

THE AETIOLOGY OF URETHRAL DISCHARGE IN MEN

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SYNOPSIS

The aetiology of urethral discharge in 94 heterosexual males was studied prospectively. *N. gonorrhoeae* was isolated in 73 (78%), *C. trachomatis* in 19 (20%), *Mycoplasma* sp in 12 (13%) and *C. albicans* in 9 (10%). Two or more pathogens were isolated in 25 (27%), and in 12 (13%) patients no pathogens were isolated. Of 73 cases with gonococcal urethritis, 25 (34%) were found to harbour other potential pathogens. *C. trachomatis* was isolated from 14 patients; 6 at initial visit and another 8 at day 14. Hence, the overall isolation rate of *C. trachomatis* from patients with gonorrhoeae was 19.2% (14/73).

Our results indicate that *N. gonorrhoeae* was the commonest cause of urethral discharge and that a significant number of these cases also harboured other potential pathogens. A significant number of these pathogens were recovered on repeat sampling at 2 weeks after treatment of gonorrhoea indicating the need for repeat sampling after the acute gonococcal infection has resolved.

INTRODUCTION

Urethritis is traditionally divided into gonococcal and non-gonococcal urethritis (NGU). NGU has become an important sexually transmitted disease (STD). Its incidence has been increasing and it has displaced gonorrhoea as the commonest STD in many European countries. In England and Wales where there has been nationwide recording of incidence data since 1951, NGU appears to be twice as common as gonorrhoea in men. Available data in Singapore (Middle Road Hospital Annual Reports) suggest that although NGU is less common than gonorrhoea, its incidence is increasing. In 1981, there were 252 cases of NGU and 1926 cases of gonorrhoea in men. The corresponding figures for 1982 were 499 and 2019. There has been, therefore, a nearly two-fold increase in the incidence of NGU. The ratio of gonococcal to non-gonococcal urethritis in men decreased from 7.6 : 1 in 1981 to 4 : 1 in 1982.

Whilst the gonococcus is an undisputed cause of urethritis, the significance of the other organisms implicated in NGU is less clear. Part of the difficulty stems from the occurrence of these organisms in normal controls. As such, the pathologic role of these organisms cannot be established unequivocally. Nevertheless, some conclusions can be made about the aetiology of NGU. Two organisms, namely *Chlamydia trachomatis* and *Ureaplasma urealyticum* are now widely accepted as causes of NGU. *Chlamydia trachomatis* is thought to be responsible for 20-50% of all cases of NGU (1-3). The isolation rate of *Chlamydia trachomatis* in heterosexual men with gonococcal urethritis is approximately 25% (1). *Chlamydia trachomatis* was isolated in 81% of men with post gonococcal urethritis (PGU) (2). In other series PGU developed in almost all men treated for gonorrhoea with penicillin, gentamicin or spectinomycin (4,5) who had concurrent *Chlamydia trachomatis* infections. Ridgway et al (16) found kanamycin to be totally ineffective against *Chlamydia trachomatis*. There is also evidence to suggest that *Ureaplasma urealyticum* may play a role in the aetiology of NGU. Although this organism has been recovered from the urethras of asymptomatic men, epidemiologic and restricted spectrum antibiotic treatment studies demonstrated that *U. urealyticum* is responsible for at least some of the *Chlamydia trachomatis* negative cases of NGU (7,8). *Mycoplasma hominis* is not generally regarded as significant in the aetiology of NGU (7,9). Certain strains of *Corynebacterium genitalium* have also been implicated in the aetiology of NGU (10). Herpes simplex virus, *Candida albicans* and *Trichomonas vaginalis* are other potential agents causing NGU but these are thought to be uncommon.

This study was conducted to determine the aetiology of acute urethral discharge in men. Careful attention was paid to *N. gonorrhoeae* and *C. trachomatis* since these organisms have an established role in the aetiology of urethritis. Cultures for *Mycoplasma sp.*, *Candida albicans* and *Trichomonas vaginalis* were also performed.

PATIENTS AND METHOD

Study Population

A restricted survey was conducted between January and March 1983. We enrolled 125 heterosexual males in this study. Only patients with new episodes of urethral discharge whose last attack was more than 3 months ago were recruited. The study was mainly microbiological and no special attempt was made to correlate our findings with the clinical appearance of the urethral discharge or the results of urethral smears. Patients who had received antimicrotherapy over the 72 hours prior to the start of the study were excluded.

Microbiologic Methods

N. gonorrhoeae

A gram stained urethral specimen was examined for gram negative intracellular diplococci. The modified Thayer Martin medium was used for the isolation of gonococci. Inoculated culture plates were incubated in a candle extinction jar for 48 hours and then examined. Colonies of typical morphology which gave a positive oxidase reaction and which contained gram-negative diplococci on gram smear examination confirmed the diagnosis.

Chlamydia trachomatis

An endourethral specimen was obtained using a cotton-tipped urethral swab. The swab was then agitated in 2 ml of antibiotic containing transport medium (2SP), and then discarded. All such specimens were then stored in ice and transported to the laboratory where they were cultured for

C. trachomatis. Thawed specimens were inoculated into cycloheximide-treated McCoy cells, incubated for 2-3 days, stained with Giemsa stain and then examined under a darkfield microscope. *C. trachomatis* was considered to be present if characteristic intracytoplasmic inclusions were seen.

Mycoplasma sp

Endourethral specimens were transported in mycoplasma transport media to the laboratory for culture on solid media. *Mycoplasma sp* was identified on colonial morphology and no attempt was made to speciate the strains further.

C. albicans and *Trichomonas vaginalis*

Endourethral specimens were obtained using cotton-tipped swabs which were then agitated in Trichocell media. These samples were incubated for 48 hours and then examined under light microscopy. Trichomonads were recognised by their oval shape, their rapidly moving flagella and jerky movements. *Candida* species was identified by the presence of budding yeast cells and pseudohyphae. Such specimens were later inoculated into rice extract agar and incubated for 48 hours. *C. albicans* was identified on finding filamentous outgrowths (pseudo-germ tubes) radiating from the previously rounded or oval yeast cells.

TREATMENT

All cases were treated on the basis of gram stained urethral smears. Gonococcal urethritis was treated with one of the following regimens:

- 1) Ampicillin 3.5g and Probenecid 1g orally and kanamycin 2g I.M.
- 2) Kanamycin 2g I.M.
- 3) Spectinomycin 2g I.M.
- 4) Amoxycillin 3g + clavulanic acid 250mg x 2 doses 4 hours apart.

All other cases with a urethral discharge in which gonococci cannot be identified were treated as for NGU with tetracycline or erythromycin in doses of 250-500 mg qds for 2 weeks.

Follow-up

All cases were seen again at day 14 after treatment. Gram stained urethral smears, cultures for *C. trachomatis*, *Mycoplasma sp.*, *C. albicans* and *T. vaginalis* were repeated. Patients with gonococcal urethritis were also seen on day 5 for assessment and repeat gram stained smears and cultures for *N. gonorrhoeae*. All patients were advised to refrain from sexual intercourse and alcohol consumption during the 2-week study period.

RESULTS

On hundred and twenty-five men with acute urethral discharge were enrolled in the study. Thirty-one patients were not evaluable due to failure to attend follow-up, re-exposure or contaminated cultures. There remained therefore 94 men for assessment.

Of the 94 with urethral discharge, 73 (77.7%) were found to have gonococcal urethritis and 21 (22.3%) non-gonococcal urethritis (see Table 1). The ratio of GU : NGU cases was approximately 3.5 : 1. The microbiological results of the 21 cases of NGU are presented in Table 2. *C. trachomatis* was the commonest pathogen with an isolation rate of 23.8% (5/21). The isolation rates for *Mycoplasma sp.* and *C. albicans* were similar — 9.5% (2/21). In the remaining 57.2% (12/21) of cases, no micro-organisms could be

TABLE 1
Diagnoses in 94 men with urethral discharge

Diagnosis	No	%
Gonococcal urethritis	73	77.7
Non gonococcal urethritis	21	22.3
Total	94	100.0

TABLE 2
Frequencies of recovery of micro-organisms from 21 men with non gonococcal urethritis

Agent	No.	% of total NGU cases
C. trachomatis	5	23.8
Mycoplasma	2	9.5
C. albicans	2	9.5
No organism	12	57.2
Total	21	100.0

identified.

The frequencies of isolation of micro-organisms in all 94 cases of urethral discharge are shown in Table 3. *N. gonorrhoeae* was isolated in 73 (77.7%), *C. trachomatis* in 19 (20.2%) *Mycoplasma* sp in 12 (12.8%) and *C. albicans* in 9 (9.6%) of these 94 cases. The total isolates exceed 94 as 25 patients had mixed infections in which more than one micro-organism was isolated.

TABLE 3
Frequencies of recovery of micro-organisms from all 94 men with urethral discharge

Agent	No. of patients with isolate (%)	No. where sole isolated
<i>N. gonorrhoeae</i>	73 (77.7)	48
<i>C. trachomatis</i>	19 (20.2)	5
<i>Mycoplasma</i>	12 (12.8)	2
<i>C. albicans</i>	9 (9.6)	2

Other potential pathogens were also isolated from 25 (34.2%) of 73 patients with gonorrhoea (Table 4). *C. trachomatis* was isolated from 19.2% (14/73), *Mycoplasma* sp from 13.7% (10/73) and *C. albicans* from 9.6% (7/73). Of 14 patients from whom *C. trachomatis* was isolated, 6 yielded positive cultures on initial sampling and another 8 on sampling on day 14.

TABLE 4
Frequencies of recovery of other potential Pathogens from 73 men with Gonococcal Urethritis

	Total	Day 1	Day 14
<i>C. trachomatis</i>	11	4	7
<i>Mycoplasma</i>	5	4	1
<i>C. trachomatis</i> + <i>Mycoplasma</i>	2	1	2
<i>Mycoplasma</i> + <i>C. albicans</i>	2	—	1
<i>C. trachomatis</i> + <i>Mycoplasma</i> + <i>C. albicans</i>	1	1	—
<i>C. albicans</i>	4	1	3
25TOTAL		11	14

DISCUSSION

The most common pathogen isolated was *N. gonorrhoeae* followed by *C. trachomatis*, *Mycoplasma* sp and *C. albicans* in that order. In no instance was *T. vaginalis* isolated. Gonococcal infections were easily identified on single initial cultures. A significant proportion (34.2%) of patients with gonorrhoea were found to harbour other potential pathogens. Theoretically, about 34% of patients with gonococcal urethritis may need treatment for co-existing pathogens as usual regimens for the treatment of gonorrhoea are unlikely to be effective against these other pathogens.

There were a total of 73 cases of gonococcal urethritis compared with 21 cases of non-gonococcal urethritis giving a ratio of 3.5:1. Unlike European countries, gonorrhoea is still the most common cause of urethral discharge in Singaporean men.

The incidence of *C. trachomatis* in heterosexual men with gonococcal urethritis was 25% in the study of Oriel et al (1). In the present study, the isolation rate of *C. trachomatis* was 19.2%. Interestingly, 6 patients were culture positive for *C. trachomatis* on initial and another 8 were identified on testing at day 14. The increase in isolation rate may be due to the advantage of repeat sampling or because the interval of 2 weeks has allowed a higher concentration of *C. trachomatis* to develop. Another possibility might be that the presence of gonococcal infection in some way adversely affects the isolation rate of *C. trachomatis*. Nevertheless, whatever the explanation, the above findings emphasize the need for repeat cultures for *C. trachomatis* after treatment of the gonococcal infection. Assuming that nearly all patients with gonococcal urethritis who have concurrent *C. trachomatis* infection go on to develop post-gonococcal urethritis, we

would expect a PGU rate of 19.2% (14/73) in our patients.

Candida albicans was isolated in 9 (9.6%) of 94 cases. In 7 cases *C. albicans* was found with other pathogens and in the remaining 2 cases it was the sole agent isolated. All such cases resolved without specific anti-candidal therapy suggesting that any urethritis present was due to other co-existing pathogens.

Mycoplasma sp was isolated in 12 (12.8%) of 94 cases. It was usually found in association with other organisms (10 cases) and as the sole agent in only 2.

This study shows that *N. gonorrhoeae* was the commonest pathogen isolated, being found in about 78% of all cases of urethral discharge. *C. trachomatis* was found in 20% and *Mycoplasma sp* in about 13%. *C. albicans* was found in nearly 10% but in all cases, the urethral discharge cleared without specific anti-candidal treatment. This suggests that other agents were responsible and that *C. albicans* was the "innocent bystander". It is also desirable to repeat sampling for other pathogens after treatment of gonococcal infections.

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