

CHLAMYDIA TRACHOMATIS URETHRITIS IN MEN ATTENDING A VENEREAL DISEASE CLINIC: A CULTURE AND THERAPEUTIC STUDY

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Abstract. Urethral specimens from 459 male patients attending a venereal disease clinic were studied for presence of *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. Of the 459 patients, 362 had symptoms suggestive of urethritis. In these 362, gonorrhoea was diagnosed in 78 (22%), while 88 (24%) harboured *C. trachomatis*; 15 harboured both organisms. Of those patients from whom *C. trachomatis* was isolated, 17% had no subjective symptoms of urethritis; the same percentage of symptomless carriers of gonococci was found. Watery discharge occurred more frequently in patients with chlamydial urethritis than in patients with gonorrhoea, while in the latter condition purulent discharge was more often found. Treatment with doxycycline for 9 days rendered 28 of 29 chlamydia-positive patients culture negative at control.

Key words: *Chlamydia trachomatis*; Urethritis; Non-gonococcal urethritis; Diagnosis; Treatment

Non-gonococcal urethritis (NGU) is known to be more common than gonococcal urethritis among men attending venereal disease (VD) clinics in the United Kingdom and the USA (3, 19). Of all patients with NGU, 25-50% harbour *Chlamydia trachomatis*. Accumulating evidence that *C. trachomatis* is an important pathogen in urethritis in males has reached convincing proportions during the last decade (1, 2, 5, 7, 13, 15, 17, 19, 20). Men with gonococcal urethritis often also harbour *C. trachomatis* (1, 7, 14, 15, 17, 19). If the gonococcal infection in these patients is treated with β -lactam antibiotics they may subsequently develop post-gonococcal urethritis (PGU); chlamydial infections being incurable by such treatment (16).

It is at present possible to isolate *Neisseria gonorrhoeae* from 20-30% of men visiting VD

clinics in Sweden. Figures on the incidence of infections with *C. trachomatis* have not yet been published.

This communication reports on the experience of a seven-month culture study in which isolation of *C. trachomatis* and *N. gonorrhoeae* was performed on a routine basis from male patients visiting a Swedish VD clinic. A new and simplified method for the isolation of chlamydia in cycloheximide-treated McCoy cells (18) was used, as was a new effective culture medium for gonococci (10). The results of doxycycline therapy on patients found to harbour *C. trachomatis* are also presented.

MATERIALS AND METHODS

Patients

All 229 male patients attending the VD clinic, University Hospital, Lund, and who complained of symptoms suggestive of urethritis, i.e. urethral discharge, itching, and painful voiding, over a 5-month period (September 1976 to January 1977) were included in the study. In addition, all men, regardless of symptoms, attending the same clinic during the subsequent 2 months (February-March 1977) were studied. During these 2 months, 133 patients with symptoms of urethritis and 97 males lacking such symptoms attended the clinic.

Most of the patients visiting the VD clinic did so voluntarily. In conformity with the Swedish Law for the control of venereal diseases, some had been requested to attend the clinic, being sexual consorts of patients in whom gonorrhoea had been diagnosed. Some had been asked by their partner having diagnosed gonorrhoea, to seek medical advice. These two latter categories made up 10-15% of the entire series of patients studied.

Symptoms of discharge, itching and painful voiding were recorded. The patients were asked to characterize their discharge, if any, as purulent or watery.

Table 1. Isolation frequency of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in 362 male patients with symptoms of urethritis attending a VD clinic

Organism isolated	Organism isolated from no. of patients	
	n	%
<i>C. trachomatis</i>	88	24
<i>N. gonorrhoeae</i>	78	22
<i>C. trachomatis</i> and <i>N. gonorrhoeae</i>	15	4

Sampling technique and transport medium

From all patients, specimens were obtained for the culture of *C. trachomatis* and *N. gonorrhoeae*. Specimens for the culture of *C. trachomatis* were collected with a calcium-alginate swab (Inolex Corp., Glenwood, Ill., USA), which was inserted 2-4 cm into the urethra and gently rotated before being withdrawn. The swabs were transported in sucrose-phosphate buffer (6) supplemented with 10 µg gentamicin (Schering) and 2.5 µg amphotericin B (Squibb) per ml. The specimens were kept at 4°C if the culture could be commenced within 24 hours of sampling. Otherwise they were stored at -80°C until required. Samples for culture of *N. gonorrhoeae* were collected from the urethra with cotton-tipped swabs. Immediately after sampling, the swabs were used to inoculate haematin agar plates (10).

During the last 2 months of our study, urethral smears, prepared from material collected by gentle curettage, were made from all patients studied. These smears were made at the patient's first attendance and were not early-morning samples. The number of leukocytes per high-power field (HPF) (×100 objective) were counted and the counts graded as follows: <10, 10-30, and >30 leukocytes per HPF.

Isolation procedures

C. trachomatis was isolated on McCoy cells which were treated with cycloheximide, according to a method we have recently devised (18).

N. gonorrhoeae was isolated on a new gonococcal medium, the composition of which we have described elsewhere (10). Immediately after inoculation, the haematin agar plates were placed in an incubator, maintained at 37°C, with regulated CO₂ atmosphere and humidity (As-sab, Gothenburg, Sweden, model Medicin T). The methods used for identification of *N. gonorrhoeae* were as reported previously (8).

Treatment

The patients from whom *C. trachomatis* had been isolated were treated with doxycycline (Vibramycin, Pfizer). On the first day of treatment, 200 mg of doxycycline was administered, while 100 mg was given on each of the following 8 days. All 88 patients treated were asked to return for check-up. Of these patients, 29 did return within

5-54 days after completion of their treatment. The mean period which had elapsed before the patients were re-examined was 15 days. Contact tracing of the sexual contacts to the chlamydia-positive men was not pursued, except in simultaneous cases of gonorrhoea.

All patients with gonorrhoea were treated with pivampicillin 1.4 g (Pondocillin, Löwens, Denmark), and probenecid 1 g (Probecid, Astra, Sweden) instituted as a single dose. All patients with gonorrhoea who also harboured chlamydia were prescribed doxycycline when they returned for control culture for gonococci.

The patients were asked to refrain from sexual intercourse until control cultures for chlamydia and/or gonococci proved negative.

RESULTS

Isolation of *C. trachomatis* and *N. gonorrhoeae*

The isolation rates of *C. trachomatis* and *N. gonorrhoeae* in the entire series of patients studied are shown in Table 1. Fifteen of the 78 (19%) patients with gonorrhoea were also found to harbour chlamydia. *C. trachomatis* was isolated from 73 (26%) of the remaining 284 men studied, who presented with symptoms suggestive of urethritis.

In the series of 230 patients who were studied regardless of symptoms of urethritis, gonococci were isolated from 30 (13%). Five of these patients had no symptoms of urethritis. Thus the frequency of symptom-free carriers of gonococci was 17%. *C. trachomatis* was isolated from 36 of these 230 patients, 6 (17%) of whom had no symptoms suggestive of urethritis.

Symptoms and signs versus results of cultures

Some of the symptoms reported by the patients as correlated to the findings of *C. trachomatis* and *N. gonorrhoeae* are presented in Table II. Purulent discharge was more common in the patients harbouring *N. gonorrhoeae* than in *C. trachomatis* cases. The reverse was found with regard to watery discharge.

The results of the leukocytes counting in urethral smears are shown in Table III. Most of the patients with gonorrhoea had more than 30 leukocytes per HPF. The numbers of patients in whom chlamydia had been found were more evenly distributed between the three leukocyte grading groups. In the 78 patients from whom neither *N. gonorrhoeae* nor *C. trachomatis* had been isolated, 45 (58%) had fewer than 10 leukocytes per HPF.

Table 11. Symptoms of urethritis correlated to isolation of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in 362 men with symptoms of urethritis visiting a VD clinic

Symptoms	<i>C. trachomatis</i> (N=73)		<i>N. gonorrhoeae</i> (N=63)		<i>C. trachomatis</i> and <i>N. gonorrhoeae</i> (N=15)		Neither organism isolated (N=211)	
	n	%	n	%	n	%	n	%
Purulent discharge	13	18	46	73	11	73	30	14
Watery discharge	38	52	13	21	3	20	112	53
Itching	12	16	1	2	0	0	23	11
Painful voiding	40	55	38	60	7	47	123	58

Effect of treatment

After the treatment with doxycycline, *C. trachomatis* could only be isolated from one of the 29 culture-positive patients who returned for check-up. In this patient, 54 days had passed since the last day of treatment until the control culture was made. Of the 28 patients with chlamydia-negative control cultures, 25 were symptom-free. Two patients still felt pain when voiding and one reported slight discharge. The control cultures from these 3 patients were made 33, 13, and 12 days, respectively, after the last day of treatment. The remaining 59 men from whom chlamydia had been isolated did not return.

DISCUSSION

Gonorrhoea was diagnosed in 22% of the 362 men studied, who had symptoms suggestive of urethritis. *C. trachomatis* was isolated from 24% of all these 362 men. Thus *C. trachomatis* did occur

more often than *N. gonorrhoeae* in these patients. Of the 284 men with NGU (18% of the total number of men presenting symptoms of urethritis), *C. trachomatis* was isolated from 26%. In reports from the United Kingdom and the USA, isolation rates of 26–49% have been given for chlamydia in men with NGU (1, 2, 5, 7, 13, 15, 17, 19, 20). The diagnostic criteria of urethritis applied in these studies have varied. Thus Smith et al. (20) found chlamydia in 26% in a series of men with subjective symptoms of urethritis, while Oriel et al. (15) isolated *C. trachomatis* from 49% of men who had more than 10 leukocytes per HPF in the urethral smear and in whom gonorrhoea had not been diagnosed. If we had employed the same criteria as Oriel and co-workers regarding leukocytes in urethral smear, 31% of our patients harbouring chlamydia would have been characterized as lacking signs of urethritis. On the other hand, the incidence of chlamydial urethritis among our patients with NGU would have risen to 38%.

Of the men from whom *C. trachomatis* had been isolated, 17% were asymptomatic. Of those men who had gonorrhoea, the same percentage were symptomless. In a series of women in the United Kingdom, three-fourths of those from whom *C. trachomatis* had been recovered from the cervix lacked subjective symptoms (11). A similar figure for asymptomatic female gonococcal carriers has been given from the same country (3).

From men with gonococcal urethritis, isolation rates for *C. trachomatis* of 11–34% have been reported (1, 7, 14, 15, 17, 19). Richmond et al. (17) found that in a series of 32 men with gonorrhoea, and from whom chlamydia had been isolated, 63% developed PGU. In our study, chlamydia was isolated from 19% of those men in whom gonorrhoea was diagnosed. This suggests that treatment of

Table 111. Number of leukocytes in urethral smears correlated to the isolation of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in 132 men with symptoms of urethritis visiting a VD clinic

Leukocytes per HPF ^a	<i>C. trachomatis</i> (N=34) ^b		<i>N. gonorrhoeae</i> (N=20) ^b		Neither organism isolated (N=78)	
	n	%	n	%	n	%
<10	10	29	3	15	45	58
10–30	13	38	5	25	16	21
>30	11	32	12	60	17	22

^a HPF=high power field ($\times 100$ objective).

^b These series include 5 patients from whom both *C. trachomatis* and *N. gonorrhoeae* were isolated from urethral specimens. One patient had <10 and 4 >30 leukocytes per HPF.

gonorrhoea with β -lactam antibiotics will result in a not-negligible number of cases with chlamydial PGU. Treatment of gonorrhoea with 2 g ampicillin plus 1 g probenecid does not eradicate a simultaneously occurring genital chlamydial infection (16).

The use of cycloheximide-treated McCoy cells has been found an effective method for the isolation of *C. trachomatis* (18) from clinical specimens. This culture technique does not involve pretreatment of the cell culture; consequently the method is convenient for use in the diagnostic laboratory. In the present study we did not pass the primary chlamydial cultures to fresh cell culturing, as Darougar et al. (4) and Oriel et al. (13) reported no advantage of a two-passage system when using irradiated McCoy cells.

The selective culture medium for *N. gonorrhoeae* employed was a dehydrated, commercially available Gc Agar Base to which, inter alia, pig serum and horse blood had been added. Trimethoprim and polymyxin B were used as antimicrobials. Our new medium was found to achieve a significantly higher isolation rate for gonococci from genital specimens than when the same specimens were cultured on the modified Thayer-Martin medium and media consisting of Gc Agar Base and additives and which were prepared according to the instructions of the manufacturers (BBL, Difco, Oxoid) (10).

Watery discharge occurred more often among the men with chlamydial urethritis than among those who had gonorrhoea (Table II), which finding is in agreement with other published results (20, 21). The men with gonococcal urethritis more often had a high leukocyte count in their urethral smears than the men with chlamydial urethritis. However, this difference could not be correlated to the character of the discharge as reported by the patients themselves.

With the diagnostic procedures undertaken in the present investigation, it was possible to obtain an aetiological diagnosis in about half of all patients studied who had symptoms of urethritis. In the remainder, no aetiological diagnoses could be obtained. No attempts were made to diagnose infections by organisms such as *Ureaplasma urealyticum*, *Trichomonas vaginalis*, candida sp. and herpes viruses which might have been aetiologically involved in some of the patients.

It is known that a large proportion of men complaining of symptoms of posterior urethritis also have mental disturbances but no evidence of somat-

ic diseases (12). In the men from whom neither gonococci nor chlamydia could be isolated, 58% had only 0-10 leukocytes per HPF in their urethral smear. In this group, some patients might have been included who had no somatic disease at all. Furthermore, among the men studied, some had probably attended the clinic merely because of a fear of having acquired a venereal infection.

A tetracycline drug has generally been considered as "the drug of choice" for treatment of genital infections with chlamydia. However, there is still no established recommendation for the duration of such a course of treatment. The eradication of chlamydia and the disappearance of symptoms in almost all of the patients treated with doxycycline for 9 days and who returned implies that the antibiotic regime administered can be recommended as an effective therapy for chlamydial urethritis.

The need for laboratory facilities to diagnose gonorrhoea is generally agreed upon. The indications are that genital infections caused by chlamydia are at least as common as those attributable to gonococci. Uncomplicated genital chlamydial infections may cause serious complications; in our hospital catchment region, *C. trachomatis* is probably a more common cause of acute salpingitis than is *N. gonorrhoeae* (9). From the clinical picture it is not, generally speaking, possible to diagnose genital chlamydial, or gonococcal, infections. Patients harbouring *C. trachomatis* and *N. gonorrhoeae* are often symptomless. The reasons given imply that it is just as necessary to perform laboratory diagnoses of chlamydial infections as of gonococcal infections.

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