made in regard to—

(a) Virulence or specific test to determine the danger of chronic carriers to themselves and others.

(b) Some differentiation of groups which would limit the work to a practical basis.

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