The prevalence of potential pathogenic bacteria in nasopharyngeal samples from individuals with a respiratory tract infection and a sore throat—implications for the diagnosis of pharyngotonsillitis

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Background. Treatment failure in patients with pharyngotonsillitis after a traditional course of penicillin V is a common finding. Several factors have been proposed to explain the failure rate, but the presence of aetiological agents other than group A β-haemolytic streptococci has attracted little attention.

Objectives. The aim of the present study was to investigate if a nasopharyngeal sample could suggest the aetiology of a sore throat in patients with a respiratory tract infection.

Methods. The prevalence of potentially pathogenic bacteria (Streptococcus pneumoniae, Haemophilus influenzae and Moraxella catarrhalis) in nasopharyngeal samples from 618 healthy individuals was compared with that from 108 patients with a respiratory tract infection and a sore throat.

Results. The prevalence of H. influenzae was higher in patients with a sore throat than in healthy individuals of the same age. For the adult patients with a sore throat, the prevalence was 27.5% compared with 2.7% for the healthy carriers (P < 10⁻⁷). The corresponding figures for schoolchildren were 31.3% versus 6.1% (P = 0.004) and for pre-school children 37.8% versus 13.2% (P = 0.0003).

Conclusions. If H. influenzae is found in a nasopharyngeal sample from a patient with a respiratory tract infection and a sore throat, it might be the aetiological agent.

Keywords. Haemophilus influenzae, Moraxella catarrhalis, nasopharyngeal culture, respiratory tract infections, Streptococcus pneumoniae.

Introduction

Pharyngotonsillitis is a respiratory tract infection causing inflammation in the pharynx and/or tonsils. The predominant symptom of pharyngotonsillitis is a sore throat. The infection, with subsequent inflammation, may be localized to the tonsils/pharynx alone or it may include several other locations as well. The most common aetiopathogenic agents are different viruses and group A β-haemolytic streptococci (GABHS). Treatment failure or recurrent infection is a common problem in acute pharyngotonsillitis. Several factors have been proposed to explain the failure rate, but the presence of aetiopathogenic agents other than GABHS has attracted little attention.

The literature does not support the idea that the clinical picture can distinguish a viral disease from a bacterial one. However, doctors do make a preliminary clinical diagnosis before confirmatory laboratory tests are taken. These preliminary diagnoses of the probability of a bacterial throat infection in the patients could be estimated as ‘unlikely’, ‘possible’ or ‘likely’. Patients diagnosed as having a ‘likely’ or ‘possible’ bacterial throat infection are usually treated with antibiotics, and those judged as having an ‘unlikely’ bacterial throat infection are not.
Patients diagnosed as having a ‘possible’ bacterial throat infection are often tested with different diagnostic tests. Of all patients with a sore throat, 34–80% are estimated to belong to the group ‘possible’ bacterial aetiology. A slightly lower number of patients, 24–65%, are actually tested for the presence of β-haemolytic streptococci (BHS) in the throat. Most probably, the diagnosis in all patients, especially those with a ‘possible’ bacterial infection, may be easier to establish if proper bacteriological testing is performed.

In the majority of patients with pharyngotonsillitis, the presence of GABHS should be checked. If GABHS cannot be found, and if the clinical picture is not convincing for a viral aetiology, the aetiology may be BHS of group C, group G or a bacterium other than BHS. Despite the fact that there is a high carrier rate of potentially pathogenic bacteria in the nasopharynx, especially among children, a nasopharyngeal culture could be of value.

The aim of the present study was to investigate whether a nasopharyngeal sample, obtained in routine medical practice, could suggest information about the aetiology of the infection in patients with a respiratory tract infection and a sore throat.

Method

During a winter period (14 January–17 February 1991) and the following summer period (15 July–15 September 1991) nasopharyngeal samples were collected from individuals living in the county of Älvsborg in the southwestern part of Sweden, a mixture of urban, village and rural populations. The ethics committee of Göteborg University approved the study.

Healthy individuals

Nasopharyngeal samples were obtained from healthy pre-school children, schoolchildren and adults. Samples from pre-school children, ≤6 years of age, were collected consecutively at visits to child welfare clinics. Samples from schoolchildren, 7–15 years of age, were obtained from children in school. Samples from adults, ≥16 years of age, were obtained consecutively at primary health care centres when the adults visited the clinic as patients with a non-infectious condition.

All individuals lacked signs of respiratory tract infections, had not received antibiotics during the previous 4 weeks and did not have known diabetes mellitus or immunodeficiency disorder. These individuals were considered to represent healthy children and adults.

Patients with respiratory tract infection and a sore throat

During the same periods, the results were registered from cultures from all the consecutive nasopharyngeal samples that were sent to the microbiological laboratory in Borås with a referral stating that the patient had a sore throat. The specimens came from the same geographical area as the specimens from the healthy individuals.

During the study periods, a special protocol was used. The doctors were asked to code the referrals to state the main symptom causing the need for a nasopharyngeal sample. The available codes were: cough >9 days; acute otitis media in a child with a middle ear ventilation tube; acute otitis media in a child not having a ventilation tube; sore throat; sneezing; sinusitis; or ‘other symptoms’. Only referrals stating a sore throat were included in this study.

Nasopharyngeal culture

The samples were collected in routine medical care by the normal staff; doctors, nurses or a medical laboratory technician trained to collect nasopharyngeal samples. The routine method was as follows: insert a thin flexible swab through one nasal aperture into the posterior wall of the nasopharynx and then put the swab into modified Stuart medium.

The samples were transported to the same microbiological laboratory in modified Stuart medium. All the samples were inoculated onto blood and haematine agar, and incubated in a 5% CO₂ atmosphere at 37°C. If no growth of relevant bacteria was seen after 48 hours, the culture was declared negative. BHS, Streptococcus pneumoniae, Haemophilus influenzae and Moraxella catarrhalis were identified by standard procedures.

Statistical analysis

Chi-square with Yates’ correction was used. When the numbers were small, Fisher’s exact test (two-tailed) was used. Relative risk with 95% confidence interval was used to compare patients with a sore throat with healthy individuals. The statistical program used was the Epi-Info version 6.04 from the Center for Disease Control (CDC) USA, and WHO.

Results

Of 108 nasopharyngeal samples with a referral stating that the patient had a sore throat, 59 stated only a sore throat, indicating that a sore throat was the only or the most predominant symptom. Among referrals stating a sore throat in combination with other symptoms, the most common combinations were a sore throat and sneezing (17 samples), a sore throat and long-standing cough (10 samples) or all these symptoms (five samples). The remaining referrals had other combinations of symptoms. There were, however, only a few referrals in each of these combinations.

We found no statistically significant difference in the prevalence of any bacterial species or in the prevalence of H.influenzae, M.catarrhalis and S.pneumoniae among patients with a referral stating only a sore throat, compared with patients with a sore throat in combination.
with other symptoms. Thus, all referrals including a sore throat were merged into one group of patients.

We could not find any statistically significant difference in the prevalence of *H. influenzae*, *M. catarrhalis* and *S. pneumoniae* among patients' samples collected during the winter season compared with the summer season. However, in the healthy population, we saw a small difference in the prevalence of *S. pneumoniae* between the winter and summer season in schoolchildren (*P* = 0.05). When we investigated the seasons separately in this age group, we could not find any statistically significant difference in the prevalence of *S. pneumoniae* between the healthy population and patients with a sore throat in any season, nor could we find any other statistically significant differences between the winter and summer season in the population of healthy individuals. Thus, the winter and summer seasons were therefore analysed together as one group.

Of the 108 samples arriving at the diagnostic laboratory, 76 (70%) came from primary health care centres, 23 (21%) from clinics for otorhinolaryngology, six (6%) from paediatric clinics, one (1%) from clinics for infectious diseases and two (2%) from other clinics. Only two of these samples (2%) came from hospitalized patients.

At least one potentially pathogenic bacterium was found in 78% of the nasopharyngeal samples from patients aged 0–6 years (Table 1). We found that both for patients with a sore throat and for healthy individuals the proportion of pathogenic bacteria decreased with age (Table 1). If potentially pathogenic bacteria were found in the nasopharynx, from adults and schoolchildren with a sore throat, it was usually only one bacterium (Table 1) and the most common finding among them was *H. influenzae* (Table 2).

### Table 1

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Symptoms</th>
<th>Total n</th>
<th>No. of bacterial species found&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Growth of any bacterium&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>0–6</td>
<td>Sore throat</td>
<td>23</td>
<td>9</td>
<td>39.1</td>
</tr>
<tr>
<td></td>
<td>Healthy</td>
<td>159</td>
<td>47</td>
<td>29.6</td>
</tr>
<tr>
<td>7–15</td>
<td>Sore throat</td>
<td>16</td>
<td>5</td>
<td>31.3</td>
</tr>
<tr>
<td></td>
<td>Healthy</td>
<td>198</td>
<td>20</td>
<td>10.1</td>
</tr>
<tr>
<td>&gt;16</td>
<td>Sore throat</td>
<td>69</td>
<td>25</td>
<td>36.2</td>
</tr>
<tr>
<td></td>
<td>Healthy</td>
<td>261</td>
<td>15</td>
<td>5.7</td>
</tr>
</tbody>
</table>

<sup>a</sup>Mean age in the age group, years (standard deviation).

<sup>b</sup>Growth of any potentially pathogenic bacteria (*S. pneumoniae*, *H. influenzae*, *M. catarrhalis* or BHS).

<sup>c</sup>Comparison between growth of any number of bacterial species between patients with a sore throat and healthy individuals.

### Table 2

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Symptoms</th>
<th>Total n</th>
<th>Growth in nasopharyngeal sample</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>S. pneumoniae</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>n</td>
</tr>
<tr>
<td>0–6</td>
<td>Sore throat</td>
<td>23</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Healthy</td>
<td>159</td>
<td>30</td>
</tr>
<tr>
<td>7–15</td>
<td>Sore throat</td>
<td>16</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Healthy</td>
<td>198</td>
<td>12</td>
</tr>
<tr>
<td>&gt;16</td>
<td>Sore throat</td>
<td>69</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Healthy</td>
<td>261</td>
<td>2</td>
</tr>
</tbody>
</table>
In all age groups, *H. influenzae* was more common in patients with a sore throat than in healthy individuals (Table 3).

**Discussion**

The main finding in this study was the strong correlation between *H. influenzae* in the nasopharynx and a sore throat, especially in adults. These findings may have implications for the diagnosis and management of patients with a sore throat.

**Methodological aspects**

The ideal situation would be to have a gold standard predicting pharyngotonsillitis caused by a specific aetiological agent, for example *H. influenzae*. Our samples from patients with a sore throat could then be compared with this gold standard. Unfortunately, there is no such gold standard. Since carriers exist among healthy individuals, estimating the prevalence of a specific aetiologic agent in just one group of patients with a sore throat is of limited value. The best information about aetiology is probably obtained by comparing the prevalence of different aetiological agents between patients with a sore throat and comparative groups of healthy individuals. Such comparisons between groups are only useful if the samples in all groups are obtained from the same geographical area and during the same periods, as was done in this study.

The advantage of defining criteria for selecting patients with a sore throat before the samples are collected is that the study population will be well defined. The disadvantage of this procedure is that our sample may reflect a population that is not the same as the patients from whom a nasopharyngeal culture would be taken as part of routine medical care. We have chosen to evaluate the outcome of nasopharyngeal cultures obtained in routine medical care without an exterior definition of how to select patients with a sore throat appropriate for obtaining a nasopharyngeal sample. Consecutive samples arriving at the microbiological laboratory stating a sore throat were used. Thus, the selection of patients in this study could be criticized, as patients were only included when their doctor thought a nasopharyngeal swab sample could be of use in the diagnostic and therapeutic procedure. However, the advantage of this procedure is that our sample will be representative of the population of patients from whom a nasopharyngeal culture would be taken in routine medical care. On the other hand, one may argue that if our findings are correct, doctors might alter their selection of patients for routine throat or nasopharyngeal samples, and then the normal clinical situation will be different from the one which we studied.

As the doctors had to characterize the patients’ symptoms on the referral slip, we postulate that nasopharyngeal sampling was preceded by a reflection on its usefulness. Thus, we assumed that doctors would not take a nasopharyngeal sample if, after a preliminary clinical evaluation, they found that the patient had a probable viral infection. When the doctors were in doubt about the aetiology of the sore throat, the routine procedure to establish the aetiology was, during the time period of this study, to test for the presence of GABHS by a rapid test or a throat culture. A nasopharyngeal culture would most probably not be obtained if the result of a preceding rapid test or throat culture showed growth of BHS. Thus, we do not have information about the simultaneous presence of BHS and *H. influenzae*.

Almost all samples (98%) came from patients who were not hospitalized. Thus, our sample represents patients with a minor illness.

The number of schoolchildren in this investigation was small and this results in wide confidence intervals for the relative risk. Furthermore, pre-school children are

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Growth in nasopharyngeal sample</th>
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</thead>
<tbody>
<tr>
<td></td>
<td><em>S. pneumoniae</em></td>
</tr>
<tr>
<td></td>
<td><em>P</em></td>
</tr>
<tr>
<td>0–6</td>
<td>NS</td>
</tr>
<tr>
<td>7–15</td>
<td>NS</td>
</tr>
<tr>
<td>≥16</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Data are from Table 2. All data are collected from the same geographical area and during the same time periods.

*P*-value when comparing prevalence of bacteria between patients with a sore throat and healthy individuals (see Table 2). NS = not significant, *P* > 0.05.

Relative risk for prevalence of bacteria in patients with a sore throat compared with healthy individuals, 95% confidence interval within parentheses.
occasionally may cause pharyngotonsillitis, and the presence of *H. influenzae*.

Previous investigations found that a high proportion (10–58%) of healthy pre-school children harbour *H. influenzae* in the throat and in the nasopharynx. Some authors found a throat sample superior to a nasopharyngeal sample for detecting *H. influenzae*. However, in a study with a control group of healthy carriers, we found no increased prevalence of *M. catarrhalis* in patients with respiratory tract infection and a sore throat compared with healthy individuals.

There are two possible pathogenic mechanisms for this; either that *H. influenzae* itself is the aetiological agent or that it produces β-lactamase and thus protects BHS from the activity of β-lactam antibiotics. If *H. influenzae* is not an aetiologic agent in patients with pharyngotonsillitis, we could expect the prevalence of *H. influenzae* among healthy individuals and patients with throat infection to be similar. Since we found a much higher prevalence in patients with a sore throat compared with healthy individuals, we conclude that, at least in adults, *H. influenzae* may act directly as an aetiological agent. The same may also be true for children, but this has to be tested further due to the few cases in this study. The correlation between a sore throat and the presence of *H. influenzae* in the nasopharynx for adults was very strong and of the same magnitude as for a sore throat and the presence of GABHS in throat samples.

**Haemophilus influenzae**

In this study, we found a high correlation in adults between a sore throat and the presence of *H. influenzae*.

**Streptococcus pneumoniae**

There are case reports indicating that *S. pneumoniae* occasionally may cause pharyngotonsillitis, and *S. pneumoniae* has been found in nasopharyngeal swabs in patients with pharyngotonsillitis. Other authors could not find *S. pneumoniae* in patients with pharyngotonsillitis. In our study, with a control group of healthy carriers, we found no support for *S. pneumoniae* being an important aetiological agent in patients with a respiratory tract infection and sore throat.

**Moraxella catarrhalis**

*Moraxella catarrhalis* has been found in tonsils or in the nasopharynx in patients undergoing tonsillectomy due to chronic tonsillitis. In a study with a control group of patients with sleep apnoea, no increased prevalence of *M. catarrhalis* could be found in removed tonsils. In patients with treatment failure of tonsillitis, *M. catarrhalis* was not found in the nasopharynx. In this study, with a control group of healthy carriers, we found no increased prevalence of *M. catarrhalis* in patients with respiratory tract infection and a sore throat compared with healthy individuals.

**Conclusions**

The findings in this study suggest that *H. influenzae* might be an aetiologic agent for sore throat. Future research, using well defined populations, should strive to clarify further the groups of patients where *H. influenzae* is an aetiological agent and subsequently determine when a nasopharyngeal sample is of clinical value. An important issue that needs to be addressed is if a nasopharyngeal sample is of value in unselected patients with a sore throat or only in those with a negative throat culture. Due to the negative ecological effects of current antibiotic usage, pharyngotonsillitis caused by *H. influenzae* should not be treated with antibiotics unless the patient has serious and/or prolonged symptoms.

**Acknowledgements**

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**References**

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