Epidemiology of Group-A $\beta$-Hemolytic Streptococci as Related to Acute Rheumatic Fever in Miami, Florida

A Six-Year Study

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Episodes of acute rheumatic fever are believed to be triggered by infections with group-A $\beta$-hemolytic streptococci, 10 to 35 days prior to the rheumatic complication. However, both rheumatic fever and rheumatic heart disease are infrequent in Miami, Florida. \(^1\) \(^2\) If the incidence rate of rheumatic disease depends on the frequency of group A streptococci, the low rheumatic rate in Miami should be accompanied by corresponding low streptococcal prevalence. A study was instituted in February 1953 to test this hypothesis.

Methods and Materials

Throat cultures were collected on swabs from 18,329 subjects between February 1953 and May 1955.\(^3\) \(^4\) \(^5\) Each swabbing was carried out by holding 2 swabs together and passing the tips over the tonsillar areas and the posterior pharynx. One of each pair of swabs was plated on beef-infusion agar fortified with 4 per cent sterile defibrinated sheep blood; the other was plated on neopeptone-infusion agar fortified similarly. During the first 3 years, plates were prepared in our laboratory; for the past 3 years, plates prepared commercially (Hyland Laboratories, Los Angeles, California) were used. After 24 hours' incubation at 37 C., plates were read for the presence of $\beta$-hemolytic colonies. Occasionally, poor growth necessitated an additional 24 hours' incubation, generally under anaerobic conditions. Colonies appearing to be $\beta$-hemolytic were subcultured until pure cultures were obtained. Verification of the nature of the organisms depended on $\beta$-hemolysis under anaerobic conditions, with identification by Gram staining after growth in Todd Hewitt broth. Pure cultures then were grouped according to the method of Lancefield,\(^7\) by use of commercial (Difeo) streptococcal antisera, groups A, B, C, F, and G.

During the same period of time, 4,265 blood samples were drawn, and antistreptolysin-O determinations performed on them, by the method of Rantz and Randall.\(^8\)

Epidemiologic procedures for these studies varied from year to year, in order to provide answers to specific questions. Thus, a small group of children were followed repetitively for 3 years, from first through third grades;\(^5\) a county-wide mass survey was conducted in children attending first through third grades;\(^3\) variations in streptococcal incidence and prevalence as related to age were observed;\(^9\) possibilities of streptococcal transmission from child to mother or mother to child were investigated;\(^10\) streptococcal findings and illness resulting in school absence were studied;\(^11\) a case registry of rheumatic fever and glomerulonephritis with intensive follow-up was instituted.\(^11\) \(^12\)

Results

Subjects were considered in the following age classes: 0 to 6, 6 to 9, 9 to 15, University students, adults, and mothers of second-grade children. The prevalence of $\beta$-hemolytic streptococci in these groups is presented in table 1. The findings indicate that the highest incidence was observed in the 6- to 9-year-old children (11.09 per cent), while the lowest was in the mothers of second-grade children (0.2 per cent). This low figure was obtained at the same time that 10.8 per cent of the second-grade children themselves harbored group-A $\beta$-hemolytic streptococci. These differences are highly significant ($p<0.0005$).

Throat swabs collected monthly for 8 consecutive months during the school year from a group of 6- to 9-year-old children yielded positive cultures for group-A $\beta$-hemolytic streptococci at least once in 30 to 40 per cent of the children studied (average 35.49 per cent).\(^5\) \(^6\)

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Table 1

Number and Per Cent of Group-A β-Hemolytic Streptococcal Isolates, According to Age of Subjects, Miami, Florida (January 1953 through June 1955)

<table>
<thead>
<tr>
<th>Age of subjects</th>
<th>No. cultures taken</th>
<th>Group-A no.</th>
<th>β-hem. strep. per cent</th>
<th>All other β-hem. strep.*</th>
<th>No. of samples</th>
<th>Antistreptoc. O titer average</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-6</td>
<td>764</td>
<td>21</td>
<td>2.8</td>
<td>47</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>6-9</td>
<td>11,248</td>
<td>1,247</td>
<td>11.09</td>
<td>2,013</td>
<td>1,808</td>
<td>96</td>
</tr>
<tr>
<td>9-15</td>
<td>2,091</td>
<td>151</td>
<td>7.2</td>
<td>394</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>18-23</td>
<td>631</td>
<td>7</td>
<td>1.0</td>
<td>63</td>
<td>631</td>
<td>96</td>
</tr>
<tr>
<td>23+ (adults)</td>
<td>1,812</td>
<td>40</td>
<td>2.2</td>
<td>195</td>
<td>1,611</td>
<td>73</td>
</tr>
<tr>
<td>Mothers of 2nd grade children</td>
<td>863</td>
<td>2</td>
<td>0.2</td>
<td>49</td>
<td>215</td>
<td>97</td>
</tr>
<tr>
<td>Epidemic=4/58</td>
<td>920</td>
<td>104</td>
<td>11.3</td>
<td>141</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Repeats (A only)</td>
<td>100</td>
<td>64</td>
<td>64.0</td>
<td>64</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Total</td>
<td>18,429</td>
<td>1,636</td>
<td>8.87</td>
<td>2,966</td>
<td>4,365</td>
<td>87</td>
</tr>
</tbody>
</table>


Throat cultures taken simultaneously from mothers and children on 863 occasions (36 pairs of participants) yielded β-hemolytic streptococci from one or both subjects 169 times. The same group of β-hemolytic streptococci was recovered from the throats of both 5 times, and only once were group-A β-hemolytic streptococci found in the cultures from both parent and child.10

Antistreptolysin-O titers performed on blood samples drawn from children 6- to 9-years-old averaged from 82 to 103 units; University students 96 units; adults 73 units; mothers of second-grade students, 97 units.4-6 All bloods were drawn when subjects were clinically well, except for 340 samples taken from children 7- to 8-years of age, among which were studies carried out during 78 respiratory absences. The average antistreptolysin-O titer of these 340 bloods was 82.

Daily absentee records were maintained on 53 second-grade students.10 Cause of absence was determined each time. Thirty-four children had 78 respiratory illnesses (table 2). Throat cultures taken within 24 to 48 hours of initial absence, and prior to administration of antibiotics (which were given only rarely), were negative for β-hemolytic streptococci from 22 subjects, accounting for 41 absences attributed to respiratory infection. Data were not available in 1 episode. Streptococci were recovered from the throats of the remaining 12 children. Four children had 15 respiratory absences, during 10 of which group-C strains were isolated; 2 had 4 illnesses during 2 of which nongroupable strains were recovered. Ten group-A strains were recovered from the throats of the remaining 6 children who suffered 17 absences due to respiratory disease. Of these 6 children, however, only 2 developed their respiratory illnesses within 24 hours of the first isolation of the group-A organisms. In the remaining subjects, group-A organisms were isolated repeatedly for 7 weeks before illness in 1 subject, 6 weeks in another, 10 days in a third, and 7 days in a fourth. Two of the 6 children showed a rise in the antistreptolysin-O titer, only 1 of whom had an illness and initial isolation associated.

Epidemics

In February and March 1955, the appearance of increased numbers of group-A type-6 organisms* led to intensive study in 2 classrooms of 1 school.6 This type of streptococcus was recovered from the throats of 46 per cent and 30 per cent respectively of those cultured. There was no indication in any other classes that these bacteria were prevalent. All but 1 of the 18 children with type-6 strains, from

*Typing was carried out by Dr. Elaine Updyke, of the Communicable Disease Center, U.S.P.H.S., Chamblee, Georgia, or with serum provided by her.
whom sufficient blood samples were available, showed a rise in antistreptolysin-O titer of 2 tubes or greater in serial studies. Despite these rises in titers, the number of absences did not increase. Absenteeism in these 2 classes was no different from that elsewhere in the school. Comparison with absence rates during other months, and with other schools, failed to show any evidence of a "clinical epidemic."

Early in April 1958, group-A type-12 organisms appeared on the increase in 1 school. Nine hundred children, the entire school population (except for 48 who refused or were out of town), had their throats cultured within 2 days. Those who were absent were reached at their homes. Group-A streptococci were isolated from 103 cultures (11 per cent), varying from 7 per cent among sixth grades to 16 per cent in the second grade. These findings are consistent with the average recovery rates previously mentioned as related to the age of children. However, data were collected by individual classes. Of the 29 rooms in the school not 1 had a group of children completely free of group-A organisms.* The range was from 3 per cent (1 of 34) up to 32 per cent (11 of 34). Five of the 7 classrooms with highest percentages (over 15 per cent) were on the first floor of the 2-story building, all emptying on to 1 portion of 1 corridor. One class with a high rate was on the second floor, at the head of the stairway leading to the same portion of the same corridor. The seventh class met on the ground floor in the school cafeteria. No correlations were evident between the streptococcal rates and absenteeism. Of the cultures taken in school, 11.2 per cent (96 of 856) were positive, whereas 17 per cent (7 of 42) of the absentees cultured were positive for group-A streptococci. This difference is not statistically significant ($p>0.20$). When there were siblings, the recovery rate paralleled the over-all school rates.

The case register\textsuperscript{11, 12} of active rheumatic episodes maintained from October 1, 1955, through September 30, 1958, revealed the occurrence of 95 cases.

\*A shortage of typing serum precluded the possibility of typing all isolated organisms.

\begin{table}
\centering
\caption{Recovery of \(\beta\)-Hemolytic Streptococci from Throats of Thirty-Four Second-Grade Children during Seventy-Eight Respiratory Illnesses (October 1956-May 1957)}
\begin{tabular}{lcc}
\hline

Total number of second-grade students studied & 53  \\
Respiratory illnesses: & children 34 & illnesses 78  \\
No. without recovery of \(\beta\)-hemolytic streptococci: & children 22 & illnesses 41*  \\
No. with recovery of \(\beta\)-hemolytic streptococci: & children 12 & illnesses 36  \\
No. positive, group-C \(\beta\)-hemolytic streptococci: & children 4 & illnesses with organism recovered 10  \\
Total illnesses & & 15  \\
No. positive, group-NG \(\beta\)-hemolytic streptococci: & children 2 & illnesses with organism recovered 2  \\
Total illnesses & & 4  \\
No. positive, group-A \(\beta\)-hemolytic streptococci: & children 6 & illnesses with organism recovered 10  \\
Total illnesses & & 17  \\
\hline
\end{tabular}
\end{table}

\textsuperscript{*}Data not available in 1 episode of illness.

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occurrence of 83 episodes, of which 53 satisfied the modified Jones criteria (table 3). One quarter of the total were observed in children under 9 years of age; an additional third, in the 10- to 15-year-old group; 23 in subjects under 30 years old, and the remainder, in patients over 30.

**Discussion**

Obvious rheumatic fever is seen infrequently in Dade County, Florida, as evidenced by the report of only 83 episodes in a 3-year period in a population averaging between 750,000 and 850,000. Group-A \( \beta \)-hemolytic streptococci, on the other hand, are recovered frequently from the throats of local school children, particularly in the 6- to 9-year-old bracket. The high streptococcal incidence and prevalence findings do not correlate with the low rheumatic fever rate.

The infrequency of rheumatic illness might be attributed to the presence of unrecognizable forms of the disease. However, previous studies in Dade County showed that rheumatic heart disease also is infrequent in native-born Miami school children, and that rheumatic heart disease is observed infrequently in autopsies performed on native-born deceased Floridians.

Certainly the small number of rheumatic episodes cannot be attributed to a dearth of group-A \( \beta \)-hemolytic streptococci. Undoubtedly, other factors—climate, socioeconomic status, environment, and heredity, to name a few—must affect the mechanism whereby these bacteria exert their etiologic effect in leading to rheumatic fever.

The ubiquity of \( \beta \)-hemolytic streptococci and the high frequency of recovery from throat cultures suggest that these findings reflect the "carrier state" rather than infections. If infection is defined in terms of clinical illness, undoubtedly the bulk of our isolations were from the throats of carriers. However, if subclinical infection is recognized as that condition in which bacterial recovery is accompanied by immunologic responses such as a rise in antistreptolysin-O titer, approximately 50 per cent of our positive children in serial studies showed a rise of 2 tubes or greater. Although this figure is lower than the 70 to 80 per cent reported from northern centers, the difference is inadequate to explain the low-incidence rate of rheumatic fever.

What about clinical infection related to streptococcal recovery? In a study of school absenteeism due to respiratory illness, the streptococcal recovery rate was significantly higher than the rate of isolation from the throats of children who were not ill. In a second study, 6 of 78 illnesses attributed to respiratory causes were associated with the recovery of group-A \( \beta \)-hemolytic streptococci. In only 2 of these 6 children did the respiratory illness develop within 24 hours of the...

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**Table 3**

*Episodes of Acute Rheumatic Fever in Dade County, Florida, as Reported by Practicing Physicians: Case Register Maintained from October 1955 through September 1958*

<table>
<thead>
<tr>
<th></th>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>3-5</td>
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<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>6-9</td>
<td>3</td>
<td>0</td>
<td>5</td>
<td>4</td>
<td>3</td>
<td>0</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>10-12</td>
<td>1</td>
<td>1</td>
<td>6</td>
<td>4</td>
<td>5</td>
<td>0</td>
<td>12</td>
<td>5</td>
</tr>
<tr>
<td>13-15</td>
<td>1</td>
<td>0</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>15+</td>
<td>4</td>
<td>4</td>
<td>10</td>
<td>8</td>
<td>6</td>
<td>2</td>
<td>20</td>
<td>14</td>
</tr>
<tr>
<td>Unlisted</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Subtotals</td>
<td>10</td>
<td>7</td>
<td>24</td>
<td>20</td>
<td>19</td>
<td>3</td>
<td>53</td>
<td>30</td>
</tr>
</tbody>
</table>

*Present = Jones criteria for Rheumatic Fever satisfied.

†Absent = Jones criteria for Rheumatic Fever not satisfied.*
initial recovery of a group-A organism; one had a rise in antistreptolysin-O titer. Mothers of the children in this portion of the investigation had their throats cultured at the same time as the children. No cross infection was apparent.

Although the group-A β-hemolytic streptococcus may be the cause of clinical illness (as seen by the higher recovery rate of these organisms from the throats of children ill with respiratory infections than from those not ill), the frequency of streptococcal isolation from the throats of well children, the failure to develop rises in antistreptolysin-O titer in respiratory illnesses occurring at the same time that group-A strains were isolated, and the observation that respiratory infections may be due often to organisms belonging to groups B, C, or G, confuse the streptococcus-illness situation in Dade County, Florida. This lack of clear-cut relationship between recovery of organisms and respiratory illness may be different in Miami from other climates, and in order to clarify the relationship between streptococcal findings, clinical respiratory involvement, and the incidence of acute rheumatic fever comparative studies in other geographic locations are essential.

Summary

Rheumatic fever and rheumatic heart disease are infrequent in Dade County, Florida.

Conversely, β-hemolytic streptococci are recovered frequently, particularly from the throats of children 6 to 9 years old.

The relationship between group-A β-hemolytic streptococci, clinical illness, and rheumatic illness may be different in South Florida from elsewhere in the United States.

Summario in Interlingua

Febre rheumatic e rheumatic morbo cardiac non es frequente in le Contato Dade in Florida.

Del altere latere, streptococcos beta-hemolytic es isolate frequentemente, super toto ab le gurgites de juveniles de inter 6 e 9 annos de etate.

Il es possibile que le relation inter streptococcos beta-hemolytic del Gruppo A, morbo clinic, e morbo rheumatic non es le mesme in Sud-Florida como alteruti in le Statos Unite.

References

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