SHORT REPORT

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

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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.

The majority of cases of non-gonococcal urethritis (NGU) remain chlamydia negative. Possible reasons for this must be explored and secondary partners treated, wherever possible.

Furthermore, as the incidence of NGU overall is decreasing, the reservoir of chlamydial infection among young sexually active men in the community will remain unchallenged until successful active male screening is introduced.

Chlamydia trachomatis (Ct) genital infection in heterosexual men, particularly when asymptomatic and undiagnosed, may have potentially serious consequences, not only for themselves but for their partners. The sequelae worldwide, particularly upper genital tract complications and facilitation of HIV infection, can seriously affect women's future health and burden welfare services. When more sensitive routine chlamydial testing, by polymerase chain reaction (PCR) was introduced, we anticipated a considerable increase in chlamydial infection in both sexes treated in our genitourinary clinic, with obvious long term benefit.

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 within the previous 3 weeks or with infected genital dermatological lesions were excluded. *C trachomatis* testing was by automated PCR.[1]

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.

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

Group	Number (average age, years)	Ct positive (average age, years)	Percentage of group	Female contacts	Percentage Ct positive
Total	283 (29)	100 (25)	35	Total 133	46
				Contacts of Ct + men 59	78
Contacts of Ct+ index females	36 (25)	24 (24)	67	36	100
Contacts of all secondary females	92 (28)	32 (28)	38	97	26
				(a) 22 concordant positive	
				(b) 3 discordant positive with Ct negative NGU partners	
With multiple female contacts	5	3		10	60
With no traceable female contacts	155 (28)	44	28	–	
Symptomatic NGU patients	143 (28)	57 (26)	40	–	
Asymptomatic NGU patients	140 (27)	43 (24)	30	–	

Ct= *Chlamydia trachomatis*

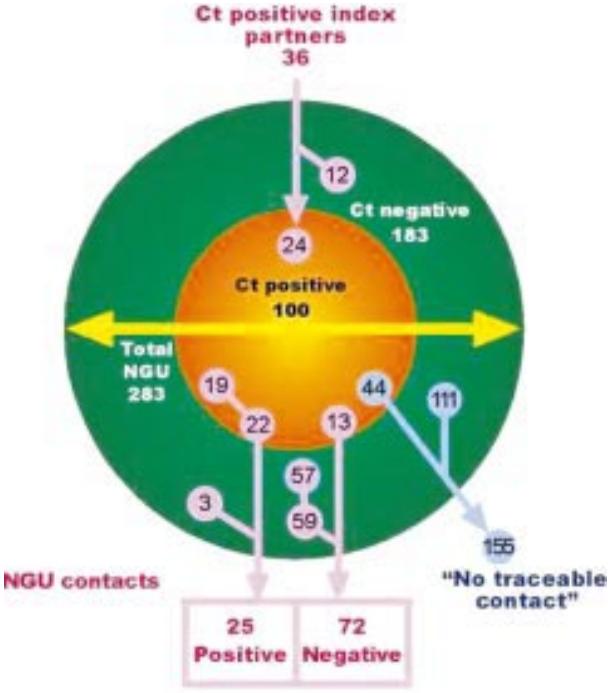

Figure 1 Heterosexual contacts of men with NGU.

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.[2] The presence of symptoms was also found relevant, as previously[3]; higher colonisation of the urogenital tract in symptomatic NGU[4] 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"[4] 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 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.[5] 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.[6] 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.[7] 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.[4] 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.[8 9] 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.

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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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