

# Genitourinary infection with *Ureaplasma urealyticum* in women attending a sexually transmitted diseases clinic

JENNIFER M HUNTER,\* HUGH YOUNG,† AND A B HARRIS†

From the \*Department of Genitourinary Medicine, Edinburgh Royal Infirmary, and the †Department of Bacteriology, University of Edinburgh, Edinburgh

**SUMMARY** *Ureaplasma urealyticum* was detected in the cervix of 49.9% and in the urine of 47.7% of women attending a department of genitourinary medicine. Isolation of *U urealyticum* was not related to diagnosis, nor was there any association between the presence of the organism and any symptoms or signs of genital tract disease. Fewer organisms were detected in the cervix of women who had a concurrent infection with *Chlamydia trachomatis* than in women who had not. A pathological role for *U urealyticum* has not been established.

## Introduction

Non-gonococcal urethritis (NGU) is now the commonest sexually transmitted disease in Britain.<sup>1,2</sup> The substantial evidence for a causative role for *Chlamydia trachomatis* in this infection has been reviewed by Taylor-Robinson and Thomas.<sup>3</sup> An aetiological role for *Ureaplasma urealyticum*, especially in non-chlamydial NGU, has been suggested,<sup>4-7</sup> but despite evidence from self-inoculation<sup>8</sup> and chemotherapeutic studies<sup>9-11</sup> the pathological significance of the organism has yet to be confirmed.

*U urealyticum* has been detected frequently and in large numbers in sexually active women.<sup>12,13</sup> Its transmission by sexual contact seems well established,<sup>14</sup> and the colonisation of the female genital tract with *U urealyticum* has been related to sexual activity and the number of sexual partners.<sup>13,15</sup> Although various reports have related *U urealyticum* infection to impaired fertility, abortion, and low birth weight,<sup>13,16</sup> its pathogenicity in the female genital tract has not yet been established.

This study describes the prevalence of *U urealyticum* in women attending a clinic for the treatment of sexually transmitted disease and attempts to correlate ureaplasma infection with signs and symptoms of genital tract disease.

Address for reprints: Dr J M Hunter, Department of Genitourinary Medicine, Black Street, Glasgow G4 0EF

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## Patients and methods

The patients studied were women who attended the department of genitourinary medicine at the Royal Infirmary, Edinburgh, for the first time between April and September 1980 and women who had attended the clinic previously but who presented during this period with a new complaint. All such women who presented between 9 am and 12 noon Monday to Friday were included unless they had received antibiotic therapy during the six weeks before their first visit.

## DIAGNOSTIC PROCEDURES

### *Gonorrhoea*

Specimens for microscopy were taken from the urethra and cervix. Specimens for culture were taken from the urethra, cervix, rectum, and throat (where indicated) and were plated directly on to Modified New York City medium.<sup>17</sup> After incubation at 36°C for 24 hours *Neisseria gonorrhoeae* was identified by rapid carbohydrate utilisation tests or delayed immunofluorescence or both.<sup>18</sup>

### *Chlamydia trachomatis*

Specimens were taken from the endocervix with sterile cotton-tipped swabs and placed in 2SP medium. They were stored at -20°C for up to three hours and at -60°C for up to three days before being cultured. Isolation was carried out by the method of Thomas *et al*<sup>19</sup> with cycloheximide-treated cells. Infected cells were incubated for three days at

35°C and the coverslips stained with iodine to detect the glycogen inclusions.

*Ureaplasma urealyticum*

**Urine.** The first 10-15 ml of voided urine were collected in a sterile universal container and stored for up to three hours at room temperature before being transported to the laboratory and processed as described by Young *et al.*<sup>12</sup> Results were expressed as total colour-changing units (ccu) present in the initial sample.

**Cervix.** Endocervical swabs were placed in 1.8 ml of TALC colour change medium<sup>12</sup> contained in bijou bottles for transport to the laboratory. On arrival, the swab was agitated in the medium and liquid expressed from the swab before it was removed from the bottle. A 200-µl volume was used to initiate a series of 10-fold dilutions up to 10<sup>10</sup> in 1.8-ml volumes of TALC medium. The medium from which the swab had been removed was considered to be a 1/10 dilution of cervical material.

**Other STDs**

Genital herpes simplex virus infection was confirmed by viral isolation and serum antibody titres. The presence of pox virus particles in molluscum contagiosum was established by electron microscopy. Vaginal secretions were examined microscopically for *Trichomonas vaginalis* and yeasts. Other STDs were diagnosed clinically.

**DIAGNOSTIC GROUPS**

Patients were assigned to one of four diagnostic groups:

- (1) Women from whom *N gonorrhoeae* was isolated;
- (2) Women who were identified as consorts of men with NGU;
- (3) Women with any other STD; and

(4) Women with no evidence of STD; this group was subdivided into women who had conditions which required treatment and those which did not.

Allocation to any diagnostic group was made independently of the culture results for *C trachomatis* and *U urealyticum*.

**CLINICAL APPEARANCE OF THE CERVIX**

The difficulties associated with interpreting clinical signs in the cervix have been discussed in detail by Rees and her co-workers,<sup>20</sup> who described a method for the standardised reporting of the clinical appearance of the cervix.

We used a similar method with the following classifications: (a) clinically healthy cervix; (b) simple cervical ectopy; and (c) cervicitis (congested oedematous cervix or cervical mucopus or pus or both).

**STATISTICAL ANALYSIS**

Statistical analysis was carried out using the  $\chi^2$  test with Yates's correction.

**Results**

Five hundred and twenty-eight women participated in the survey. Valid results for ureaplasma isolation were obtained from the cervix in 413, from the urine in 375, and from both sites in 359 women. Several women from whom cervical specimens were obtained were unable to pass urine at their initial visit, and a batch of almost 100 specimens from both sites was contaminated accidentally.

**PREVALENCE**

*U urealyticum* was isolated from the cervix in 206/413 (49.9%) of women and from the urine in 179/375 (47.7%). Ureaplasmas were detected with equal frequency among all diagnostic groups (table 1). The isolation rate was not affected by age. *U*

TABLE 1 Prevalence of ureaplasmas in the cervix and urine in relation to diagnosis

Diagnosis	Cervix						Urine							
	Total No of patients	Ureaplasma - positive		With <10 <sup>5</sup> ccu		With ≥10 <sup>5</sup> ccu		Total No of patients	Ureaplasma - positive		With <10 <sup>5</sup> ccu		With ≥10 <sup>5</sup> ccu	
		No	%	No	%	No	%		No	%	No	%	No	%
Gonorrhoea	75	40	53.3	25	33.3	15	20.0	67	32	47.8	15	22.4	17	25.4
NGU contact	58	29	50.0	15	25.9	14	24.1	56	31	55.4	17	30.4	14	25.0
Other STD	113	51	45.1	37	32.7	14	12.4	96	43	44.8	30	31.3	13	13.5
Other conditions: requiring treatment	84	44	52.4	32	38.1	12	14.3	78	38	48.7	19	24.4	19	24.4
not requiring treatment	83	42	50.6	28	33.7	14	16.9	78	35	44.9	21	26.9	14	17.9
Total	413	206	49.9	137	33.2	69	16.7	375	179	47.7	102	27.2	77	20.5

ccu = colour-changing units

*urealyticum* was found in the cervix of 10 of 30 women over 35 years of age compared with 49 of 91 aged 15-19 years ( $\chi^2 = 3.02$ ;  $0.1 > P > 0.05$ ) and in 45.8% (11/24) of the youngest women (aged 15-17 years) compared with 56.7% (38/67) of those aged 18-19 years ( $\chi^2 0.46$ ;  $P = 0.5$ ). Large numbers ( $\geq 10^5$  ccu) of ureaplasmas were present in the cervix in 16.7% and in the urine in 20.5% of women. The number of ureaplasmas present in either site was not related to age or diagnosis.

There was a significant correlation between isolation of ureaplasmas from the cervix and from the urine ( $\chi^2 = 204$ ;  $P < 0.001$ ); 46.2% of women had positive results in both sites, 6.1% in the cervix alone and 5.8% in the urine alone; 41.8% had negative results in both sites. This association was also quantitative; 45.3% of women had ureaplasmas present in both urine and cervix in numbers  $\geq 10^5$  ccu and 30% had small numbers at both sites (table II). In only four (1.1%) women were large numbers of ureaplasmas detected at one site if the other showed no growth.

TABLE II *U urealyticum* isolation in urine and cervical specimens

Urine culture	Cervical culture			
	-	+	<10 <sup>5</sup> ccu	≥10 <sup>5</sup> ccu
Negative	166	22	21	1
Positive	21	150	96	54
<10 <sup>5</sup> ccu	18	77	68	9
≥10 <sup>5</sup> ccu	3	73	28	45

ccu = colour-changing units  
+ = ureaplasma-positive; - = ureaplasma-negative

RELATION OF UREAPLASMAS TO SYMPTOMS AND SIGNS

In 179 women in whom other STDs were excluded the presence of *U urealyticum* was analysed in relation to symptoms and signs of genital tract disease. No significant association was found, either quantitatively or qualitatively, between the presence of ureaplasmas in the cervix or urine and any symptom or sign (tables III and IV). In particular,

large numbers of ureaplasmas were as common in those with a healthy cervix as in those with cervicitis. Of 34 women in whose urine *U urealyticum* was present in numbers  $\geq 10^5$  ccu, three (8.8%) complained of dysuria compared with 11/89 (12.4%) women whose urine was ureaplasma-negative.

CONCURRENT CHLAMYDIAL INFECTIONS

Ureaplasmas were detected in the cervix of 43/81 (53.1%) of chlamydia-positive women and in 157/319 (49.2%) of chlamydia-negative women (table V). Numbers  $\geq 10^5$  ccu were detected in nine (11.1%) chlamydia-positive women and in 17.9% (57/319) of chlamydia-negative women. This difference just fails to reach statistical significance at the 0.5% level ( $\chi^2 2.9$ ;  $0.1 > P > 0.05$ ). If, however, only the groups with the highest incidence of *C trachomatis* (contacts of NGU and women with gonorrhoea) are considered, the difference in numbers of ureaplasmas present in chlamydia-positive and chlamydia-negative women is significant (table V;  $\chi^2 4.5$ ;  $0.05 > P > 0.02$ ). No such difference was noted in women with other conditions, sexually transmitted or otherwise.

The presence of *C trachomatis* in the cervix was not correlated with the isolation of ureaplasmas from the urine, either quantitatively or qualitatively, in any diagnostic group.

Discussion

Braun *et al*<sup>21</sup> reported a strong association between the presence of *U urealyticum* in the cervix and in the urine. Our results confirm this association and demonstrate its quantitative nature. Braun, however, isolated ureaplasmas from the cervix alone in 18% of patients, whereas in this study ureaplasmas were detected in the cervix alone in only 6.1%. A similar number (5.8%) had positive results in the urine alone; the results suggest that if screening women for the presence of ureaplasmas is a useful investigation, samples from either the urine or the cervix would give equally valid results. Numbers of ureaplasmas  $\geq 10^5$  ccu were detected significantly more often in the urine than in the cervix, but this may simply reflect

TABLE III Frequency of ureaplasma isolation from the cervix in relation to its clinical appearance

Clinical appearance	Total No of specimens	Ureaplasma - positive					
				With <10 <sup>5</sup> ccu		With ≥10 <sup>5</sup> ccu	
		No	%	No	%	No	%
Healthy	51	27	52.9	17	33.3	10	19.6
Simple cervical ectopy only	47	24	51.1	17	36.2	7	14.9
Vaginitis only	23	8	34.8	5	21.7	3	13.0
Cervicitis	58	31	53.4	17	29.3	14	24.1

ccu = colour-changing units

TABLE IV *Ureaplasma* isolation from urine in relation to symptoms

Symptoms	Total No of specimens	<i>Ureaplasma</i> - positive		With <10 <sup>5</sup> ccu		With ≥10 <sup>5</sup> ccu	
		No	%	No	%	No	%
No symptoms	71	30	42.3	16	22.5	14	19.7
Vaginal discharge	77	41	53.2	23	29.9	18	23.4
Genital irritation	60	34	56.6	20	33.3	14	23.3
Dysuria	19	8	42.1	5	26.3	3	15.8

ccu = colour-changing units

the difference in sampling procedures; an initial specimen of urine may contain a greater proportion of the organisms present than does an endocervical swab.

The overall prevalence of ureaplasmas found in this study (47.7% in the urine and 49.9% in the cervix) is slightly lower than that previously reported in similar populations.<sup>12,13</sup> We were unable to detect any difference in isolation rates among the various diagnostic groups, and the number of ureaplasmas present was similar in every group. Young *et al*<sup>12</sup> reported that women whose consorts had NGU had a significantly higher incidence of ureaplasma infection, but they were also unable to detect any quantitative differences.

It might have been expected that the organism would occur less frequently among the youngest women, but no difference was found between those aged 15-17 years and the other age groups, presumably because sexual activity is already established in girls of this age attending the clinic. The only age group in which ureaplasmas were isolated less frequently was that over 35 years of age; these women comprised less than 10% of the study population and the difference was not statistically significant.

The lack of association, quantitative or otherwise, between the presence of ureaplasmas and any sign or symptom of genital tract disease makes a pathological role for the organism in women seem unlikely. In the same series of patients we noted an association

between chlamydial infection and the clinical appearance of the cervix. These findings (unpublished observations) are similar to those reported by Rees and her co-workers.<sup>20</sup>

Concurrent infection with *C trachomatis* seems to affect adversely the number of ureaplasmas detected, although this effect is less clear-cut in women than it was in men with NGU.<sup>22</sup> The presence of chlamydia may inhibit the multiplication of ureaplasmas, perhaps by preventing their association with cells; alternatively, ureaplasmas may be present in chlamydia-infected cells but are more difficult to detect. Masover *et al*<sup>23</sup> reported that the single identifying property of *U urealyticum*—the ability to hydrolyse urea—was lost or not expressed after association with mammalian cells in vitro. The mechanism of the association between ureaplasmas and cells in vivo is not known, but the possibility that it might be influenced in some way by the presence of *C trachomatis* deserves further study.

This study confirms that *U urealyticum* is common in the urine and cervix of sexually active women, but it has not established a pathological role for the organism.

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TABLE V *Ureaplasma* and chlamydial isolation in relation to diagnostic groups

Diagnosis	Chlamydial isolation	Total No of specimens	<i>Ureaplasma</i> - positive		With <10 <sup>5</sup> ccu		With ≥10 <sup>5</sup> ccu	
			No	%	No	%	No	%
All groups	+	81	43	53.1	34	42.0	9	11.1
	-	319	157	49.2	100	31.3	57	17.9
Gonorrhoea	+	30	14	46.7	11	36.7	3	10.0
	-	45	26	57.8	14	31.1	12	26.7
NGU Contact	+	21	12	57.1	9	42.9	3	14.3
	-	34	16	47.1	6	17.6	10	29.4

ccu = colour-changing units  
+ = positive; - = negative

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