Gonorrhoea in men with homosexual contacts

Serogroups of isolated gonococcal strains related to antibiotic susceptibility, site of infection, and symptoms

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SUMMARY In 37 homosexual men the incidences of urethral, rectal, and pharyngeal gonorrhoea were 45·9%, 56·8%, and 27% respectively. Local symptoms were present in all men with urethral gonorrhoea but in only 25% of those with pharyngeal or rectal gonorrhoea or both. Infection at two sites was found in 29·7% of the patients.

Forty-nine gonococcal isolates from the 37 patients were serogrouped by coagglutination into one of the serogroups WI, WII, or WIII, and their susceptibility to benzylpenicillin, ampicillin, cefuroxime, doxycycline, and spectinomycin tested. Only one gonococcal isolate from each patient was counted when two isolates belonged to the same serogroup and had the same antibiotic susceptibility. Thus, 15·4%, 76·9%, and 7·7% of the gonococcal strains belonged to serogroups WI, WII, and WIII respectively. There was a significantly lower incidence of WI strains and a significantly higher incidence of WII strains among men with homosexual contacts than among other patients with gonorrhoea from the same geographical region. Gonococcal strains of serogroup WI were significantly more resistant to all antibiotics tested, except to spectinomycin, than randomly chosen WI strains. Among WII and WIII strains the incidence of diminished susceptibility to all antibiotics tested was about the same.

Introduction

Gonococcal infections of the anorectum and the pharynx are often asymptomatic¹⁻⁴ and more difficult to treat than infections of the urethra or cervix.^{1-4,7} Homosexual men have a higher rate of pharyngeal^{1,6,8,9} and anorectal^{3,8} gonorrhoea than heterosexual men or women. Gonococcal strains from homosexual men are reported to be more resistant to penicillin than gonococcal isolates from heterosexual patients.⁸

Serogrouping of gonococci based on a stable class of antigens, the W antigens, was described by Danielsson and Sandström^{10,11} and by Sandström and Danielsson.^{12,13} Strains could be classified into at least three antigen groups, WI, WII, and WIII. Serological classification of gonococci with this technique showed differences in prevalence of the three serogroups between geographical areas¹⁴ and between strains of different auxotypes.¹⁵ Significant

differences were found in the antibiotic susceptibility of strains in the three serogroups.

The aim of this study was to investigate the incidences of the different W serogroups in strains isolated from men with homosexual contacts in Stockholm. The serogroup patterns were related to antibiotic susceptibility, site of infection, and symptoms. The incidence of gonococcal infection at the three sites—the urethra, rectum, and pharynx—and of symptoms in relation to the sites of infection was also studied.

Patients and methods

GONOCOCCAL ISOLATES

All gonococcal strains from men with known homosexual contacts attending the outpatient clinic for venereal diseases at Södersjukhuset, Stockholm, were included in the study during three study periods—the end of November to mid-December 1979, mid-May to mid-June 1980, and July to the end of December 1980. Patients were questioned about symptoms relating to the urethra, anorectum, and pharynx, and

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Accepted for publication 22 April 1981

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about homosexual contacts. In all homosexual men specimens for culture were taken from all three sites. Thus, 49 gonococcal isolates from 37 men were included in the study (table I).

TABLE I Sites of the gonococcal infections in 37 men with homosexual contacts and the serogroups of the strains isolated

Sites of infection	No of patients	No of strains of serogroups:		
		WI	WII	WIII
Urethra only	11	1	10*	1
Rectum only	12	2	10	
Pharynx only	3	1	2	
Urethra + rectum	4	1*	3	
Urethra + pharynx	2		2	
Rectum + pharynx	5†	1	3	2
Total No	37	6	30	3

*One man had two gonococcal infections within six months and different serogroups of the gonococcal isolates.

†In one man the isolate from the rectum belonged to serogroup WI and that from the pharynx to serogroup WII.

Specimens were inoculated directly on to selective and non-selective hematin agar plates, which were put into candle jars at 37°C and later the same day delivered to the bacteriological laboratory, where they were incubated at 37°C for about 40 hours in 5% CO₂ atmosphere. Gonococci were identified and stored as described.^{15 16}

SEROGROUPING

Serogrouping by coagglutination (COA) was performed as described.^{11 13 15} The gonococcal major outer membrane protein (MOMP) reference strains¹⁷ and an NRL (Neisseria Reference Laboratory) strain (labelled 7122 and obtained from K K Holmes, Seattle, USA) were used for immunising rabbits and for the absorption of antisera. Those strains which were selected for the preparation of COA reagents for the serogroups WI, WII, and WIII are listed in table II, which also shows the COA patterns of the isolates from the 37 patients. All 49 gonococcal

isolates were serogrouped but only one strain from each patient was counted when different isolates from the same patient had the same COA pattern. In one patient the two strains from the pharynx and rectum had different serogroups. One man had two infections with different strains within six months. Thus, 39 isolates were included in the study.

ANTIBIOTIC SUSCEPTIBILITY

Susceptibility tests were performed with benzylpenicillin, ampicillin, cefuroxime, doxycycline, and spectinomycin in two-fold dilutions by an agar dilution technique.¹⁶ The concentrations tested were 0.004-4.0 mg/l of benzylpenicillin and ampicillin, 0.002-4.0 mg/l of cefuroxime, 0.016-4.0 mg/l of doxycycline, and 0.5-512 mg/l of spectinomycin. Antibiotic-free control plates and strains with known minimum inhibitory concentrations (MIC) of the antibiotics¹⁶ were included. The MIC was determined as the lowest concentration that inhibited growth; a faint haze or growth of a single colony was disregarded.

STATISTICAL ANALYSIS

χ^2 tests with Yates's correction were used.¹⁸

Results

SITES OF INFECTION AND SYMPTOMS

Seventeen of the 37 (45.9%) men had gonococcal infection of the urethra, 21 (56.8%) of the rectum, and 10 (27%) of the pharynx (table I). In 11 (29.7%) patients gonococci were isolated from two sites. All the 11 men with gonorrhoea in the urethra only (table I) had symptoms referable to the urethra. The six patients infected in the urethra and rectum or pharynx all attended because of urethral symptoms. Of the eight men with positive culture results from the pharynx or the pharynx and rectum, two had a sore throat and one of these two also had anorectal symptoms. Among the 17 patients with gonococci in the rectum or rectum and pharynx, only four had

TABLE II The gonococcal reference strains used for immunising and absorptions for preparation of coagglutination reagents representing serogroups WI, WII, WIII. Coagglutination patterns for the 39 gonococcal isolates.

Serogroup	Coagglutination reagents	Combinations of coagglutination patterns					
		WI		WII		WIII	
WI	Anti W-16 absorbed with N-10 and F-6	+	-	-	-	-	-
WI	Anti D-4 absorbed with C-3 and F-6	+	+	-	-	-	-
WII	Anti N-10 absorbed with F-6 and B-2	-	-	+	+	-	-
WII	Anti A-1 absorbed with F-6 and 7122	-	-	+	-	+	-
WIII	Anti F-6 absorbed with U-14, A-1, and 7122	-	-	-	-	-	+
No of isolates		5	1	6	21	3	3

+ Positive; - negative

symptoms referable to the anorectum. Thus, of the 20 men with gonococcal infection in the rectum or pharynx or both, only five (25%) attended because of symptoms of gonorrhoea and 15 (75%) for other reasons. Overall, 15 of the 37 (40.5%) patients were asymptomatic.

SEROGROUPING

Six of the 39 (15.4%) gonococcal isolates belonged to serogroup WI, 30 (76.9%) to WII, and three (7.7%) to serogroup WIII (tables I and II). No correlation between the presence or absence of symptoms and the serogroup of the infecting strains could be shown. Isolates from three known contact pairs belonged to the same serogroup. In 10 of the 11 men with infection at two sites both isolates belonged to the same serogroup. One patient, however, had a strain of serogroup WI in the rectum and one of serogroup WII in the pharynx. A serogroup WII strain was isolated from a man who returned six months later with infection of the urethra and rectum with gonococci of serogroup WI.

ANTIBIOTIC SUSCEPTIBILITY

The two isolates from 10 of the 11 men with infections at two sites had the same antibiotic susceptibility. The strains from the man with isolates of different serogroups in the rectum and pharynx had different MICs of all antibiotics except doxycycline; the rectal strain was the most resistant.

All six gonococcal strains of serogroup WI and all three of serogroup WIII had diminished sensitivity to benzylpenicillin (MIC ≥ 0.125 mg/l) and MICs of

ampicillin and cefuroxime of ≥ 0.25 mg/l and ≥ 0.06 mg/l respectively (table III). The MICs of all these three antibiotics for serogroup WII strains had a bimodal distribution with the two peaks at 0.016 and 0.25 mg/l for benzylpenicillin, at 0.06 and 0.25 mg/l for ampicillin, and at 0.016-0.03 mg/l and 0.125 mg/l for cefuroxime (table III and figure). In all, 66.7% of the 39 strains and 56.7% of the WII isolates had diminished sensitivity to benzylpenicillin.

All six strains of serogroup WI had an MIC of doxycycline of 0.5 mg/l (table III). Two of the three strains of serogroup WIII had an MIC of 0.25 mg/l and one of 1 mg/l. The MICs of doxycycline for WII strains also had a bimodal distribution with two peaks at 0.25 and 1 mg/l (table III and figure). In all, 30.8% of the 39 strains and 36.7% of the WII isolates had an MIC of ≥ 1 mg/l of doxycycline.

There was no difference in susceptibility to spectinomycin between strains of the different serogroups; all were sensitive. Seventeen of the 39 (43.6%) isolates had an MIC of 8 mg/l and the remainder of 16 mg/l.

Thirty (76.9%) of the 39 isolates had the same MIC ($\pm$ one dilution step) of benzylpenicillin and cefuroxime. Nine of the isolates, five of which belonged to serogroup WI, had a difference of two dilution steps with the MIC of benzylpenicillin always the higher.

About 60-64% of isolates from the urethra and pharynx had diminished sensitivity to benzylpenicillin compared with 71% of isolates from the rectum (not significant).

TABLE III *In-vitro* susceptibility to benzylpenicillin, ampicillin, cefuroxime, and doxycycline of 39 gonococcal isolates of serogroups WI, WII, and WIII from 37 men with homosexual contacts

	No* (%) of isolates with MICs (mg/l) of:								
Serogroups	0.016	0.03	0.06	0.125	0.25	0.5	1.0	2.0	Total
<i>Benzylpenicillin</i>									
WI					5	1			6
WII	12 (40.0)	1 (43.3)	0 (43.3)	2 (50.0)	14 (96.7)	1 (100)			30
WIII				1	1	1			3
<i>Ampicillin</i>									
WI					1	2	2	1	6
WII			12 (40.0)	1 (43.3)	13 (86.7)	2 (93.3)	2 (100)		30
WIII					1	1	1		3
<i>Cefuroxime</i>									
WI			5	0	0	1			6
WII	8 (26.7)	6 (46.7)	3 (56.7)	8 (83.3)	4 (96.7)	1 (100)			30
WIII			1	1	1				3
<i>Doxycycline</i>									
WI						6			6
WII				1 (3.3)	12 (43.3)	6 (63.3)	10 (96.7)	1 (100)	30
WIII					2	0	1		3

* Cumulative frequencies

FIGURE *In-vitro* susceptibility to benzylpenicillin, cefuroxime, and doxycycline of gonococcal isolates of serogroup WII from men with homosexual contacts compared with those from randomly chosen patients.

Discussion

Bro-Jørgensen and Jensen¹ reported an incidence of 25% of pharyngeal gonorrhoea in homosexual men with gonorrhoea compared with 7% in Danish heterosexual men. Corresponding figures for homosexual men were 19-25% in studies by Handsfield *et al.*⁸ Kraus,⁶ and Wiesner *et al.*⁹ Handsfield *et al.*⁸ and McMillan and Young³ found incidences of 41% and 51% respectively of anorectal gonorrhoea in homosexual men. The incidence in this study of 27% of pharyngeal and about 57% of rectal gonorrhoea in men with homosexual contacts corresponds well with these reports.

Bro-Jørgensen and Jensen¹ and Stolz and Schuller⁴ reported that about 76% and 83% of patients with pharyngeal gonorrhoea were asymptomatic. McMillan and Young³ found that 70% of homosexual men with anorectal gonorrhoea had no anorectal symptoms. In this study 75% of the men with pharyngeal or rectal gonorrhoea or both were asymptomatic, a figure which is in agreement with these findings.

Handsfield *et al.*⁸ found 64% of urethral infections in homosexual men with gonorrhoea, of whom 2%

were asymptomatic. Crawford *et al.*¹⁹ have correlated asymptomatic gonorrhoea in men with strains of the Arg-Hyx-Ura (AHU) auxotype. Handsfield *et al.* explain the low rate of asymptomatic urethral gonorrhoea in homosexual men by a low incidence of strains of the AHU auxotype. AHU strains were reported to belong to serogroup WI,²⁰ but strains of serogroup WI are not always of the AHU auxotype.¹⁵ In this study only about 46% of the men had urethral infections and none was asymptomatic. Only two of the isolates from the urethra belonged to serogroup WI (table I).

In a recent study of gonococcal strains isolated in Stockholm during two periods in 1979 and 1980 from 124 consecutive patients (48 women and 76 men, of whom 13 were homosexuals)¹⁴ the incidence of gonococcal strains of serogroups WI, WII, and WIII from men were 36.8%, 57.9%, and 5.3% respectively. Corresponding figures for all patients (men and women) were 40.3%, 56.5%, and 3.2%. The difference in incidence of 40.3% of WI strains from these patients compared with 15.4% from men with homosexual contacts is statistically significant ($\chi^2 = 7.1$; $P < 0.01$). The corresponding incidences for WII strains were 56.5% and 76.9% ($\chi^2 = 4.4$;

$P < 0.05$) and for WIII isolates 3.2% and 7.7% (not significant).

In a previous study of unselected strains from 68 women and 53 men (nine of whom were homosexuals) it was found that 93.5% of the 46 WI strains were sensitive to < 0.125 mg/l of benzylpenicillin, 95.7% to cefuroxime, 93.5% to < 0.25 mg/l of ampicillin, and 93.5% to < 0.5 mg/l of doxycycline.¹⁶ WI isolates from men with homosexual contacts seem to differ in this respect and were significantly more resistant to these antibiotics (table III) than the unselected WI strains in general (benzylpenicillin, ampicillin, and doxycycline; $\chi^2 = 26.2$, $P < 0.001$; cefuroxime, $\chi^2 = 20.2$, $P < 0.001$). The antibiotic susceptibility of WII strains in the present study did not differ from that in the previous one (figure).¹⁶ WIII isolates in the previous study had MICs of ≥ 0.125 mg/l of cefuroxime and ≥ 0.25 mg/l of benzylpenicillin and ampicillin, and 66.7% of them were resistant to ≥ 0.5 mg/l of doxycycline.¹⁶ This corresponds well with the antibiotic susceptibility of WIII strains in the present study (table III).

Treatment failures with penicillin, ampicillin, and tetracycline have been correlated with increased resistance of gonococci.^{5 21 22} The high incidence of gonococcal strains with diminished sensitivity among homosexual men, therefore, constitutes a therapeutic problem. Spectinomycin was the only antibiotic tested with about the same MIC for all gonococcal strains tested. High failure rates, however, have been reported when spectinomycin was used to treat pharyngeal gonorrhoea.^{5 6}

Sandström and Danielsson¹⁷ and Sandström *et al.*²⁰ showed that more than 90% of gonococcal strains isolated from patients with disseminated gonococcal infection (DGI) belonged to serogroup WI. The low rate of WI strains among homosexual men in Stockholm could mean a lower risk of such patients acquiring DGI, but little is known about other complications.

The value of a serological classification of gonococci to demonstrate double infections, to distinguish reinfections from treatment failures, and to identify gonococcal strains from contact pairs was also demonstrated in this study.

This work was supported by grants from the Swedish Medical Research Council (Project No 16X-6583) and from the Swedish Society of Medical Sciences (Project No 45, 1980). I am indebted to my colleagues at the Department of Dermatology, Södersjukhuset, for their collaboration in this study, to Assistant Professor Dan Danielsson, Department of Clinical Microbiology and Immunology, Central County Hospital, Örebro, for his valuable advice, his

encouragement, and his help with the manuscript, to Mr Arne Hultgren for skillful technical assistance, and to Mrs Elisabeth Hallmert for typing the manuscript.

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