Acute Otitis Media Caused by *Streptococcus pyogenes* in Children

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(See the editorial commentary by Shulman and Tanz on pages 42–4)

**Background.** *Streptococcus pyogenes*, or group A β-hemolytic Streptococcus (GAS), is an important causative agent of bacterial pharyngotonsillitis and skin, soft-tissue, and invasive infections. Although it is also an important pathogen in acute otitis media (AOM), its exact role has not been determined.

**Methods.** Patients aged 0–18 years with AOM, from whom a specimen of middle-ear fluid was obtained and cultured during 1999–2003, were enrolled. *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, and GAS were considered pathogens. Information collected included demographic characteristics, clinical history, and signs and symptoms.

**Results.** GAS otitis was observed in 350 (3.1%) of 11,311 episodes (of which 117 were also culture-positive for other pathogens). The other 10,961 episodes involved *H. influenzae* only ( ), *S. pneumoniae* only ( ), dual infection with *H. influenzae* and *S. pneumoniae* ( ), *M. catarrhalis* only ( ), and other combinations of pathogens (n = 271). Increased age and Jewish ethnicity were independent, significant, positive risk factors for GAS AOM, and fall season was a negative risk factor. Episodes of GAS infection were less frequently bilateral, febrile, and accompanied by other systemic findings than were other episodes of other types of infection. Most patients with GAS AOM presented with acute drainage from the ears. A lower proportion of cases of AOM were due to GAS in children with recurrent AOM and in patients recently treated with antibiotics, compared with patients with AOM who did not have these factors. The risk for mastoiditis was highest among patients with GAS AOM, compared with patients infected with other pathogens: 11.6 episodes per 1000 episodes of GAS AOM, compared with 2.2, 0.3, and 0 episodes of mastoiditis per 1000 episodes of AOM due to *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*, respectively.

**Conclusion.** Compared with AOM caused by pathogens other than GAS, GAS AOM is characterized by older age and higher local aggressiveness manifested by lower rates of fever and respiratory symptoms and higher rates of tympanic perforation and mastoiditis.

*Streptococcus pyogenes* (or group A β-hemolytic *Streptococcus* GAS) is well recognized as the most common causative agent of bacterial pharyngotonsillitis in school-aged children. It is one of the most important pathogens that cause skin and soft-tissue infections [1] and is also associated with septicemia and other severe complications [2, 3]. In the first half of the 20th century, GAS was the pathogen most frequently isolated from people with acute otitis media (AOM), especially in cases where it was complicating scarlet fever and measles [4]. However, since the 1950s, it has been rapidly replaced by *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*, and it is now ranked only fourth among pathogens that cause AOM and in recent years has caused <10% of all cases [5]. Because of this small proportion, it has, in the past, not been possible to study the characteristics of GAS AOM, even in a relatively large case series.

During the past 5 years, a large database on cases of AOM for which tympanocentesis was performed to obtain culture specimens was compiled by our study group. The database has enabled us to compare various characteristics of GAS AOM with those of AOM caused by other pathogens and attempt to determine whether GAS AOM has some unique epidemiological and clinical features.
METHODS

Study population and setting. The Negev region is a heterogeneously populated area, with ∼500,000 inhabitants (of whom >150,000 are children) belonging to 2 major ethnicities, Jewish and Moslem Bedouin. The Jewish population’s lifestyle and standards of living can be compared with those of developed countries, whereas the Bedouin population is still in transition from a semi-nomadic lifestyle to permanent settlement. About 40% of the Bedouins are still scattered in shanty towns. This population can be compared to that of a developing nation. The Soroka University Medical Center is the only hospital for the entire region, and its clinical microbiology laboratory provides services both to the hospital and to >60% of the community. Thus, >95% of all middle ear fluid cultures from the region are performed in this laboratory [6].

Patients and procedures. We enrolled patients aged 0–18 years with AOM from whom a specimen of middle-ear fluid was obtained and cultured during January 1999–December 2003. Culture specimens were obtained either by tympanocentesis or by collection of pus that drained from the ear. The diagnosis of AOM was made by a pediatrician, a family physician, or an otolaryngologist. Demographic and clinical information was prospectively obtained from children with cultures positive for S. pneumoniae, H. influenzae, and/or M. catarrhalis from January 1999 through December 2003, and from children with cultures that were performed from November 2001 through December 2003 and were positive for GAS.

For each episode, we collected information on the patient’s age, sex, and ethnicity; the season the episode occurred; the patient’s body temperature and symptoms, including vomiting and symptoms of upper-respiratory infection; the laterality of the AOM (i.e., whether it was unilateral or bilateral); the method of acquisition of the culture specimen (i.e., during tympanocentesis or from pus draining from ear after spontaneous perforation of the middle-ear cavity); and the patient’s recent history of antibiotic treatment. Data were obtained from the medical charts, the child’s physician, or the child’s parents, as appropriate.

For an episode of infection to be classified as new, it had to occur >30 days after any previous episode caused by the same organism. If caused by a different organism (including β-lactamase-positive H. influenzae versus β-lactamase-negative H. influenzae or different serotypes of S. pneumoniae), an episode was classified as new even if it occurred <30 days after the previous episode.

Tympanocentesis and transport of specimens. Tympanocentesis was performed by an otolaryngologist using a specially curved needle attached to a tuberculin syringe that acts as a suction trap. The material obtained by tympanocentesis or by collection of pus drained from the ear canal was applied onto a sterile swab that was sent to the clinical microbiology laboratory of Soroka University Medical Center in a transport medium (MW 173 Amies Medium Transwab, Medical Wire and Equipment; Polty, United Kingdom) within 12 h.

Bacteriologic analysis. The swabs were plated on trypticase agar containing 5% sheep blood and 5.0 μg/mL gentamicin and on chocolate agar. The plates were incubated aerobically at 35°C for 48 h. Presumptive identification of S. pneumoniae was based on the presence of α-hemolysis and inhibition of optochin and was confirmed by positive results from a slide agglutination test (Phadebact; Boule Diagnostics AB).

H. influenzae was identified on the basis of Gram staining, growth on chocolate agar, failure to grow on trypticase agar with added sheep blood, and nutritional requirement of both hemin and nicotine adenine dinucleotide. β-Lactamase production was tested by determined by the chromogenic cephalosporins method by using nitrocefin as the substrate [7]. M. catarrhalis was identified on the basis of Gram staining, positive oxidase reaction, and characteristic biochemical profiling, as determined by the API NH kit (BioMérieux), and was confirmed by the NET kit (Carr Scarborough Microbiologicals) [7]. Streptococcus pyogenes was identified on the basis of the presence of β-hemolysis, susceptibility to bacitracin, and positive coagglutination with the streptococcal grouping kit manufactured by Oxoid.

Only S. pneumoniae, H. influenzae, M. catarrhalis, and GAS were considered pathogens. An infection was defined as mixed if >2 pathogens grew from cultures of specimens obtained from the same ear or if different pathogens grew from cultures of specimens obtained from different ears during the same visit.

Statistical analysis. Data were recorded using Microsoft Office Access 2000 software (Microsoft). Statistical analysis was performed with SPSS 10.0 software (SPSS). Contingency table analysis was performed using the χ² test or Fisher’s exact test, as appropriate. We also performed χ² testing to calculate linear trend in proportions and goodness of fit testing to compare mean ages. Relative risk and 95% CI values were used to compare the risk of isolation of GAS between age groups. OR values, as estimates of the relative risks from multivariate logistic regression models, were used to define independent risk factors associated with isolation of GAS. We calculated 95% exact binomial CIs according to criteria established by Clopper and Pearson [8]. P < .05 was considered significant for all calculations.

RESULTS

A total of 11,311 episodes of AOM were recorded during the 5-year period from January 1999 through December 2003. Of these, culture specimens from 6170 episodes (54.5%) were obtained by tympanocentesis, culture specimens from 1810 episodes (16.0%) were obtained by collection of pus that drained from the ear, and no information regarding the source of cul-

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A. Proportion of episodes with culture positive for any pathogen and episodes with culture positive for group A β-hemolytic Streptococcus (with or without a pathogen causing otitis).

B. Proportion of episodes with culture positive for GAS (with or without other pathogens).

**Figure 1.** Culture results for 11,263 episodes of acute otitis media, by patients’ age group. A, Proportion of episodes with culture positive for any pathogen and episodes with culture positive for group A β-hemolytic Streptococcus (with or without a pathogen causing otitis). B, Proportion of episodes with culture positive for GAS (with or without other pathogens). *P < .001 for decrease. **P < .001 for increase.
Table 1. Comparison of mean age and ethnicity of patients with episodes of acute otitis media (AOM) caused by group A β-hemolytic Streptococcus (GAS) and episodes of AOM caused by GAS and other pathogens.

<table>
<thead>
<tr>
<th>Variable</th>
<th>GAS only</th>
<th>GAS and other pathogens</th>
<th>Haemophilus influenzae only</th>
<th>Streptococcus pneumoniae only</th>
<th>H. influenzae and S. pneumoniae</th>
<th>Moraxella catarrhalis only</th>
<th>Other combinations of pathogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of episodes</td>
<td>233</td>
<td>117</td>
<td>2507</td>
<td>2131</td>
<td>1290</td>
<td>129</td>
<td>271</td>
</tr>
<tr>
<td>Mean age of patient, months ± SDa</td>
<td>23.4 ± 26.3</td>
<td>18.4 ± 18.8</td>
<td>12.1 ± 10.5</td>
<td>12.4 ± 14.2</td>
<td>12.5 ± 9.4</td>
<td>10.7 ± 11.7</td>
<td>12.0 ± 11.2</td>
</tr>
<tr>
<td>Jewish ethnicity of patient, % of episodesb</td>
<td>57.5</td>
<td>44.4</td>
<td>43.3</td>
<td>43.8</td>
<td>31.9</td>
<td>54.3</td>
<td>37.3</td>
</tr>
</tbody>
</table>

a P < .001 for comparison of GAS AOM (infection with GAS only or with GAS and another pathogen) with all non-GAS categories of AOM, except comparison with "other combinations of pathogens," for which P = .065.
b P < .001 for difference in distribution between ethnic groups.

tarrhalis (n = 1), and combinations of >2 pathogens (n = 27).

The median ages of patients with AOM due to GAS only (median age, 16.7 months) and of patients with mixed infection involving GAS and other pathogens (median age, 15.2 months) were higher than the median ages of all other patient groups, which were as follows: infection with S. pneumoniae only, 9.4 months; infection with H. influenzae only, 10.0 months; mixed infection with S. pneumoniae and H. influenzae, 10.7 months; infection with M. catarrhalis only, 7.2 months; and infection with other combinations of pathogens, 9.1 months. Although the proportion of episodes that were culture-positive for ≥1 pathogen decreased with increased age, the proportion of episodes positive for GAS increased with increased age (figure 1). The proportion of episodes that were culture-positive for GAS increased from 122 (1.9%) of 6406 episodes in patients aged <12 months to 122 (3.5%) of 3467 episodes in patients aged 12–23 months and to 103 (7.4%) of 3190 episodes in patients aged ≥24 months (P < .001). For episodes that were culture-positive for any pathogen, the chance that GAS would be isolated was 3.1% for patients aged <12 months, 6.1% for patients aged 12–23 months, and 15.3% for patients aged ≥24 months (P < .001). In other words, the relative risk (RR) of an episode involving GAS in patients aged 12–23 months and those aged ≥24 months, compared with that of patients aged <12 months, was 1.85 (95% CI, 1.44–2.37) and 3.89 (95% CI, 3.01–5.02), respectively. The respective RR and 95% CI for GAS otitis, for culture-positive episodes, was 2.0 (95% CI, 1.57–2.56) and 5.03 (95% CI, 3.92–6.45).

For further analysis, we divided episodes with cultures positive for ≥1 pathogen into 7 categories: GAS only (n = 233), GAS and other pathogens (n = 117), H. influenzae only (n = 2507), S. pneumoniae only (n = 2131), H. influenzae and S. pneumoniae (n = 1290), M. catarrhalis only (n = 129), and other combinations of pathogens (n = 271) (table 1). Patients with the highest ages were those with GAS AOM, followed by patients with mixed infection with GAS and other pathogens (P < .001 for patients with infection caused by GAS only and patients with mixed infection involving GAS and other pathogens, against all other non-GAS groups; P = .065 for patients with mixed infection involving GAS and other pathogens vs. patients with other combinations of mixed infection).

The distribution of the 7 categories was different between the 2 ethnic groups (Jews and Bedouins) (table 1). Mixed GAS infection (i.e., infection involving GAS and other organisms), as well as infection caused by S. pneumoniae only, infection caused by H. influenzae only, and mixed infection with S. pneumoniae and H. influenzae were more common among the Bedouins, but infection caused by GAS only and M. catarrhalis only were significantly more common among Jews.

We attempted to determine whether GAS AOM had a different seasonality distribution than the other categories of AOM. For all categories of AOM, the highest rate of culture-positivity was during winter (December–February; 2406 [62.6%] of 3844 episodes), and the lowest rate was during summer (June–August; 1032 [53.3%] of 1935 episodes; P < .01 compared with the rate in winter). All 7 categories of AOM showed similar seasonal distribution; the rate peaked during winter, declined during spring (March–May), and reached the nadir during summer or fall (September–November). However, the proportion of episodes positive for GAS (GAS only or mixed) was higher during summer than the proportions of

### Table 2. Risk factors for acute otitis media (AOM) caused by group A β-hemolytic Streptococcus (GAS) or caused by GAS and other pathogens in children: result of a multiple regression analysis.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>OR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in monthsa</td>
<td>1.01</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Jewish ethnicityb</td>
<td>1.54</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Fall seasonc</td>
<td>0.553</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

a Because this is a continuous variable, the chance of having GAS AOM increases by 1.01 for each 1-month increase in age, and the chance of having GAS AOM increases by 1.13 for each 1-year increase in age.

b Versus Bedouin ethnicity.

c Versus occurrence during another season.
Table 3. Clinical data associated with episodes of acute otitis media (AOM) caused by group A β-hemolytic *Streptococcus* (GAS) only and/or other pathogens (*n* = 4,832).

<table>
<thead>
<tr>
<th>Causative pathogen(s)</th>
<th>No. of episodes with finding present / no. with data available (%)</th>
<th>No. of episodes with data available (%)</th>
<th>Causative pathogen(s)</th>
<th>No. of episodes with finding present / no. with data available (%)</th>
<th>No. of episodes with data available (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Body temperature ≥38°C</td>
<td>Upper respiratory infection</td>
<td>Pneumonia</td>
<td>Vomiting</td>
<td>Unilateral infection</td>
</tr>
<tr>
<td>GAS only</td>
<td>39/66 (59.1)</td>
<td>27/77 (35.1)</td>
<td>1/87 (1.1)</td>
<td>8/88 (9.1)</td>
<td>70/87 (80.5)</td>
</tr>
<tr>
<td>GAS and other pathogens</td>
<td>24/35 (68.6)</td>
<td>20/40 (50)</td>
<td>2/43 (4.7)</td>
<td>7/44 (15.9)</td>
<td>27/44 (61.4)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em> only</td>
<td>773/960 (80.5)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>498/842 (59.1)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>56/1016 (5.5)</td>
<td>290/1080 (28.2)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>516/1020 (50.6)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em> only</td>
<td>636/778 (81.7)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>379/701 (54.1)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>39/844 (4.6)</td>
<td>213/853 (25.0)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>462/863 (53.5)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td><em>H. influenzae</em> and <em>S. pneumoniae</em></td>
<td>389/495 (78.6)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>249/439 (56.7)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>34/536 (6.3)</td>
<td>153/543 (28.2)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>265/546 (48.5)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td><em>Moraxella catarrhalis</em> only</td>
<td>43/59 (72.9)</td>
<td>31/48 (64.6)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0/62 (0)</td>
<td>23/62 (37.1)&lt;sup&gt;b,c&lt;/sup&gt;</td>
<td>33/61 (54.1)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Other combinations</td>
<td>92/119 (77.3)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>64/117 (54.7)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>10/133 (7.5)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>42/135 (31.1)&lt;sup&gt;b,c&lt;/sup&gt;</td>
<td>67/136 (49.3)&lt;sup&gt;b&lt;/sup&gt;</td>
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</tbody>
</table>

<sup>a</sup> The ear fluid specimen consisted of pus that drained out of the middle-ear cavity after spontaneous perforation of the tympanum.

<sup>b</sup> *P* < .05 compared with episodes caused by GAS only.

<sup>c</sup> *P* < .05 compared with episodes caused by GAS only and GAS and other pathogens.
episodes of other etiological groups and lower during fall than those of all other groups (P < .05 for seasonal distribution; P = .06 for the distribution of GAS-positive episodes vs. episodes of infection with M. catarrhalis only).

We attempted to determine whether ethnicity, sex, age, and season were each independent risk factors for GAS-positive episodes. Multiple logistic regression analysis was performed with GAS infection as the dependent variable. Increased age (each additional month of age increased the risk of GAS AOM by 1.01 times, thus each additional year increased the risk by 1.13 times), ethnicity (being Jewish), and season (all 3 seasons except fall) were all independent, significant risk factors (table 2).

During the period November 2001–December 2003 (during which associated clinical and demographic data where prospectively collected for all culture-positive episodes involving children), 4832 episodes, with appropriate data were recorded. We compared clinical data obtained from patients with AOM caused by GAS only and patients with AOM caused by a combination of GAS and other pathogens with data obtained from patients with non-GAS episodes (table 3). Episodes of AOM caused by GAS only differed in several aspects from episodes of infection caused by other pathogens. (1) Episodes of GAS AOM were significantly less frequently associated with fever, compared with episodes caused by other pathogens (P < .01 compared with each group, except episodes of infection caused by M. catarrhalis only). (2) Episodes of GAS AOM were significantly less often associated with other signs of upper respiratory tract infection, compared with episodes caused by all other pathogens (P < .01 compared with each group). (3) Patients with GAS AOM had the lowest rates of vomiting (P < .001 compared with each group) (4) episodes of GAS AOM were more often unilateral than were all other episodes (P < .001 compared with each group). (5) Episodes of GAS AOM were less frequently associated with antibiotic treatment in the previous month than were other episodes (P < .001 compared with each group). Finally, (6) episodes of GAS AOM were less frequently associated with previous AOM episodes than were episodes of mixed infection with S. pneumoniae and H. influenzae (P = .013). These findings remained significant after correction for age. With regard to the proportion of episodes with a temperature of ≥38°C, upper respiratory infection, vomiting, unilateral otitis media, and use of antibiotics in the past month, episodes of mixed GAS infection (i.e., caused by GAS and other pathogens) usually showed values that were in between the values for episodes caused by GAS only and values for episodes caused by other pathogens.

The great majority of patients with episodes of AOM culture-positive for GAS (GAS only or mixed) presented with spontaneously draining ears, and the great majority of patients with non-GAS infection had intact ear drums and needed to undergo tympanocentesis for culture specimens to be obtained (P < .001 for GAS culture-positive episodes vs. all other groups).

Eleven (0.2%) of 4832 episodes were associated with mastoiditis. In 6 (54.5%) of 11 episodes, the pathogen was S. pneumoniae; in 4 episodes (36.4%), GAS was the causative organism (3 were caused by GAS only and 1 was caused by GAS and S. pneumoniae), and in 1 episode (9.1%) the causative organisms were H. influenzae and S. pneumoniae. The risk for development of mastoiditis if GAS was causing AOM was 11.6 cases per 1000 episodes (mastoiditis developed in 4 of 346 episodes; 95% CI, 3.2–29.3 cases per 1000 episodes). The mastoiditis risk for episodes of S. pneumoniae infection was 2.2 cases per 1000 episodes (mastoiditis developed in 8 of 3651 episodes; 95% CI, 0.9–4.3 cases per 1000 episodes); for episodes of H. influenzae infection, the risk was 0.3 cases per 1000 episodes (mastoiditis developed in 1 of 3999 episodes; 95% CI, 0.0–1.4 cases per 1000 episodes); and for episodes of M. catarrhalis infection, the risk was 0 case per 1000 episodes (mastoiditis developed in 0 of 394 episodes; 95% CI, 0.0–3.0 per 1000 episodes). Therefore, GAS AOM presented the highest risk of developing into mastoiditis, followed in descending order by AOM due to S. pneumoniae, H. influenzae, and M. catarrhalis (P < .001). These findings remained after correction for age.

DISCUSSION

Our extensive database of prospectively studied, culture-positive episodes of AOM permitted the characterization of GAS AOM, which usually constitutes <10% of all episodes of AOM. Although the expected overlap is quite extensive, several unique features of GAS AOM could be characterized.

First, the proportion of episodes of AOM caused by GAS increased with increased age, whereas AOM caused by other pathogens showed the opposite trend. Children >2 years of age were almost at a 4-fold higher risk of having GAS AOM, compared with children <1 year of age. Furthermore, if an episode of AOM was culture-positive, the risk of GAS infection for children >2 years of age was 5-fold higher than for children <12 months of age. The GAS group had the highest median age of all groups.

Second, episodes of GAS AOM had the sharpest contrast in seasonal distribution, having distinct peaks during winter and summer, compared with AOM due to other pathogens. This pattern seems to mimic the colonization pattern of GAS, which achieves peak levels in the throat during winter and peak levels on the skin during summer [9].

Third, and probably most important, the clinical features of GAS AOM were significantly different than those of AOM caused by other pathogens. Episodes of GAS were less frequently bilateral, febrile, and accompanied by other systemic findings, such as upper-respiratory and lower-respiratory infections. These characteristics, which were also observed by
Palmu et al. [10], suggest that GAS may be more locally aggressive than are the other 3 pathogens we studied (namely, S. pneumoniae, H. influenzae, and M. catarrhalis), and that GAS infection may require a preceding viral infection less often than does infection with other pathogens. Such features may explain the above-mentioned signs and symptoms [11, 12].

Further support that GAS may be more locally aggressive than are the other 3 pathogens is provided by 3 important findings. (1) The majority of patients with GAS AOM presented with acute drainage from the ears, suggesting a rapid and virulent progression to tympanic perforation, compared with the progressions of infections caused by other pathogens. This feature was also noted by Palmu et al. [10] and Spingarn et al. [13]. (2) Among children with recurrent AOM problems and patients who were recently treated with antibiotics, occurrence progressed was also noted by Palmu et al. [10] and Spingarn et al. [13]. (3) The risk of developing mastoiditis, the most frequent complication of AOM, was 11.6 related to age, it suggests that GAS is more capable of attacking even after correction for age. Although this finding might be other pathogens. This finding remained statistically significant even after correction for age. Although this finding might be related to age, it suggests that GAS is more capable of attacking noncompromised ears than are other pathogens, thus suggesting GAS has a higher virulence. (3) The risk of developing mastoiditis, the most frequent complication of AOM, was 11.6 cases per 1000 episodes of GAS AOM, compared with only 2.2, 0.3, and 0 cases per 1000 episodes of AOM caused by S. pneumoniae, H. influenzae, and M. catarrhalis, respectively, demonstrating again the relative virulence of GAS. The important role of GAS in mastoiditis has also been noted in previous studies by our group [14], as well as by others [15–17], and may partially explain the high frequency of mastoiditis in the past, compared with the relative rarity of mastoiditis at the present, even in patients with untreated episodes of AOM [18–20]. To the best of our knowledge, our study is the first to demonstrate prospectively that GAS causes mastoiditis more frequently than other pathogens.

We found that AOM due to GAS alone was more frequent in the Jewish population, but that S. pneumoniae infection and mixed infection caused by GAS and other pathogens were more frequent in the Bedouin population. Because we only studied children from whom ear-fluid specimens were obtained (mostly by tympanocentesis in the pediatric emergency department) and cultured, we could not calculate the true incidence of these episodes. Therefore, although the differences between the 2 ethnic groups were significant, we cannot conclude whether these differences derived from a higher true incidence of GAS infection in the Jewish population or a relative higher percentage of incidence due to a higher incidence of GAS infection caused by another pathogen, such as S. pneumoniae, in the Bedouin population.

In conclusion, a large series of 346 episodes of AOM caused by GAS was characterized by higher patient age and higher local aggressiveness of the pathogen, manifested by lower rates of fever and respiratory manifestations and higher rates of eardrum perforation and mastoiditis.

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