

STUDIES UPON MINUTE HEMOLYTIC STREPTOCOCCI

II. THE DISTRIBUTION OF MINUTE HEMOLYTIC STREPTOCOCCI IN NORMAL AND DISEASED HUMAN BEINGS*

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In an accompanying communication (1) we have described the primary isolation and the cultural characteristics of a hitherto undescribed group of minute *beta* hemolytic streptococci. In this report, we shall discuss the occurrence of these organisms and that of ordinary *beta* hemolytic streptococci in the throats of normal and diseased human beings.

Methods

The technique of obtaining throat cultures and the methods of primary isolation already described (1) were followed in this study, save in the case of those cultures obtained from the throats of individuals ill with scarlet fever or septic sore throat. The throat swabs from these patients were shaken in 3 cc. of sterile physiological saline instead of the usual 1 cc.

The period of time covered by this study dates from March 29, 1933, until June 12, 1934, 80 per cent of the cultures being taken between October 1, 1933, and April 8, 1934. All of the cultures from normal individuals were obtained during the first 3 months of 1934, that is, during the period of the year in which the incidence of ordinary *beta* hemolytic streptococci is at a high level in Baltimore (2). With the exception of the group of patients ill with glomerular nephritis and a special group of 40 normal individuals, almost all of the cultures were single. Many of the individuals in the nephritic group were swabbed repeatedly at weekly intervals, and in order to have results from a similar group of normal subjects we swabbed 40 individuals once a week for a 12 week period.

Over 75 per cent of the throats were swabbed by one individual and when it was possible the cultural results were checked independently by two of us. Repeatedly we have obtained cultures containing the minute organisms when routine throat

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cultures failed to show them. In practically all instances the identity of the ordinary *beta* hemolytic streptococci and of the minute hemolytic streptococci was confirmed by the morphological appearance of the organisms and their production of hemolysin in sugar-free rabbit's blood broth.

RESULTS

Minute hemolytic streptococci were infrequently found in single cultures from the throats of normal individuals. As is shown in Table I, in a series of 404 cultures from a like number of normal

TABLE I
Incidence of Beta Hemolytic Streptococci and Minute Beta Hemolytic Streptococci in the Throats of Normal and Diseased Human Beings

Status of subjects	No. of subjects in series	No. of cultures	Cultures positive for <i>beta</i> streptococci		Cultures positive for minute streptococci		Subjects positive for <i>beta</i> streptococci		Subjects positive for minute streptococci	
			No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
Normal—single culture.....	404	404	44	11	24	6	44	11	24	6
Normal—multiple culture...	40	471	61	13	37	8	29	73	9	23
Chronic diseases.....	102	102	4	4	4	4	4	4	4	4
Acute respiratory tract diseases.....	108	125	16	13	10	8	15	14	9	8
Scarlet fever.....	110	117	75	68	4	4	70	64	4	4
Acute tonsillitis.....	22	37	37	100	3	8	22	100	3	14
Rheumatic infection.....	59	93	22	24	41	44	18	31	25	43
Recovered from glomerular nephritis.....	19	48	12	25	2	4	9	47	2	11
Glomerular nephritis.....	42	274	103	34	108	36	23	55	33	79

individuals, minute streptococci were found in the throats of 44 of these individuals (11 per cent).

A second group of 40 normal individuals was studied at weekly intervals during the first 3 months of 1934. As will be seen in Table II, 471 throat cultures were obtained and of these 37 (8 per cent) were positive for minute streptococci while 61 (13 per cent) were positive for ordinary *beta* hemolytic streptococci. In this group 9 (23 per cent) individuals showed the minute organisms at one time or the other and 29 (73 per cent) were positive one or more times for ordinary hemolytic streptococci. It is interesting to note that of the 9 indi-

TABLE II

Incidence of Beta Hemolytic Streptococci and of Minute Beta Hemolytic Streptococci in the Throats of 40 Normal Individuals as Determined by Weekly Throat Cultures during a Period of 12 Weeks

Subject	Results of cultures											
	1st. wk.	2nd wk.	3rd wk.	4th wk.	5th wk.	6th wk.	7th wk.	8th wk.	9th wk.	10th wk.	11th wk.	12th wk.
1	—	—	—	—	—	B	—	—	—	—	—	—
2	—	M	M	—	—	—	B	M	—	M	M	M
3	—	—	—	—	B	—	—	B	—	—	—	—
4	—	—	—	—	—	—	—	B	—	—	B	B
5	B	—	—	—	—	—	—	B	—	B	—	—
6	—	—	—	—	—	—	—	—	—	—	—	—
7	—	—	—	—	—	—	—	—	—	—	—	—
8	—	—	—	—	—	M	—	—	—	—	—	—
9	—	—	—	B	—	—	—	—	—	—	—	—
10	—	—	B	B	B	B	B	B	B	B	B	B
11	—	—	—	—	—	—	—	B	—	—	—	—
12	—	BM	M	—	B	—	M	B	—	M	M	M
13	—	—	—	—	—	M	—	—	—	—	—	—
14	—	—	—	—	—	—	B	—	—	—	—	—
15	—	—	—	—	—	—	—	—	B	—	—	—
16	—	—	—	—	—	—	—	B	—	—	—	—
17	—	—	—	—	—	—	—	—	—	—	—	—
18	—	—	—	—	—	—	—	B	B	B	B	B
19	—	—	—	—	—	—	B	—	—	—	—	—
20	—	—	—	—	—	B	—	—	—	—	—	B
21	—	—	—	—	M	—	B	—	M	M	M	M
22	—	B	B	—	—	—	B	—	—	—	B	B
23	B	—	—	—	—	—	—	—	—	—	—	—
24	—	—	—	—	—	—	—	—	—	—	—	—
25	—	—	—	—	—	—	—	—	—	—	—	—
26	—	—	M	M	M	M	M	BM	M	—	M	—
27	—	—	—	—	—	—	B	B	B	B	—	—
28	—	—	—	—	—	B	—	—	—	—	—	—
29	—	—	—	—	—	—	B	—	B	B	—	—
30	—	—	—	—	—	—	B	—	—	—	—	—
31	—	—	—	—	M	—	—	—	B	—	M	M
32	—	—	M	—	—	—	—	—	B	—	—	M
33	—	—	—	—	—	—	—	—	—	—	—	—
34	B	B	—	—	—	—	—	—	—	—	B	—
35	—	—	—	—	—	—	—	—	—	—	—	—
36	—	—	—	—	—	—	B	B	—	—	—	—
37	—	—	—	—	—	—	—	—	—	—	—	—
38	—	—	—	—	—	—	—	—	—	B	B	—
39	—	BM	B	M	—	—	M	M	—	—	—	—
40	B	B	—	—	—	—	—	—	—	—	—	—

B = beta hemolytic streptococci.

M = minute hemolytic streptococci.

— = negative for minute and beta hemolytic streptococci.

viduals in whom the minute organisms were demonstrated, 5 showed definite evidence of chronic infectious processes in the lymphoid tissue of their rhinopharynges.

In a group of ward patients suffering from essentially chronic disease, *e.g.* carcinoma, diabetes, hypertension, 102 single cultures were made from 102 individuals. Only 4 of these cultures (4 per cent) were positive for minute hemolytic streptococci and the same number showed ordinary hemolytic streptococci. Studies of the throat flora of individuals ill with acute respiratory tract affections in which the hemolytic streptococcus does not generally play an important rôle, for instance diphtheria, lobar pneumonia, influenza, colds, measles, hay fever, revealed a low incidence of the organisms, for only 9 (8 per cent) of 108 subjects in this group yielded minute hemolytic streptococci, while 15 (14 per cent) harbored the ordinary hemolytic streptococci.

Studies of the throat flora of individuals who were ill with diseases of proven streptococcus etiology, for example scarlet fever and septic sore throat, showed that these diseases were not associated with a high incidence of minute hemolytic streptococci, a fact demonstrated in Table I. 117 throat cultures were obtained from 110 individuals ill with scarlet fever and only 4 (about 4 per cent) cultures were positive for minute hemolytic streptococci. 75 (68 per cent) cultures showed ordinary *beta* hemolytic streptococci. These last figures on the incidence of *beta* hemolytic streptococci in scarlet fever may seem somewhat low, but as the cultures were obtained from the 1st to the 21st day of the disease, the high incidence of hemolytic streptococci found when cultures are taken during the first days of scarlet fever would not be expected. During the past year we were able to obtain 37 throat cultures from 22 individuals who were suffering from acute follicular tonsillitis. All of the cultures were positive for ordinary *beta* hemolytic streptococci, while 3 (8 per cent) cultures from 3 (15 per cent) individuals showed minute streptococci.

A group consisting of 59 individuals suffering from acute rheumatic fever or from rheumatic heart disease was studied for the presence of *beta* hemolytic streptococci in their rhinopharynges. In 25 (43 per cent) of these individuals minute hemolytic streptococci were found, while only 18 (31 per cent) patients were positive for ordinary hemolytic

tic streptococci. As no attempt was made in this series of patients to correlate the degree of activity of the rheumatic process with the time of the throat cultures, the relatively high incidence of the minute hemolytic streptococci is of interest.

Our final studies were made upon a group of 61 individuals who either had had glomerular nephritis and had recovered or who were suffering from either acute, latent or progressive glomerular nephritis at the time the investigations upon their throat flora were conducted. Of the 61 individuals 19 were considered as being well and in this group minute streptococci were found once in each of 2 individuals, while ordinary hemolytic streptococci were found in 9 individuals in this group.

Table III shows the results of 274 throat cultures obtained from 42 individuals who have been under observation because of the presence of an acute, latent or progressive glomerular nephritis during the past 14 months. From these 42 individuals we have secured 108 (36 per cent) cultures which were positive for minute streptococci and 103 (34 per cent) cultures which showed ordinary *beta* hemolytic streptococci. The minute streptococci were found in 33 (79 per cent) of the members of this group, and in 14 (33 per cent) of the patients they were the only hemolytic streptococci isolated during the period of investigation. Ordinary *beta* hemolytic streptococci were found alone in 4 (10 per cent) members of this group, while 19 (45 per cent) individuals showed both organisms in their throat cultures at various times during the period of study. In 5 (12 per cent) individuals neither representative of the hemolytic streptococcus group was found during the course of our investigation.

DISCUSSION

Minute hemolytic streptococci were infrequently isolated from the throats of a large group of normal individuals, from whose throats only single cultures were taken. However in a smaller group of normal individuals in whom an investigation of the throat flora was made at weekly intervals over a period of 3 months, the organisms were found to occur more frequently although their incidence was considerably lower than that of the ordinary *beta* hemolytic streptococcus.

In individuals who were suffering from a variety of chronic diseases

the incidence of both ordinary and minute *beta* hemolytic streptococci was low and the same was essentially true of individuals ill with acute respiratory tract affections of non-streptococcal origin. The minute organisms were infrequently isolated from the throats of patients who were suffering from scarlet fever or severe acute tonsillitis. In purulent diseases we have on three occasions isolated the minute organisms in pure culture—once from an abscess in the deep tissues of the chest wall and twice from acutely inflamed paranasal sinuses, thus showing that they are capable in themselves of producing infections.

These minute hemolytic streptococci have been isolated most frequently from the throats of individuals who were suffering from glomerular nephritis or from chronic rheumatic infection. In view of the well known association of ordinary *beta* hemolytic streptococci with the progression of these diseases we believe that our findings assume added importance because in 14 of the nephritis group and in 17 of the rheumatic group, minute *beta* hemolytic streptococci were the only members of the hemolytic streptococcus family isolated during the period of investigation. Possibly a careful examination of throat cultures from all subjects ill with these two diseases will eventually reveal all of them to be chronically infected with one or the other type of *beta* hemolytic streptococcus. We feel that the burden of proof, especially in regard to the association of hemolytic streptococci with the progression of glomerular nephritis, rests upon those who state that evidence of *beta* hemolytic streptococcal infestation is lacking in this group of patients.

CONCLUSIONS

1. Minute *beta* hemolytic streptococci were found to occur from one-third to one-half as frequently in normal individuals as do ordinary *beta* hemolytic streptococci.
2. They were rarely isolated from the rhinopharynges of individuals suffering from chronic disease.
3. In acute respiratory tract infection other than that due to the ordinary *beta* hemolytic streptococcus the incidence of minute streptococci was slightly higher than in normal individuals.
4. In acute streptococcal infections, scarlet fever and acute tonsillitis, for example, the incidence of minute hemolytic streptococci did

not significantly vary from the incidence found in normal human beings.

5. Minute *beta* hemolytic streptococci were found in the throats of 33 out of 42 patients ill with glomerular nephritis and in 25 out of 59 patients who were suffering from the various manifestations of rheumatic fever.

6. In glomerular nephritis and rheumatic infection the minute *beta* hemolytic streptococci were isolated from the throats of more patients than were the ordinary *beta* hemolytic streptococci.

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