Clinical Paper

Gonorrhoea in men: clinical and diagnostic aspects

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Aim: To review the features of gonococcal infection in men in the 1990s.

Methods: A retrospective study of all men with gonorrhoea presenting to an inner city department of genitourinary medicine in the years 1990 to 1992.

Results: 1749 cases of gonorrhoea were seen in 1382 men. A high incidence of gonorrhoea was found in attenders of African or Caribbean extraction. In 228 men with a known date of infection, the incubation period, a mean of 8.3 days, was longer than previously described. The mean infectious period was 12.0 days. By 14 days 86.2% of men had developed symptoms. Of 1615 men with urethral infection 81.9% complained of discharge, while dysuria occurred in 52.8%. Discharge with dysuria were present in only 48.1% of patients. In 10.2% episodes of urethral infection the patients had no symptoms referable to their gonorrhoea. Urethral gonorrhoea was diagnosed by microscopy in 94.4% of symptomatic men and in only 81.1% of asymptomatic men. Microscopy of rectal samples were positive in 46.4% of cases. In this population, a dose of 2g of ampicillin with 1g of probenecid gave a high cure rate of gonorrhoea as long as infection was not due to penicillinase-producing organisms.

Conclusions: These data suggest that the incubation and infectious period of urethral gonorrhoea has increased compared with previous studies and that symptoms have altered. Only 48.1% of men described the classical symptoms of discharge with dysuria. Microscopy of urethral smears remains useful in symptomatic men but is less sensitive in those without symptoms.

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Keywords: gonorrhoea; diagnosis; incubation period; post gonococcal urethritis; men

Introduction

There has been little published work on clinical aspects of gonococcal infection in men since before the 2nd World War and much that is written reflects received information, passed down from previous authorities. The continuing drift towards decreased antibiotic sensitivity of *Neisseria gonorrhoeae* is well documented but one might expect to see changes in the organism (as has been shown in women),¹ with regard to the symptoms it produces and its incubation period, as a result of the widespread use of effective anti-gonococcal therapy. A selective advantage might accrue to those strains of the gonococcus that produce fewer symptoms, at a later stage.

We have undertaken a review of all cases of gonorrhoea in men seen in the Department of Genitourinary Medicine at St Thomas' Hospital during the three years 1990 to 1992. In this study attention was paid to symptoms at presentation, their duration, and demographic details.

Methods

Following clinical examination, all patients underwent standard investigations.² A sample of urethral material was gram-stained and examined microscopically for the presence of gram-negative intracellular diplococci (GNID). A rectal sample from homosexual men was similarly examined and in all cases confirmation of gonorrhoea was sought from

the laboratory by sending samples, including those from the oropharynx, plated directly on to a selective but non-inhibitory lysed blood agar medium containing vancomycin, colistin, amphotericin and trimethoprim. A pharyngeal swab was taken routinely from all homosexual men, and from heterosexual men either at the time GNID were seen on the urethral smear or, if the smear was negative, at the time of treatment following a positive culture for gonorrhoea. A diagnosis of gonorrhoea was made if the oxidase test and the Phadebact monoclonal antibody test were positive. Samples that showed GNID on microscopy but which failed to grow *N. gonorrhoeae* were not counted as cases of gonorrhoea. Isolates were tested for sensitivity using penicillin, ciprofloxacin and nalidixic acid discs. Penicillin resistant strains were examined for beta-lactamase production and those isolates found to have reduced zone sizes to ciprofloxacin and nalidixic acid had MIC measured.

All patients had urethral swabs taken for *Chlamydia trachomatis* at the initial visit, and in all cases the test used was cell culture.

Patients with gonorrhoea were treated with ampicillin 2g and probenecid 1g, unless there was a history of penicillin hypersensitivity or a suspicion that the organism was penicillinase-producing *N. gonorrhoeae* (PPNG), when ciprofloxacin 250mg was administered (the clinic operates a policy of predicting PPNG in those with a history of overseas connections).³

Patients were seen for tests of cure at 1-3

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Table 1 Ethnic group of heterosexual patients with gonorrhoea (GC)

	Heterosexuals GC	Clinic population*	Odds Ratio
Black	1227 (87.6%)	11904	15.03
White	148 (10.6%)	21576	95% CI (12.65–17.85)
Asian	12 (0.9%)		
Oriental	10 (0.7%)		

*Figures for diagnoses in male heterosexuals attending the clinic in 1990–92.

and 10 days after treatment. A diagnosis of post gonococcal urethritis was made at this second test of cure in men who had a negative chlamydia culture from the initial visit, and whose urethral smear was negative for GNID, but where there were five or more polymorphonuclear leucocytes (PMN) per high power field, and in the absence of another cause of urethritis, such as meatal warts, balanitis or herpes infection.

Results

Full data were missing for 12 episodes, which were excluded from the analysis. There were 1749 episodes of gonorrhoea in 1382 men, including 88 (5.0%) due to PPNG.

Coincidental infection of the urethra with *C trachomatis* was found in 212 (15.3%) of 1387 cases of gonorrhoea in heterosexuals. Heterosexual men with gonorrhoea were significantly ($p < 0.001$) more likely to be black (of African or Caribbean extraction) than the general clinic population (table 1).

There were 362 episodes of gonorrhoea in 293 homosexual men, of whom 272 were white. Sixty eight (23.2%) men were known to be HIV seropositive prior to the diagnosis of gonorrhoea. In eight (2.2%) of these episodes *C trachomatis* was isolated.

In 127 (7.3%) cases, the gonorrhoea was directly acquired overseas of which 53 (41.7%) of organisms were PPNG, mainly from regions where this is endemic. Imported gonorrhoea was seen from five continents, including 25 from Europe, 28 from the West Indies of which 15 (53.6%) were PPNG, 13 from North America, 30 from West Africa of which 23 (76.7%) were PPNG and 18 cases

from South East Asia of which nine were PPNG.

A past history of gonorrhoea was given by 426 (30.8%) patients, and 259 men had repeated infections (626 episodes) during the three years of the study, with a maximum of nine episodes in one individual.

The mean age of men with gonorrhoea was 26.7 years (range 14–67).

Incubation period and infectious period

Out of 1615 episodes of urethral gonorrhoea, it was possible to identify the date of infection accurately in 228. These were individuals in whom there was a history of a single contact with an individual on a known date, after which symptoms developed, and where any other partners (usually a long term regular partner) were screened in the department on at least two occasions and found to be free of infection. The incubation period in these men had a range of one to 57 days, with a mean of 8.3 and a median of 5.8 days. When those with coexistent chlamydial urethritis were excluded, the mean incubation period was 8.1 days with a median of 5.6 days. The mean infectious period was 12.0 days (median 8.2) in those with gonorrhoea alone with a range of two to 90 days, and 12.8 days (median 8.1) if chlamydia was also present. By 14 days 86.2% of men had developed symptoms (fig 1).

Symptoms

Information on symptoms were available for 1615 episodes of gonococcal infection of the urethra (table 2). The most common symptom was urethral discharge in 1323 (81.9%) cases, while dysuria occurred in 853 (52.8%). Discharge with dysuria occurred in 777 (48.1%) cases. The average duration of symptoms in patients with urethral infection prior to attending the clinic was 6.2 days with a range of one day to one year. Patients with coexistent chlamydial infection were less likely to complain of urethral discharge and more likely to be asymptomatic when compared with those with gonorrhoea alone. Fifty one (3.2%) patients with urethral gonorrhoea complained of other symptoms related to their gonococcal infection including eleven with pain or swelling of the testes and one with disseminated gonococcal infection who presented with a rash. In 164 (10.2%) episodes of urethral infection, the patients had no symptoms referable to their gonorrhoea, most probably being in the pre-symptomatic stage of gonorrhoea.⁴ A majority (89) of these patients attended as contacts of partners known to have gonorrhoea and a further 42 patients presented with symptoms unrelated to gonorrhoea such as warts or herpes. The remaining 33 patients with symptoms unrelated to gonorrhoea attended for "a check up" or expressing concerns about a recent sexual contact.

Twenty seven (19.6%) of 138 homosexual patients with rectal gonorrhoea had noticed some symptoms with 10 (7.2%) complaining of perianal or anal pain and discomfort, 16 (11.6%) of anal discharge and one (0.7%) of diarrhoea. Gonorrhoea was isolated from the

Figure 1 Infectious and incubation period of urethral gonorrhoea ($n = 228$)

Table 2 Historical incubation periods of urethral gonorrhoea in men

	Year of study	No patients	Mean Incubation	Treatment
Lodin ¹¹	1932	115	4.9 days	topical
Lodin ¹¹	1942	220	4.6	sulphonamides
Lodin ¹¹	1952	193	6.0	penicillin
Lodin ¹¹	1954/5	145	6.1	penicillin
Schofield ¹²	1978	242	6.2	penicillin
Sherrard and Barlow ⁶	1989	113	7.9	penicillin
This study	1990/2	228	8.2	penicillin

oropharynx in 37 (2.7%) heterosexual men and in 67 (18.5%) homosexual men. Four (4.1%) patients with oropharyngeal infection had symptoms referable to the throat.

A total of 15 (0.8%) complications of gonorrhoea were recorded, with 13 cases of epididymo-orchitis, one thrombosis of the dorsal vein of the penis and one disseminated infection. This figure is comparable to the 1.1% rate reported nationally in the 1994 KC60 returns.⁵

Diagnosis

Urethral gonorrhoea was diagnosed by microscopy in 1503 (93.1%) of 1615 episodes. When asymptomatic men were excluded the number of cases of urethral infection diagnosed by microscopy rose to 1370 (94.4%) of 1451 episodes. In asymptomatic urethral infection the diagnosis was made by microscopy in only 133 (81.1%) of 164 episodes. In six of the 31 asymptomatic episodes, where microscopy was negative for GNID, there were less than 5 PMNs per high power field.

Microscopy of rectal samples was less sensitive, with 64 positives (46.4%) out of 138 cases: this is a higher figure than the 30.6% found in women.¹

Treatment

Ampicillin 2g with probenecid 1g was prescribed in 1406 episodes of gonorrhoea, and

failed to eradicate the infection in 51 (4.2%) of the 1211 cases where there was at least one test of cure performed. PPNG was isolated from 28 of these treatment failures and two further isolates were penicillin resistant. Excluding those with PPNG, our regimen of low dose ampicillin with probenecid, gave a cure rate of 1160 (98.1%) of 1183 cases where there was follow up. Of the 21 treatment failures in patients with penicillin sensitive organisms, seven failures were in the oropharynx and four in the rectum; all these patients were asymptomatic. There were 10 episodes of failure to eradicate urethral infection and eight of the patients were asymptomatic, having previously been symptomatic. Nine patients with PPNG were treated with ampicillin and probenecid and cured with this regime.

Ciprofloxacin 250 mg was the initial treatment in 149 episodes, with three (2.0%) failures, two of which were with ciprofloxacin resistant organisms, one of which was additionally PPNG. The third treatment failure occurred in a case of oropharyngeal infection. Other treatments included co-trimoxazole, spectinomycin, and tetracycline when microscopy had been negative for *N gonorrhoeae*. Seven (0.4%) patients who were microscopy negative and had no urethritis received no treatment as they defaulted from follow up, and subsequent attempts to contact them were unsuccessful.

Follow up

Following a diagnosis of gonorrhoea patients were given an appointment to reattend in 24–48 hours, and again 10 days later. Despite the efforts of the Health Advisers 235 (13.5%) of the 1742 patients receiving treatment failed to attend for any follow up, and a further 332 (19.1%) defaulted their second test of cure. There was complete follow up in 1175 (67.2%) episodes.

Other infections

C trachomatis was isolated in 220 (12.6%) episodes of which 212 were heterosexually acquired. Forty six (20.9%) of patients with coexistent chlamydial urethritis defaulted follow up and therefore were not treated. Of the 1075 patients with urethral gonococcal infection who completed follow up 174 had chlamydia and 639 (70.9%) of the remaining 901 were diagnosed as having post gonococcal urethritis.

Other coexistent infections included genital warts in 3.3% patients, HIV infection (both previously known and newly diagnosed) in 86 (4.9%) men, genital herpes in 26 (1.5%) patients, *Trichomonas vaginalis* in 33 (1.9%) and 38 men with scabies, *Pediculosis pubis* or candidiasis. Three men were found to have early infectious syphilis and six cases of late latent disease were diagnosed.

Discussion

It appears that gonorrhoea in men is a changing disease which confirms earlier studies from 1989.⁶ The "classical" presentation of gonor-

Figure 2 Symptoms of urethral gonorrhoea in men (n = 1615)

rhoea is discharge with dysuria.⁷⁻¹⁰ In this study these symptoms were found together in only 48.1% of all those with urethral infection, or 54.7% of patients with gonorrhoea without chlamydia. It was not possible to quantify the severity of the dysuria but very few of the case-notes refer to the severe burning discomfort ("chaudepisse") of yesteryear.

The incubation period of gonorrhoea is given (unreferenced) in textbooks as 2 to 5 days but there have been few attempts to study this systematically. Lodin¹¹ suggested in 1955 that the incubation period of gonorrhoea might be increasing. Previous studies¹¹⁻¹² have used the mean incubation period, a less meaningful measure than the median, in our view. However, it is clear that this has steadily increased since the introduction of antibiotics (table 2) and it is of note that the incubation period is longer than that seen in the same clinic in 1989.⁶ A prospective study in 1974,¹³ using a captive population which had been exposed to gonorrhoea in the Far East, gave a mean incubation period of 3.4 days but all participants had been briefed (and screened) before exposure and may have been on the lookout for symptoms. It may be that there are significant educational and social differences between the various study populations, but the published data do not allow for comparison. It is likely that very few of Lodin's population were black, as the study was conducted in Scandinavia in the 1930s to 1950s. It has been suggested in the past that blacks may have fewer symptoms from gonorrhoea for a variety of reasons including an observation that there may be differences in auxotypes found in black and white men.¹⁴ Whilst the typing data on this population are currently incomplete, a study among men with gonorrhoea attending the same clinic in 1989 found no difference in auxotype between black and white men.¹⁵

Lodin¹¹ noted that the period between development of symptoms and presentation at clinic had increased from 1.8 days in 1938 to 3.5 days in 1955. Our figure of 6.2 days, (from a walk-in, no appointment clinic) suggests that this trend continues. This steady increase is hard to explain but could result from a gradual lessening in the severity of symptoms.

Microscopy of a gram-stained urethral sample is confirmed as a highly sensitive examination for gonorrhoea in symptomatic men, although its sensitivity is much reduced in asymptomatic men, even when most of these are presenting as known contacts of gonorrhoea, and the index of suspicion of the microscopist is high.

Gonorrhoea is seen disproportionately in black clinic attenders and the rates of black men attending the clinic are higher than the figures from the census data for the local population. It may be that local heterosexual white men attend GU clinics elsewhere, or that they are more likely to seek care outside GUM clinics. However, the high rates of gonorrhoea in black men concur with other studies in both the USA and UK¹⁶⁻¹⁷ including two recent prospective studies,¹⁸⁻¹⁹ and, as has been previously reported, most cases of repeated infec-

tion occurred in black men.²⁰⁻²² Additionally, data from the national gonorrhoea audit in 1995 found most gonorrhoea in heterosexual men in London to occur in black men (Mark Fitzgerald, personal communication), making it unlikely that white men are seeking care away from their area of residence. Additionally, during the three years of the study there were only seven positive cultures for gonorrhoea in the department of microbiology that did not come from the GUM department, making it unlikely that patients are having the infection diagnosed by their local general practitioners.

Gonorrhoea, like most other sexually transmitted diseases, is accepted as an independent cofactor in the transmission of HIV infection²³ and our findings give cause for concern since high HIV seroconversion rates are already being seen in the USA among a group of heterosexuals who return to an STD clinic with repeated infections.²⁴ This is especially the case as much of the imported gonorrhoea seen at this clinic comes from areas of the world where heterosexual transmission of HIV predominates.

The high default rate from follow up of patients with gonorrhoea is well documented.²⁰ In this clinic population the practice is to withhold antichlamydial treatment until after a second test of cure, but this has resulted in 46 (20.9%) of coexistent chlamydial infections being untreated. The majority of chlamydial infection was found in heterosexual men and the lower incidence of chlamydial infection in homosexual men is in accordance with other studies.²⁵ We have observed patients with concurrent infection to be more likely to have fewer symptoms or to be asymptomatic than patients with gonorrhoea alone which implies they are unlikely to seek medical attention in the future for their chlamydia infection and thus act as a source of infection to others. In addition, if the figures for post gonococcal urethritis in men completing follow up are extrapolated to those defaulting a further 362 patients with urethral infection may have undiagnosed postgonococcal urethritis. However, the rates of postgonococcal urethritis seen in patients completing follow up are higher than described in other studies.²⁶ It may be that such individuals are more likely to remain symptomatic and therefore return for follow up and those defaulting may have lower rates of postgonococcal urethritis. If the rates of postgonococcal urethritis were as high in defaulters, 25% (408) of men with urethral infection may have required additional treatment, and in this clinic consideration needs to be given to treating patients with gonorrhoea concurrently with an antichlamydial agent.

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A cobblestone

A 29 year old Afro-Caribbean man presented with a four month history of episodic, painful swelling of the prepuce occurring during penile erection. He was employed as a male stripper and his stage act culminated in a display of his erect phallus. Immediately before a performance he would produce an erection by masturbation and ligate the base of the penis with a rubber band to prevent detumescence. The first episode of preputial swelling occurred after his show unexpectedly over-ran by several minutes, delaying release of the ligature.

He described the swelling as resembling a tense, fluid-filled ring around the base of the glans penis; the swelling subsided after removal of the ligature allowed detumescence, leaving small linear fissures in the foreskin. Since this initial episode, he had suffered from

intermittent preputial swelling not only at work but also after sexual intercourse with his female partner.

On examination the only abnormal physical finding was a slightly tight prepuce. There was no evidence of lichen sclerosus of the penis and routine investigations excluded sexually transmitted infections.

The patient's history was consistent with recurrent paraphimosis and we informed him that circumcision was advisable, particularly as he wished to continue working as a stripper. In men who are predisposed to paraphimosis, delayed penile detumescence as described in this case may precipitate the problem. Paraphimosis may, therefore, be added to the list of occupational health hazards.

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