Low Rates of Streptococcal Pharyngitis and High Rates of Pyoderma in Australian Aboriginal Communities Where Acute Rheumatic Fever Is Hyperendemic

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(See the editorial commentary by Kaplan and Bisno on pages 690–2)

Background. Acute rheumatic fever is a major cause of heart disease in Aboriginal Australians. The epidemiology differs from that observed in regions with temperate climates; streptococcal pharyngitis is reportedly rare, and pyoderma is highly prevalent. A link between pyoderma and acute rheumatic fever has been proposed but is yet to be proven. Group C β-hemolytic streptococci and group G β-hemolytic streptococci have also been implicated in the pathogenesis.

Methods. Monthly, prospective surveillance of selected households was conducted in 3 remote Aboriginal communities. People were questioned about sore throat and pyoderma; swab specimens were obtained from all throats and any pyoderma lesions. Household population density was determined.

Results. From data collected during 531 household visits, the childhood incidence of sore throat was calculated to be 8 cases per 100 person-years, with no cases of symptomatic group A β-hemolytic streptococci pharyngitis. The median point prevalence for throat carriage was 3.7% for group A β-hemolytic streptococci, 0.7% for group C β-hemolytic streptococci, and 5.1% for group G β-hemolytic streptococci. Group A β-hemolytic streptococci were recovered from the throats of 19.5% of children at some time during the study. There was no seasonal trend or correlation with overcrowding. Almost 40% of children had pyoderma at least once, and the prevalence was greatest during the dry season. In community 1, the prevalence of pyoderma correlated with household crowding. Group C and G β-hemolytic streptococci were rarely recovered from pyoderma lesions.

Conclusions. These data are consistent with the hypothesis that recurrent skin infections immunize against throat colonization and infection. High rates of acute rheumatic fever were not driven by symptomatic group A β-hemolytic streptococci throat infection. Group G and C β-hemolytic streptococci were found in the throat but rarely in pyoderma lesions.

Acute rheumatic fever (ARF) remains an important cause of heart disease among Aboriginal people in tropical Australia. ARF rates of >300 cases per 100,000 persons per year (among children 5–14 years old) in this population contrast sharply with rates <5 cases per 100,000 persons per year in the non-Aboriginal population [1], a rate that is similar to those in other wealthy countries [2]. Yet the epidemiology appears to differ from that observed in regions with temperate climates [3]. Despite having some of the highest documented rates of ARF and rheumatic heart disease (RHD) in the world, pharyngeal carriage rates of group A β-hemolytic streptococci (GAS) appear to be low [4], classic rheumatic M serotypes are absent [5], and the distinction between strains that cause ARF and glomerulonephritis, on the basis of genotype and site of recovery, is ill-defined [6]. Similar patterns of throat carriage and/or infection and pyoderma have been found.
in other regions with high burdens of ARF and RHD, including Ethiopia, Jamaica, and southern India [7, 8].

A possible causal relationship between GAS skin infection and ARF and RHD in the tropics was suggested 25 years ago [9] and has been investigated in Australia since the mid-1990s [10]. The hypothesis has been challenged [11], and the question remains unresolved. A key piece of missing evidence has been documentation that GAS pharyngitis is truly uncommon in these communities.

In countries with temperate climates, GAS pharyngitis and throat carriage are seasonal and are associated with overcrowded housing. In tropical regions, the picture is less clear. Nevertheless, wherever there is overcrowding, the community burden of β-hemolytic streptococci (BHS) tends to be high. This increases the opportunity for genetic diversity, by intraspecies and interspecies transfer of key virulence factors and by blurring of established genotypic and phenotypic boundaries [12].

*S. pyogenes* group C β-hemolytic streptococci (GCS)- or group G β-hemolytic streptococci (GGS)–specific polysaccharides. Some strains are capable of causing classic streptococcal diseases and their sequelae [13]. They are commonly recovered from throat specimen cultures, especially in tropical regions, and they exchange genetic determinants with GAS, including those for virulence factors [14, 15]. Their potential role in poststreptococcal disease prompts further investigation.

The aim of our study was to conduct prospective surveillance for streptococcal infection and colonization of the throat and skin among families of people with known previous cases of ARF and/or RHD in remote Aboriginal communities to further elucidate the potential relationship between pyoderma and ARF. Specifically, we sought to document the burden of GAS pharyngitis and pyoderma, age distribution, seasonal variation, and the link to domestic overcrowding. A secondary aim was to assess the contributions of GCS and GGS to throat infection and colonization, as well as their roles in pyoderma.

**METHODS**

**Study sites and consultation.** The study was conducted in 3 remote Aboriginal communities in the Top End of the Northern Territory of Australia, a vast and sparsely populated region. It has a wet season that extends from November to April and a dry season that extends from May to October. Surveillance was conducted from August 2003 to June 2005 (inclusive). Households in community 1 were included for the whole surveillance period. Surveillance commenced in community 2 in August 2003 but was transferred to community 3 in July 2004, because of difficulties with transport and waning community support. The study was approved by the local ethics committee before community, family, and individual consent was obtained.

**Definition of a household.** These communities have highly mobile populations. Following up each enrolled individual for a prolonged period was considered to be an impossible task. For this reason, we decided to follow up households. Households with a known history of ARF and/or RHD were selected to increase chances of encountering additional cases of ARF. One aim was to obtain appropriate information and perform cultures in the months prior to the onset of symptoms, should someone in the study develop ARF. A household was defined as a family group that lived in 1 house or 2 houses on adjacent quarter-acre blocks. For the purposes of calculating household size, people were considered to belong to a household if they said they belonged at the time of enrollment and were present when the household was visited on at least 2 subsequent occasions. We also determined the number of occupants per bedroom.

**Household visits.** Researchers visited households on a monthly basis. Participants present at the time were asked whether they had a sore throat or skin sores. Each throat was examined, and swab specimens were obtained for culture. Limbs and exposed areas were examined for pyoderma and other skin conditions, and swab specimens were obtained according to a standard protocol. This process was called a "consultation." Pyoderma was defined as the presence of ≥1 pustular, crust, or vesicular lesion or dry-but-inflamed skin ulcers ≥1 cm in diameter. Noninfected insect bites and noninflamed, partly-healed pyoderma lesions were excluded. People with pyoderma, symptomatic pharyngitis, or other medical conditions of concern were taken to the health center for treatment. Swab specimens were inoculated onto culture plates (horse blood agar and a selective media containing colistin and nalidixic acid) and transported by aircraft to the laboratory in Darwin, Australia [16].

**Laboratory methods.** Culture plates were incubated at 37°C in 5% CO₂. They were examined after 24 h and after 48 h. Subculture was performed for later identification of BHS using a Streptococcal Grouping Kit (Oxoid Diagnostic Reagents). One colony was selected for typing, unless there were obvious differences in colonial morphology and/or intensity of hemolysis. Beginning in May 2004, *Staphylococcus aureus* was also identified from pyoderma swab specimens using colonial morphology and Staphytec Plus (Oxoid).

**Data analysis.** Data were analyzed using Stata software, version 8.0 (Stata). Period prevalence was calculated by dividing the number of episodes of throat specimen cultures positive for BHS or skin sores by the number of consultations for the study period. Monthly visits to communities provided point prevalence rates; median point prevalence was calculated using data collected from all visits over the study period for each community. Incidence density for sore throats was calculated by assuming a duration of 3.5 days [17] and using the following equation: incidence per
100 person-years = ST ÷ OB ÷ 3.5 × 365 × 100 (where ST is the number of episodes of sore throat and OB is the number of observations). Crowding was defined in terms of the number of people per bedroom and was related to episodes of BHS throat carriage or pyoderma per household observation using Pearson’s correlation coefficient (r²). The 95% CIs were calculated using standard methods, and χ² analysis was used to compare observed differences in proportions.

RESULTS

Enrollment. Forty-nine households and 1173 people were enrolled. There were 531 household visits. A total of 787 people had purulent pharyngitis. GGS was recovered from another which was 26% (interquartile range [IQR], 15%–33%).

Assessment of sore throat. Of 4842 consultations, sore throat was reported on 9 occasions (0.19%; 95% CI, 0.10%–0.35%). Purulent pharyngitis was observed on only 2 occasions (0.03%). GAS was recovered from 2 people who reported having a sore throat, both of whom were adults, one of whom had purulent pharyngitis. GGS was recovered from another adult with a sore throat in the absence of purulent pharyngitis.

The incidence density for sore throat was 19 episodes per 100 person-years (95% CI, 12–28 episodes per 100 person-years) and for symptomatic GAS pharyngitis, the incidence density was 4 episodes per 100 person-years. In children, the incidence density for sore throat (on the basis of 2 reported episodes of sore throat) was 8 episodes per 100 person-years (95% CI, 4–15 episodes per 100 person-years), and for symptomatic GAS pharyngitis, the incidence density was 0.

Recovery of BHS from the throat. One or more BHS isolates were recovered from the throat on 558 occasions (11.5%), as follows: GAS, 216 specimens (4.5%); GCS, 80 specimens (1.7%); and GGS, 262 specimens (5.4%) (table 2). Two BHS isolates were recovered from the same specimen on 13 occasions, and 3 isolates (GAS, GCS, and GGS) were recovered on 1 occasion. The median point prevalence for BHS throat carriage in children was 9.6% (IQR, 7.4%–15.8%), as follows: GAS, 3.7% (IQR, 2.3%–6.0%); GCS, 0.7% (IQR, 0%–2.6%); and GGS, 5.1% (IQR, 2.8%–7.8%). GAS was recovered from the throat on at least 1 occasion in 126 children (19.5%), on 2 occasions in 20 children (3.1%), and on 3 occasions in 3 children (0.5%). GGS was recovered at least once from 130 children (20.2%); GGS was recovered from 3 children on 4 occasions and from 2 children on 5 occasions. Throat carriage of all BHS peaked in the 10–14-year-old age group, with a sharp drop off in late adolescence (figure 1).

Almost all (75 of 80) GCS isolates came from community populations with household crowding.

Table 1. Community populations with household crowding.

<table>
<thead>
<tr>
<th>Community</th>
<th>Approximate community population</th>
<th>No. of households enrolled (no. of people enrolled)</th>
<th>Median no. of people per house (range)</th>
<th>Median no. of people per bedroom (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2500</td>
<td>18 (548)</td>
<td>17 (9–33)</td>
<td>6.9 (2.8–16.5)</td>
</tr>
<tr>
<td>2</td>
<td>800</td>
<td>12 (84)</td>
<td>7 (2–14)</td>
<td>2.3 (1–4.7)</td>
</tr>
<tr>
<td>3</td>
<td>1800</td>
<td>19 (541)</td>
<td>14 (6–27)</td>
<td>7.5 (1.5–13.0)</td>
</tr>
</tbody>
</table>

Table 2. Recovery rates of β-hemolytic streptococci (BHS) from the throat.

<table>
<thead>
<tr>
<th>Total no. of throat swab specimens, by community and age group</th>
<th>BHS</th>
<th>No. [%] of throat swab specimens (95% CI)</th>
<th>GAS</th>
<th>GCS</th>
<th>GGS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community 1 (n = 3016)</td>
<td>387</td>
<td>[12.8] (11.7–14.1)</td>
<td>134</td>
<td>[4.4] (3.7–5.2)</td>
<td>75</td>
</tr>
<tr>
<td>Children &lt;15 years old (n = 1701)</td>
<td>274</td>
<td>[16.1] (14.4–17.9)</td>
<td>88</td>
<td>[5.2] (4.2–6.3)</td>
<td>55</td>
</tr>
<tr>
<td>Community 2 (n = 295)</td>
<td>12</td>
<td>[4.1] (2.1–7.0)</td>
<td>6</td>
<td>[2.0] (0.8–4.4)</td>
<td>...</td>
</tr>
<tr>
<td>Children &lt;15 years old (n = 135)</td>
<td>10</td>
<td>[7.4] (3.6–13.2)</td>
<td>5</td>
<td>[3.7] (1.2–8.4)</td>
<td>...</td>
</tr>
<tr>
<td>Community 3 (n = 1531)</td>
<td>159</td>
<td>[10.4] (8.9–12.0)</td>
<td>76</td>
<td>[5.0] (3.9–6.2)</td>
<td>5</td>
</tr>
<tr>
<td>Children &lt;15 years old (n = 858)</td>
<td>113</td>
<td>[13.2] (11.0–15.6)</td>
<td>58</td>
<td>[6.8] (5.2–8.7)</td>
<td>4</td>
</tr>
<tr>
<td>Total (n = 4842)</td>
<td>558</td>
<td>[11.5] (10.6–12.5)</td>
<td>216</td>
<td>[4.5] (3.9–5.1)</td>
<td>80</td>
</tr>
<tr>
<td>Total for children &lt;15 years old (n = 2694)</td>
<td>397</td>
<td>[14.7] (13.4–16.1)</td>
<td>151</td>
<td>[5.6] (4.8–6.5)</td>
<td>59</td>
</tr>
</tbody>
</table>

NOTE. GAS, group A β-hemolytic streptococci; GCS, group C β-hemolytic streptococci; GGS, group G β-hemolytic streptococci.

* No date of birth was available for 13 people.
Figure 1. Age distribution and throat carriage of β-hemolytic streptococci (BHS) and pyoderma. The peak age group for throat carriage of BHS is the 10–14-year-old group, and the peak age group for throat carriage of pyoderma is the 5–9-year-old group. The number of people enrolled in each age group is shown in parentheses. GAS, group A β-hemolytic streptococci; GCS, group C β-hemolytic streptococci; GGS, group G β-hemolytic streptococci.

Table 3. Prevalence of pyoderma by community and recovery of β-hemolytic streptococci (BHS).

<table>
<thead>
<tr>
<th>Community</th>
<th>No. of consultations, by community and age group</th>
<th>No. of episodes of pyoderma (period prevalence, 95% CI)</th>
<th>Median point prevalence (IQR)</th>
<th>No. (%) of occasions on which BHS was recovered</th>
<th>No. of isolates GAS GCS GGS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community 1 (n = 3034)</td>
<td>287 [9.5] (8.4–10.6)</td>
<td>7.3 (5.4–10.3)</td>
<td>80 (27.9)</td>
<td>86</td>
<td>3</td>
</tr>
<tr>
<td>Children &lt;15 years old (n = 1711)</td>
<td>260 [15.2] (13.5–17.0)</td>
<td>11.9 (8.2–20.6)</td>
<td>73 (28.1)</td>
<td>77</td>
<td>3</td>
</tr>
<tr>
<td>Community 2 (n = 299)</td>
<td>38 [12.7] (9.2–17.0)</td>
<td>11.8 (6.2–12.9)</td>
<td>5 (13.2)</td>
<td>5</td>
<td>...</td>
</tr>
<tr>
<td>Children &lt;15 years old (n = 138)</td>
<td>35 [25.4] (18.3–33.4)</td>
<td>20.0 (0–28.5)</td>
<td>5 (14.3)</td>
<td>5</td>
<td>...</td>
</tr>
<tr>
<td>Community 3 (n = 1533)</td>
<td>130 [8.5] (7.1–10.0)</td>
<td>6.1 (3.5–10.8)</td>
<td>33 (25.4)</td>
<td>34</td>
<td>...</td>
</tr>
<tr>
<td>Children &lt;15 years old (n = 859)</td>
<td>118 [13.7] (11.5–16.2)</td>
<td>14.1 (7.9–19.3)</td>
<td>30 (25.4)</td>
<td>31</td>
<td>...</td>
</tr>
</tbody>
</table>

**NOTE.** GAS, group A β-hemolytic streptococci; GCS, group C β-hemolytic streptococci; GGS, group G β-hemolytic streptococci; IQR, interquartile range.
Why are observed rates of GAS pharyngitis so low among Aboriginal children when rates of ARF and RHD are so high? One explanation is that it is an uncommon disease in this population. If so, recurrent pyoderma may be playing an immunizing role, with a subsequent reduction in the rate of GAS pharyngitis. Alternatively, it may be that GAS pharyngitis is largely asymptomatic in Aboriginal children, more so than in other populations. This would be difficult to prove, because the use of serial phlebotomy to measure increases in antistreptococcal antibody levels is unacceptable in Aboriginal communities, and children already have high background titers of antistreptolysin O antibodies and anti-DNase B [26]. Infection with GCS or GGS can also raise antistreptolysin O titers [13]. An additional explanation is that children are reluctant to admit having a sore throat because of shyness, stoicism, or the threat of a painful injection. It has also been suggested that children may not understand the question “do you have a sore throat,” especially in regions where multiple languages are spoken. We believe that this problem has been minimized in our study, because Aboriginal researchers asked the questions using the local language. Rather than a clinic-based survey that depends on health-seeking behavior, our study is more likely to ascertain all cases of sore throat, mild or severe.

In regions with temperate climates, throat carriage rates of GAS in school-age children range from 15% to 30% [18, 20, 23, 27, 28]. In tropical and subtropical regions, the picture is more varied and ranges from 4% to 17% [29, 30]. The prevalence of childhood GAS throat carriage in our study is in step with the low end of the reported range.

Throat carriage rates of GCS and GGS can be equal to or surpass those of GAS in tropical and subtropical regions, yet
they often have been ignored, because they are not considered to be a cause of ARF [31]. In this study, the rate of throat carriage of GGS was high in communities 1 and 3, and the rate of throat carriage of GCS was relatively high in community 1. Given that interspecies transfer of virulence genes (between GAS, GCS, and GGS) is likely to be more intense in regions with high endemicity [15], GCS and GCS could well play an immune-priming role in ARF in these settings.

Overall seasonal variations in the rate of throat carriage of GAS and GGS were minimal, although it is difficult to draw conclusions, because communities 2 and 3 were each followed up for only 1 year. In most regions with temperate climates, the rate of throat carriage peaks in the cooler months [18, 23, 25, 32]. Notably, there is no seasonal variation in the incidence of ARF in the Top End region [33].

There was no correlation between GAS throat carriage and household crowding, although there was a correlation between the prevalence of pyoderma and crowding in community 1. Crowding has been associated with worse health outcomes, including those for skin infection in Top End Aboriginal communities [34]. In early US military studies, acquisition of pharyngeal GAS was inversely proportional to the distance between barracks beds [35], and crowding has been identified by some authors [36] (but not all [22]) as being a risk factor for ARF and RHD. A link between household crowding and pyoderma has also been reported [37–39]. In this study, the correlation between crowding and pyoderma in community 1 may have been influenced by a number of unidentified confounding factors. The seasonal result is paradoxical, because community populations are usually reduced in the dry season; this is demonstrated by school attendances (M.I.M., unpublished observation) and the number of people present at the monthly household visits. The dry season brings increased outdoor activity and a greater chance of minor skin trauma; at the same time, children tend to avoid swimming during these months, because they find the water to be too cold.

The prevalence of pyoderma in children was high (11.9%–20%) but much lower than previously reported in the region [40]. This could be a result of recently introduced “healthy skin” programs and “scabies days,” especially in community 1. Not only were rates of pyoderma lower, but there were higher rates of GAS pharyngeal carriage than were previously documented [4, 26], further supporting the premise that they may be reciprocal, one protecting against the other. GAS was the predominant BHS recovered from pyoderma lesions, and reasons for the absence of GCS and GGS are not obvious. Human strains of GCS and GGS have the M protein and can cause pharyngitis [13]. Almost invariably, these strains also possess class I mmm genes, which are supposedly associated with throat rather than skin colonization [41]. GGS and/or GCS can cause poststreptococcal glomerulonephritis, reactive arthritis, and invasive soft-tissue infections [13], but information about their role in pyoderma is scant.

Although this study had limitations, including variability in the technique of collecting and processing swab specimens [16], a high turnover of household participants, and the move from community 2 to community 3, the size of the study and the consistency of the data over the duration of surveillance suggest that our findings likely represent the true epidemiology of BHS infection and carriage in this population. Because we targeted households with an established risk for ARF and RHD, our findings may not represent the epidemiology for the whole community.

In summary, in this tropical region with high rates of ARF and RHD, GAS pharyngitis is rare, whereas pyoderma is common and possibly associated with domestic overcrowding and the dry season. These data are consistent with the hypothesis that recurrent skin infections immunize against throat colonization and infection. They provide additional support for the contention that, in this population at least, ARF does not invariably follow symptomatic GAS throat infection. GGS and GCS are commonly found in the throat, but not on the skin, and their pathogenic role has yet to be elucidated.

Acknowledgments

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Potential conflicts of interest. All authors: no conflicts.

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