**SHORT REPORT**

**Chlamydia trachomatis** in non-gonococcal urethritis patients and their heterosexual partners: routine testing by polymerase chain reaction

I A Tait, C A Hart

**Objectives:** To identify the proportion of cases of non-gonococcal urethritis (NGU) in which *Chlamydia trachomatis* was detected in patients and their partners, using DNA amplification testing; and to relate the importance of age and symptoms to the presence of chlamydial infection and so clarify the aetiology and epidemiology of NGU, with a view to reducing the prevalence of chlamydial infection in general.

**Methods:** A 6 month cohort of all newly registered heterosexual men diagnosed with NGU, shortly after the introduction of polymerase chain reaction (PCR) chlamydial testing in 1997, was reviewed, with particular reference to their age and presence of symptoms; where possible, their women partners’ data were traced.

**Results:** Of 283 NGU patients, 35% were chlamydia positive and significantly younger than the chlamydia negative cases (mean ages 25 and 29 years respectively). 51% NGU patients were symptomatic, of whom 40% were chlamydia positive. 43% of all chlamydia positive NGU patients were asymptomatic. 36 men had had chlamydia positive index partners. 26% of the 97 secondary female contacts were chlamydia positive; three had had a negative male partner. From 155 men (28% chlamydia positive) no contacts were traceable.

**Conclusions:** In comparison with a previous similar study in 1987–90, using less sensitive diagnostic methods, a higher rate of chlamydial infection in NGU was detected. Young age and the presence of symptoms were confirmed as important factors for chlamydial positivity.

**SUBJECTS AND METHODS**

To assess this, we carried out a retrospective survey of 6 months of unselected cases of NGU in heterosexual men, commencing 4 weeks after *Ct* PCR testing had been adopted (28 April 1997).

The case sheets of all 1628 newly registered male patients were reviewed. Those with heterosexually acquired NGU (283) were selected and their female contacts’ case sheets sought. Women previously diagnosed with chlamydial infection whose partners had subsequently attended (secondary male cases) and were in this NGU group were “female index cases.” Women attending consequent on their partners’ NGU diagnosis were “female secondary cases.” Difficulties in achieving contact attendance meant that virtually all secondary contacts, of either sex, were regular partners although the exact sexual transmission history was not always clear.

*Ct* testing had been performed by endourethral swabs in both sexes and endocervical in women. NGU was defined as five or more polymorphonuclear leucocytes (PMNL) per high power field, with or without symptoms of a urethral discharge and/or dysuria. Men who were currently taking antibiotics or who had been treated for chlamydial or gonococcal infections and/or dysuria. Men who were currently taking antibiotics or who had been treated for chlamydial or gonococcal infections within the previous 3 weeks or with infected genital dermatological lesions were excluded. *C trachomatis* testing was by automated PCR.

**RESULTS**

See table 1 and figure 1.

The rate of chlamydial infection in NGU in the 6 months under review was 35% (100/283). *Ct* positive NGU men (average age 25 years) were significantly younger than the negative cases (average age 29 years, *p* = 0.001).

The 51% of cases of NGU who were symptomatic had a higher chlamydial positivity rate (40%) than the asymptomatic cases (30%, *p* = 0.019).

The average age of the asymptomatic *Ct* positive NGU men (24 years) was considerably less, but not significantly so, than the asymptomatic *Ct* negative men (28 years).

Partner status was examined to elucidate further the role of *Ct* in NGU. In 13% (36) of couples, of whom 24 men were *Ct* positive, the woman had been the index partner. Ninety seven secondary women contacts had been traced and screened, of whom 25 were positive. It is noteworthy that three of these women had had a *Ct* negative NGU partner. Of the 72 *Ct* negative secondary women contacts, 13 had had *Ct* positive partners. The 32 male index *Ct* positive cases yielded 22 *Ct* positive secondary female contacts, a transmission rate of 69%.

No contact was traceable from 155 men (28% *Ct* positive) and five men had had two each, resulting in 22 positive secondary contacts from 19 index positive men and 59 negative secondary contacts from 57 index negative men.

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C. trachomatis in NGU patients and their heterosexual partners

Table 1 Different groups of NGU patients, their Ct status, and female contacts

<table>
<thead>
<tr>
<th>Group</th>
<th>Number (average age, years)</th>
<th>Ct positive (average age, years)</th>
<th>Percentage of group</th>
<th>Female contacts</th>
<th>Percentage Ct positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>283 (29)</td>
<td>100 (25)</td>
<td>35</td>
<td>133</td>
<td>46</td>
</tr>
<tr>
<td>Contacts of Ct+ index females</td>
<td>36 (25)</td>
<td>24 (24)</td>
<td>67</td>
<td>36</td>
<td>78</td>
</tr>
<tr>
<td>Contacts of all secondary females</td>
<td>92 (28)</td>
<td>32 (28)</td>
<td>38</td>
<td>97</td>
<td>26</td>
</tr>
<tr>
<td>With multiple female contacts</td>
<td>5</td>
<td>3</td>
<td>28</td>
<td>10</td>
<td>60</td>
</tr>
<tr>
<td>With no traceable female contacts</td>
<td>155 (28)</td>
<td>44</td>
<td>28</td>
<td>26</td>
<td>100</td>
</tr>
<tr>
<td>Symptomatic NGU patients</td>
<td>143 (28)</td>
<td>57 (26)</td>
<td>40</td>
<td>60</td>
<td>100</td>
</tr>
<tr>
<td>Asymptomatic NGU patients</td>
<td>140 (27)</td>
<td>43 (24)</td>
<td>30</td>
<td>71</td>
<td>40</td>
</tr>
</tbody>
</table>

**Ct+ Chlamydia trachomatis**

**Figure 1** Heterosexual contacts of men with NGU.

**DISCUSSION**

The chlamydial infection rate in NGU in this study, 35%, showed only a marginally significant (p = 0.07) increase over 28% in a prospective study, under similar conditions in 1987–90, with ELISA and DIF testing (Dr OP Arya, personal communication).

Age was a significant factor for chlamydial positivity, confirming earlier findings. The presence of symptoms was also found relevant, as previously; higher colonisation of the urogenital tract in asymptomatic NGU is a possible explanation. It is of interest that the Ct positive asymptomatic cases were considerably younger than the others. Symptoms may have gone unnoticed among younger men owing to “genital unawareness” or the presence of a Ct positive female index partner may have reduced the perceived need for a detailed history.

Despite the increased diagnostic sensitivity, there remained 65% NGU cases who tested negative for chlamydia. If, as the presence of the discordant Ct positive secondary women contacts suggests, some men had an undetected chlamydial infection, there may have been a previous exposure to Ct (or C. pneumoniae). No longer immunologically naive, they had eradicated it more rapidly. Another possible effect of previous Ct infection is an immune response to chlamydial heat shock protein (hsp) 60 and cross reaction with host hsp; this has been associated with persistent or recurrent urethritis within the following 3 months without reinfection. Other agents including Mycoplasma genitalium, Ureaplasma urealyticum, and those associated with oral sex and with bacterial vaginosis may trigger subsequent episodes of NGU if their hsp similarly cross react. These two possibilities encourage the greater pursuit of accuracy in the sexual history and also epidemiological treatment of all NGU secondary contacts at their first clinic attendance in conjunction with empirical treatment of NGU patients and avoidance of intercourse until both index and secondary patients have completed treatment. Such epidemiological treatment of secondary female contacts, where chlamydial infection is present, reduces the risk of reinfection and of gynaecological complications. Adverse reactions are not serious; however, any benefits in the absence of chlamydial infection await proof.

Other NGU may indeed be Ct negative, due directly to Mycoplasma genitalium or Ureaplasma urealyticum infections, urethral strictures, or urinary tract infections; none are routinely excluded in NGU investigations.

Interpersonal relationships may be seriously stressed by Ct negative NGU, particularly recurrent or persistent cases, and women question the need to treat “an infection you don't know we have” and the fidelity of a long term partner who “keeps bringing back this infection.” Convoluted explanations from healthcare workers and further investigations may not help.

Although the proportion of Ct positive cases in NGU had risen, probably because of adoption of more sensitive diagnostic testing, the incidence of NGU has decreased since the 1980s. The number of Ct positive sexually active young men identified is, therefore, unlikely to increase and so the community reservoir remains untapped.

Another approach is opportunistic LCR/PCR screening of asymptomatic sexually active young adults of both sexes. In the Portsmouth pilot project (preliminary data from Dr J Tobin, personal communication) of around 14 000 women (16–24 years) screened, approximately 10% tested Ct positive; no less than 70% of the positive women's traceable male contacts were tested and about 43% were positive. This contact tracing level was extremely demanding of time and effort and, with wider screening programmes, will be difficult to maintain.

Primarily targeting young men is more difficult, however, because they do not, in general, regularly attend a healthcare unit (for example, for contraception) and the response has been poor, both in the United Kingdom and abroad. Male acceptance of increased responsibility for contraception, particularly in an established relationship, and subsequent attendance at related clinics would permit more screening opportunities. Other locations, such as the commencement of tertiary education, should be explored.
ACKNOWLEDGEMENTS
Some preliminary findings, later expanded and diversified, were presented at the IV European Chlamydia Congress, Chlamydia 2000, held in Helsinki, Finland in August 2000.
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Conflict of interest: None.

CONTRIBUTORS
IAT had the original idea, reviewed the case sheets, analysed the data, and wrote the first draft; CAH had introduced the change to PCR testing and supervised the laboratory work, and contributed to interpreting the results, and commented on previous drafts of this paper.

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