

Chlamydia trachomatis and Ureaplasma urealyticum in men attending a sexually transmitted diseases clinic

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SUMMARY Urethral specimens from 480 heterosexual patients were examined for *Chlamydia trachomatis*. Chlamydia were isolated from 32.7% of men with non-specific urethritis (NSU), from 16.1% of men with gonorrhoea, and from 4.1% of men without urethritis. Chlamydial isolation was not related to duration of symptoms, presence of discharge, or past history of attendance at the clinic.

Urine from 176 heterosexual patients was examined for *Ureaplasma urealyticum*. Ureaplasmas were present in 53.8% of men with NSU, in 28% of men with gonorrhoea, and in 32.9% of men with no urethritis. Detection rates for ureaplasmas in patients with chlamydia-negative and chlamydia-positive NSU were similar, but ureaplasmas were present in significantly greater numbers in patients with chlamydia-negative NSU than in those with chlamydia-positive NSU.

Introduction

Non-specific urethritis (NSU) is now the commonest sexually transmitted disease in the United Kingdom,^{1,2} but the aetiology in many cases is still obscure. The association of *Chlamydia trachomatis* with nongonococcal urethritis was first described by Dunlop *et al*³ in 1965 and the causal nature of this relationship now seems established, with *C trachomatis* being isolated in 30-70% of cases.⁴⁻¹²

Ureaplasma urealyticum has also been implicated in the aetiology of nongonococcal urethritis and has been isolated from 40-60% of patients with NSU.¹³⁻¹⁶ This association has been said to be particularly strong in chlamydia-negative NSU,¹⁷ but despite evidence from studies with antibiotics which differentiate between chlamydial NSU and ureaplasma NSU¹⁸⁻²⁰ and from the self-inoculation study reported by Taylor-Robinson *et al*,²¹ the aetiological role of ureaplasmas in NSU is still in doubt.¹⁶ The results of quantitative studies have also been conflicting.^{13, 16, 17}

The present study was performed to determine the prevalence of *C trachomatis* and *U urealyticum* infection in male patients attending a clinic for the

treatment of sexually transmitted diseases. An attempt has also been made to evaluate the relationship between chlamydia and ureaplasmas in NSU.

Patients and methods

STUDY POPULATION

The study population was composed of 480 heterosexual male patients who attended the department of sexually transmitted diseases at the Edinburgh Royal Infirmary between October 1979 and January 1980. Those included were new patients and old patients returning with a fresh infection who presented between 9 am and 12 noon Monday to Friday and who had not received antibiotics during the six weeks preceding their initial visit.

DIAGNOSTIC CRITERIA

Gonorrhoea was diagnosed on the basis of positive urethral culture results for *Neisseria gonorrhoeae* with or without Gram-negative diplococci present on microscopy.

Non-specific urethritis was diagnosed irrespective of symptoms in patients in whom microscopical examination of Gram-stained urethral material or threads from the first specimen of urine showed 10 or more leucocytes per high power field ($\times 1000$),⁸ when gonorrhoea was excluded as above.

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Accepted for publication 8 September 1980

Asymptomatic patients were those who complained of neither discharge nor dysuria and in whom there was no microscopical evidence of urethritis.

Patients with symptoms but without signs of urethritis were excluded from both of the last two diagnostic groups.

ISOLATION PROCEDURES

Gonorrhoea

Samples for microscopy and culture were taken with plastic disposable bacteriological loops (Nunc Products). Specimens for culture were plated directly on to modified New York City medium.²² After incubation at 36°C for 24 hours *N gonorrhoeae* was identified by rapid carbohydrate utilisation tests and delayed immunofluorescence or both.²³

Chlamydia trachomatis

Specimens from the anterior urethra were taken using a sterile ENT swab (Medical Wire and Equipment Company) and placed in 2SP medium. They were stored at -20°C for up to three hours and at -60°C in the laboratory for up to three days before being cultured. Isolation was carried out by the method of Thomas *et al*²⁴ with cycloheximide-treated cells. Incubation of the infected cells was continued for three days at 35°C and the coverslips stained with iodine to detect the glycogen inclusions.

Ureaplasma urealyticum

The first-voided sample of urine, usually 7-10 ml, was collected in a sterile universal container. The sample was stored at room temperature for up to three hours before being transported to the laboratory and processed as described by Young *et al*.²⁵ Results were expressed as the total number of colour-changing units (ccu) present in the initial urine sample. In the absence of any evidence to suggest otherwise, it was assumed that the total number of organisms present in the initial urine specimen was an accurate reflection of the numbers present in the anterior urethra.

STATISTICAL ANALYSIS

Statistical significance was determined by the χ^2 test with Yates's correction or Student's *t* test.

Results

CHLAMYDIA TRACHOMATIS

C trachomatis isolation was attempted in 480 heterosexual men; the organism was isolated from 48 (32.7%) of 147 men with NSU and from eight of 195 men with no evidence of urethritis (table I). This difference is highly significant ($\chi^2_1 = 48.8$; $P < 0.001$). Ten (16.1%) of the 62 men with gonorrhoea also harboured chlamydia.

TABLE I *Chlamydia trachomatis* in heterosexual men

Primary diagnosis	No	% Of all diagnoses	Chlamydia-positive	
			No	%
Gonorrhoea	62	12.9	10	16.1
NSU	147	30.2	48	32.7
No symptoms	195	40.6	8	4.1
Other*	76	16.3	11	14.1
Total	480	100.0	77	16.0

*Patients with symptoms but without signs of urethritis at the time of initial examination.

The presence of a clinically detectable discharge and the duration of symptoms had no significant effect on the recovery of *C trachomatis*. Indeed among the 21 patients with NSU who had no symptoms the organism was isolated from 10 (47.6%) patients.

C trachomatis was isolated from 10 (35.7%) of 28 patients with ureaplasma-positive NSU and from 10 (41.7%) of 24 patients with ureaplasma-negative NSU. This difference is not significant.

CONTACT TRACING

Although the study was not designed to include the contacts of the men examined, consorts of 14 of the 77 men infected with chlamydia were seen. Chlamydia were isolated from the seven cases tested.

UREAPLASMA UREALYTICUM

U urealyticum was looked for in 176 heterosexual men; the organism was detected in 28 (53.8%) of 52 men with NSU but in only 32.9% of 73 asymptomatic men. This difference is significant ($\chi^2_1 = 4.67$; $0.02 < P < 0.05$). Ureaplasmas were present in 18 (56.3%) of 32 men with chlamydia-negative NSU and in 10 (50%) of 20 men with chlamydia-positive NSU (table II). This difference is not significant ($\chi^2 = 0.02$; $P > 0.5$).

Marked differences between chlamydia-negative and chlamydia-positive NSU occurred, however, when the number of ureaplasmas present was taken into account. Of patients with chlamydia-negative NSU 53.1% had large numbers ($\geq 10^5$ ccu) of ureaplasmas present in their urine compared with 15.0% of patients with chlamydia-positive NSU (table II). This difference is significant ($\chi^2_1 = 6.03$; $0.01 < P < 0.02$). The mean number of ureaplasmas present in men with chlamydia-negative NSU was $10^{7.1}$ compared to $10^{4.6}$ in men with chlamydia-positive NSU ($t = 2.13$; $P < 0.05$). The distribution of ureaplasmas in patients with chlamydia-positive and chlamydia-negative NSU is shown in the figure.

Although *U urealyticum* was found less often in men with gonococcal urethritis and in men without urethritis (table II), it was usually present in large

TABLE II *Ureaplasma urealyticum* in heterosexual men

Primary diagnosis	No	Ureaplasma-positive		With ureaplasmas (<10 ⁵ ccu)		With ureaplasmas (≥10 ⁵ ccu)	
		No	%	No	%	No	%
Gonorrhoea	25	7	28.0	2	8.0	5	20.0
Chlamydia-negative NSU	32	18	56.3	1	3.1	17	53.1
Chlamydia-positive NSU	20	10	50.0	7	35.0	3	15.0
No symptoms	73	24	32.9	8	11.0	16	21.9

ccu = colour-changing units

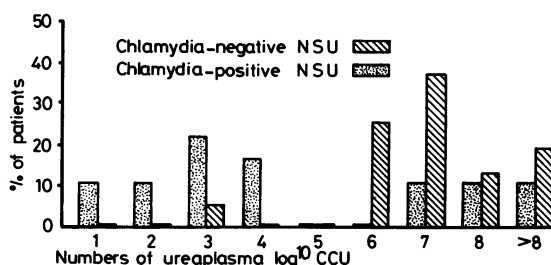


FIGURE Number of ureaplasmas in patients with NSU

numbers. Ureaplasmas were present in numbers equal to or greater than 10⁵ ccu in five of the men with gonococcal urethritis who harboured ureaplasmas and in 16 of the men without urethritis.

Discussion

Any consideration of non-specific urethritis is complicated by the lack of universally accepted criteria for its diagnosis; even within England and Wales²⁶ there are marked variations in the criteria applied. This may partly account for the differences in reported isolation rates for *C trachomatis*, which range from 26%¹⁰ to 58.5%¹¹ in recent surveys; there is a tendency for the highest isolation rates to be reported by those authors who restrict their diagnosis of urethritis to patients whose urethral exudates contain more than 20 leucocytes per high power field on microscopical examinations. The isolation rate of 33% for *C trachomatis* in NSU in the study reported here is similar to that obtained by others using the same diagnostic criteria.^{8 10}

Unlike other authors^{7 8} we were unable to relate isolation of *C trachomatis* to either severity or duration of symptoms, and we obtained particularly high isolation rates in patients with NSU who had no symptoms.

The significance of *U urealyticum* in NSU is much less well established. The overall isolation rate of 53.8% reported here agrees with the 52.9% reported

by Taylor-Robinson *et al.*¹⁶ but he found no significant difference between chlamydia-positive and chlamydia-negative NSU in terms of the numbers of organisms present. However, the results of quantitative studies have been conflicting, and Hare *et al.*¹³ detected "high numbers" of ureaplasmas in chlamydia-negative NSU more frequently than in chlamydia-positive NSU.

In the present study we found that *U urealyticum* could be detected fairly frequently in sexually active men, and large numbers (≥10⁵ ccu) could be present without causing any evidence of urethritis. Nevertheless, the organism is isolated more often from men with NSU, and a causative role for *U urealyticum* in some cases cannot be excluded. The factors which might influence the pathogenicity of the organism are not known, but the observation that ureaplasmas were found in low numbers in chlamydia-positive NSU might indicate some inhibitory action of *C trachomatis*. It seems unlikely that detection of the organism is influenced by the presence of urethritis, as detection rates and numbers of the organisms present are similar for patients with gonococcal urethritis and those without urethritis.

This study provides further support for the aetiological role of *C trachomatis* in NSU, but the case for such a role for *U urealyticum* is still not proved.

We are grateful to our medical and non-medical colleagues in the University Department of Genitourinary Medicine, Edinburgh Royal Infirmary, for their help in the collection of specimens and data and in the preparation of this paper.

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