Neisserial colonisation of the pharynx

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SUMMARY The spectrum of neisserial colonisation of the pharynx was determined from 3557 throat exudates cultured on modified New York City (MNYC) medium. Oxidase positive Gram-negative diplococci (GNDc) were isolated from 1204 (33·8%) of the throat cultures. Neisseria gonorrhoeae, N meningitidis, and N lactamica accounted for 20·3%, 74·2%, and 3·7% of the oxidase positive GNDc respectively. The observed coexistence of gonococci and meningococci in the pharynx (0·39%) was significantly different (p<0·001) from the theoretical expected value (1·7%). The prevalence of pharyngeal infection in patients with gonorrhoea was 4·3% for all men, 11% for homosexual men, and 7·9% for women.

Despite the risks of disseminated infection and spread to sexual partners, the detection of pharyngeal gonorrhoea is less important than that of endocervical infection in women, urethral infection in heterosexual men, and anorectal infection in homosexual men.

Introduction

The lack of correlation between pharyngeal colonisation with gonococci and symptoms of pharyngitis,1 combined with the reluctance of many patients to admit to orogenital contact, makes it difficult for the clinician to use these criteria in selecting patients from whom to take throat cultures. Because of the possible presence of other neisseriae in the pharynx, the microbiological examination of throat cultures is much more time consuming and technically demanding than the examination of material from genital sites. The use of a selective medium aids the examination of cultures from all anatomical sites but is particularly helpful in the diagnosis of rectal and pharyngeal infection. Since its introduction in 1977 modified New York City (MNYC) medium has improved the efficiency and the rapidity of cultural diagnosis in Edinburgh.2 3 Workers in other countries4 5 have also noted an improvement in culture results with MNYC medium and have adopted this medium for routine use.

Pharyngeal colonisation with penicillinase producing Neisseria gonorrhoeae (PPNG) may be of particular importance because of the potential for transfer of the TEM β-lactamase plasmid from N gonorrhoeae to N meningitidis if both organisms inhabit the same pharynx.5 The incidence of meningococcal colonisation of the pharynx is known to be higher (about 26%) in patients with genital gonorrhoea than in those without (about 11%).7 8 Pharyngeal colonisation with gonococci ranges from 3·2% to 7·0% of men with gonorrhoea and from 2·9% to 11·3% of women with gonorrhoea.9 From these data simultaneous pharyngeal colonisation with gonococci and meningococci would be expected in 1-2·5% of patients with gonorrhoea.

Patients and methods

The study population included all men and women from whom samples were taken for microbiological diagnosis of gonorrhoea at the department of genitourinary medicine, Edinburgh Royal Infirmary, during 1978 to 1981.

Gram-stained smears of material from the urethra in men and the urethra and cervix in women were examined microscopically while the patient was at the clinic. Cultures were made from urethral specimens in all men, whereas anorectal specimens were also taken from homosexual men. Urethral, cervical, and anorectal specimens were taken routinely from women. Pharyngeal specimens were taken from all women with gonorrhoea in a genital site, those who were contacts of men with gonorrhoea, and those who had a history of orogenital contact; pharyngeal specimens were also taken from patients considered to be at high risk of acquiring infection because of multiple sexual partners. Likewise, pharyngeal
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specimens were taken from all male patients who were contacts of women with gonorrhoea, those with positive Gram-stained smears of urethral discharge, and those who gave a history of orogenital contact; pharyngeal cultures were taken routinely from all homosexual patients. If the first set of cultures from women were negative for *N gonorrhoeae* the tests were normally repeated twice at one or two weekly intervals. Test-of-cure cultures were normally carried out at one, two, and four weeks after treatment.

All specimens were inoculated directly on to MNYC medium at the clinic. After inoculation plates were held at 36°C in a carbon dioxide (10%) enriched atmosphere and transferred to the laboratory within four hours. Cultures were incubated and examined for oxidase positive Gram-negative diplococci (GNDC) which were tested for penicillin production and further identified by carbohydrate utilisation and fluorescent antibody tests as described.

Details of patients with pharyngeal infection were obtained retrospectively from the case notes. Statistical analysis was by the $\chi^2$ method with Yates's correction.

Results

Table I shows the total number of cases of gonorrhoea diagnosed over the four year period 1978-81. Although the annual number of cases of gonorrhoea decreased during the four year period, the proportion of patients from whom throat cultures were taken remained fairly constant. There was a slight increase in the proportion of patients with pharyngeal gonorrhoea. The increase between 1978 and 1981, however, although more noticeable in women, was not statistically significant ($p>0.1$).

INCIDENCE

Men

The 93 separate episodes of pharyngeal gonorrhoea (table I) occurred in 88 patients and yielded 107 isolates of gonococci. The average age of the patients was 24-8 years. Sixty nine (78.4%) of the patients were single, 11 (12.5%) married, and eight (9.1%) separated or divorced. Most patients (69.3%) had one or more casual sexual partners.

Rectal cultures were taken from 272 homosexuals, of whom 30 (11%) had pharyngeal gonorrhoea compared with 4.3% of all men.

Of 92 episodes of pharyngeal infection for which data were available, 80 (87.0%) were diagnosed at the first diagnostic test and seven (7.6%) at the second. In five (5.4%) patients pharyngeal gonorrhoea was diagnosed after treatment for anogenital infection.

Urethral infection was also present in 63 (68.5%) and rectal infection in 11 (12.0%) patients. The throat was the only site giving positive results in 21 (22.8%) patients: this corresponds to 1.0% of all patients with gonorrhoea in whom throat cultures were taken. The throat was the only site to give positive results in 13 (4.8%) of the 272 homosexuals.

Women

The 106 separate episodes of pharyngeal infection (table I) occurred in 105 patients and yielded 137 isolates of gonococci. The average age of the patients was 22.4 years. Sixty nine (65.7%) women were single, 17 (16.2%) married, 18 (17.1%) separated or divorced, and one (1.0%) widowed: 31.4% had one or more casual partners and 81% of the women were known contacts of men with gonorrhoea.

Of the 106 episodes of pharyngeal infection, 101 (95.3%) were diagnosed at the first diagnostic test and three (2.8%) at the second. Pharyngeal infection was diagnosed in two patients (1.9%) after treatment for anogenital infection. The throat was the only site giving positive results in 11 (10.4%) patients: this corresponds to 0.8% of all patients with gonorrhoea in whom throat cultures were taken.

SIGNS AND SYMPTOMS

Five (5.4%) of the 93 episodes of pharyngeal infection in men were associated with signs or symptoms referable to the throat compared with 14 (13.2%) of the 106 episodes of pharyngeal infection in women: this difference was not statistically significant ($\chi^2 = 2.7; p = 0.1$). None of the patients had any symptoms relating to disseminated gonococcal infection.

**Table I** Number of patients with gonorrhoea and pharyngeal gonorrhoea detected over the four year period 1978-81

<table>
<thead>
<tr>
<th>Year</th>
<th>No of patients with gonorrhoea</th>
<th>No (%) of patients with throat cultures taken</th>
<th>No (%) of patients with pharyngeal gonorrhoea</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
</tr>
<tr>
<td>1978</td>
<td>702</td>
<td>453</td>
<td>639 (91.0)</td>
</tr>
<tr>
<td>1979</td>
<td>598</td>
<td>424</td>
<td>557 (93.1)</td>
</tr>
<tr>
<td>1980</td>
<td>583</td>
<td>403</td>
<td>517 (88.7)</td>
</tr>
<tr>
<td>1981</td>
<td>549</td>
<td>331</td>
<td>484 (88.2)</td>
</tr>
<tr>
<td>Total</td>
<td>2432</td>
<td>1611</td>
<td>2197 (90.3)</td>
</tr>
</tbody>
</table>

*Expressed as a percentage of patients in whom throat cultures were taken.*

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RESULTS OF TREATMENT

The effectiveness of different dosages of ampicillin in treating pharyngeal infection in men and women is shown in Table II: patients who were treated with other antibiotics and those cases without test-of-cure cultures were excluded.

In men the cure rate with a single dose of ampicillin was not significantly different from that after a course of treatment (p>0.5). In women, however, there was a highly significant difference between the cure rates obtained with a single dose and with a course of treatment ($\chi^2 = 19.5; p<0.001$).

TABLE II Results of treatment of pharyngeal gonorrhoea in 47 men and 72 women

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No (%) of patients</th>
<th>Treated</th>
<th>Cured</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td>Ampicillin 2 g (single dose)*</td>
<td>7</td>
<td>30</td>
<td>6 (85.7)</td>
</tr>
<tr>
<td>Ampicillin 2 g + oxytetracycline 250 mg four times daily (5 days)</td>
<td>23</td>
<td>22</td>
<td>22 (95.7)</td>
</tr>
<tr>
<td>Ampicillin 2 g + ampicillin 250 mg four times daily (5 or 7 days)</td>
<td>13</td>
<td>42</td>
<td>12 (92.3)</td>
</tr>
<tr>
<td>Ampicillin 3 g + ampicillin 250 mg four times daily (5 or 7 days)</td>
<td>4</td>
<td>4</td>
<td>4 (100)</td>
</tr>
<tr>
<td>Total</td>
<td>47</td>
<td>44</td>
<td>44 (93.6)</td>
</tr>
</tbody>
</table>

*Probenecid 1 g orally was given with ampicillin in each case.

NEISSERIAL IDENTIFICATION

As indicated in Table I, 3557 pharyngeal specimens were taken for culture from 4043 patients with gonorrhoea. Oxidase positive GNDC were cultured from 1204 (33.8%) of the 3557 pharyngeal cultures; Table III shows the identity of these organisms.

Of the 244 isolates of gonococci from the pharynx, 107 were from men and 137 from women. Gonococci and meningococci were isolated together at only 14 (0.39%) of the 3557 examinations. The theoretical proportion of patients in whom we would expect both organisms to be isolated together is 0.017, calculated on the basis that meningococci were isolated from 25.1% of patients and gonococci from 6.9% of patients (Table III). The calculation of $\chi^2$ from a comparison between the actual and theoretical distribution showed a highly significant difference ($\chi^2 = 37.8; p<0.001$).

PENICILLINASE-PRODUCING NEISSERIA GONORRHOEAE (PPNG)

Of the total of 2432 gonococcal infections only eight (0.33%) were due to PPNG and the throat was affected in only one case, when N meningitidis was also isolated from the throat.

TABLE III Identity of 1204 oxidase positive Gram-negative diplococci (GNDC) isolated from 3557 throat cultures

<table>
<thead>
<tr>
<th>Organism</th>
<th>No of isolates</th>
<th>% of total throat cultures</th>
<th>% of oxidase positive GNDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neisseria gonorrhoeae</td>
<td>244</td>
<td>6.9</td>
<td>20.3</td>
</tr>
<tr>
<td>Neisseria meningitidis</td>
<td>894</td>
<td>25.1</td>
<td>74.2</td>
</tr>
<tr>
<td>Neisseria lactamica</td>
<td>44</td>
<td>1.2</td>
<td>3.7</td>
</tr>
<tr>
<td>Neisseria flavescens</td>
<td>1</td>
<td>&lt;0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Neisseria perflava</td>
<td>6</td>
<td>0.2</td>
<td>0.5</td>
</tr>
<tr>
<td>Branhamella catarrhalis</td>
<td>12</td>
<td>0.3</td>
<td>1.0</td>
</tr>
<tr>
<td>Unidentified</td>
<td>3</td>
<td>0.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Total</td>
<td>1204</td>
<td>33.8</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Discussion

The importance of diagnosing pharyngeal infection should be evaluated in relation to: the spread of infection from the throat to genital or other sites in a sexual partner; the risk to the individual of developing a disseminated gonococcal infection (DGI); the potential for transfer of the TEM beta-lactamase plasmid from N gonorrhoeae to N meningitidis if both organisms inhabit the same pharynx; and the resources available.

The prevalence of pharyngeal gonorrhoea in Edinburgh (4.3% of men and 7.9% of women with gonorrhoea) is comparable with that found elsewhere. The much higher incidence of pharyngeal infection (11%) in homosexual men, in 4.8% of whom the throat was the only site giving positive results, has also been noted by others.

Thompson1 considered that transmission from the throat to any other body site of the sexual partner was undocumented. Others considered that mouth-to-mouth transfer and mouth-to-genital transfer may occasionally have taken place. Mouth-to-genital transfer probably occurs more frequently in certain geographical areas.

The possibility of transfer of the TEM beta-lactamase plasmid from the gonococcus to the meningococcus obviously depends on the prevalence of PPNG and the incidence of pharyngeal colonisation with gonococci and meningococci. The observed association of gonococci and meningococci in this study was significantly different (p<0.001) from the predicted value. This difference is particularly interesting in view of the strong positive association between genital gonorrhoea and meningococcal colonisation of the pharynx.5,6 Our finding requires corroboration since it implies that the opportunities for transfer of genetic material between gonococci and meningococci in the pharynx are much fewer than might be expected.

The above difference between the expected and observed values could be explained by technical
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difficulties in detecting gonococci and meningococci in the same specimen; for example prolific growth of one organism might mask the presence of the other. Alternatively, meningococcal colonisation of the pharynx may have an inhibitory effect on gonococcal colonisation. The possible protective effect of meningococcal urethritis against gonococcal infection by bacteriocin production has been reported.15

Although effective treatment may eliminate the risks associated with pharyngeal gonorrhoea, infection at this site is often resistant to treatment.11 16 Single-dose treatment, which was effective in about 95% of genital infections, failed in over 50% of women with pharyngeal infection. The same treatment was effective in 85% of men with pharyngeal gonorrhoea: all but one of the men treated with a single dose had acquired their pharyngeal infection from heterosexual contacts. As most heterosexual men attended the clinic because of symptomatic urethritis, the outcome of single-dose treatment may be influenced by the duration of pharyngeal colonisation.

Pharyngeal gonorrhoea can only be diagnosed by identifying N gonorrhoeae in cultures of pharyngeal exudate. It is good practice also to identify, whenever possible, all non-gonococcal oxidase positive GNDC. The spectrum of oxidase positive GNDC encountered after culture on MNYC medium (table III) indicates the microbiological workload involved in this task. N meningitidis and Branhamella catarrhalis were the two organisms most often confused with N gonorrhoeae when suspected gonococcal isolates were submitted to a reference diagnostic laboratory for confirmation.17 In this study, despite the large numbers of isolates examined, we did not encounter either of these problems with the rapid carbohydrate utilisation system.10 Identification of problem cultures by both biochemical and immunological methods has been highly recommended.17 In our experience the sensitivity and specificity of immunofluorescence and coagglutination are similar, although the latter has several advantages in performance.18 N lactamica which occurred in 1-3% of all throat cultures may produce a cross-reaction in the coagglutination test.19 To prevent mis-identification an O-nitrophenyl-β-D-galactopyranoside (ONPG) test should be performed on all non-genital isolates which are positive by coagglutination. Other non-pathogenic neisseriae were rarely isolated, suggesting that MNYC medium is effective in inhibiting these organisms.

In this geographical area there seems to be little risk associated with pharyngeal gonorrhoea, either to the individual or to their sexual partner(s). In general, the detection of endocervical infection in women, urethral infection in heterosexual men, and anorectal infection in homosexual men is much more important than the detection of pharyngeal gonorrhoea in either sex and should have priority of resources. Careful monitoring of PPNG and pharyngeal gonorrhoea should, however, be undertaken by certain centres to provide valuable epidemiological data.

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