

## ORIGINAL ARTICLE

Antimicrobial susceptibility of *Neisseria gonorrhoeae* strains isolated in Guangzhou, China, 1996–2001

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**Objective:** To investigate the in vitro antimicrobial susceptibility and resistant trends of *Neisseria gonorrhoeae* strains isolated in Guangzhou, from 1996 to 2001.

**Methods:** The agar dilution method was used to determine the minimum inhibitory concentrations (MICs) to four antimicrobials, penicillin G, ciprofloxacin, ceftriaxone, and spectinomycin. The resistance of all strains to four antibiotics was interpreted according to criteria used in the project of surveillance of gonococcal antibiotic susceptibility in the WHO Western Pacific Region. Penicillinase producing *N gonorrhoeae* (PPNG) was analysed by the paper acidometric method.

**Results:** 793 consecutive *N gonorrhoeae* isolates collected in Guangzhou were studied from 1996 to 2001. A total of 55 strains of PPNG were identified and the prevalence rapidly spread from 2% to 21.8%. Of the four antibiotics examined, ceftriaxone and spectinomycin appeared to be the most effective agents although two spectinomycin resistant strains were isolated in 1996. Their MIC<sub>50</sub>, MIC<sub>90</sub>, and geometric mean MIC (MIC<sub>mean</sub>) were all between the sensitive ranges of the interpretative criteria and remained stable over the years. However, resistance increased continuously to penicillin G and dramatically to ciprofloxacin. In 1996–2001, MIC<sub>50</sub>, MIC<sub>90</sub>, and MIC<sub>mean</sub> of penicillin G increased from 1 µg/ml to 2 µg/ml, 4 µg/ml to 32 µg/ml, and 0.68 µg/ml to 2.35 µg/ml, respectively; those of ciprofloxacin steeply increased from 0.12 µg/ml to 4 µg/ml, 2 µg/ml to 32 µg/ml, and 0.14 µg/ml to 2.62 µg/ml in 1996–9, respectively, and then declined slightly in 2000–1. The prevalence of resistant isolates spread from 57.2% to 81.8% for penicillin G and from 17.6% to 72.7% for ciprofloxacin over the 6 years.

**Conclusion:** Resistance to penicillin and ciprofloxacin increased greatly during 1996–2001. Ceftriaxone and spectinomycin should be used as the first line agents in treating gonorrhoea. It is of great importance to continuously survey the susceptibilities of *N gonorrhoeae* to antibiotics in controlling the spread of gonococcal infections.

*Neisseria gonorrhoeae* infections represent one of the most widely disseminated sexually transmitted diseases in China. A total of 837 400 cases of gonorrhoea were reported in 1999, which accounted for 40.7% of all STDs and increased by 32.3% over 1998,<sup>1</sup> Guangdong, located in the far south of China, was one of the provinces with the highest prevalence. During 1996–2000, 131 738 cases were reported, with epidemiological links to Hong Kong and other south east Asian countries because of increasing travel to and from those destinations.<sup>2</sup>

The national guideline for therapy in 1993 recommends one of the following single doses regimens as first line therapy for uncomplicated gonorrhoea: ciprofloxacin 500 mg or ofloxacin 400–600 mg orally, ceftriaxone 250 mg or spectinomycin 2 g intramuscularly. Penicillin is only recommended if resistance is known to be rare and tetracycline is chosen if the patients are allergic to these antibiotics. With the emergence and spread of resistant strains, penicillin and tetracycline are no longer listed as first line agents for treatment of gonorrhoea in the new guideline since August 2000.

Prompt and appropriate antimicrobial treatment is important in eliminating the pathogen and limiting its transmission. However, the antibiotic resistance of *Neisseria gonorrhoeae* is constantly changing as a result of the extensive use and/or abuse of antibiotics for treatment of gonorrhoea and importation of resistant strains. An early survey showed that the rate of penicillin resistant strains increased from 47.8% in 1987 to 64.5% in 1992 in China.<sup>3</sup> Recently, the strains with high level resistance to quinolones were found in Guangzhou.<sup>4</sup> Therefore, the need for epidemiological study

of this organism and surveillance of its susceptibility to common antibiotics is reinforced. A project on the surveillance of gonococcal antibiotic susceptibility in the WHO Western Pacific Region has been carried out in China. As one of the members of the research group, we annually determine the in vitro susceptibility of *N gonorrhoeae* isolates in Guangzhou, the capital city of Guangdong province. This paper analysed the prevalence of penicillinase producing *N gonorrhoeae* (PPNG), the antimicrobial susceptibilities, and resistant trends of *N gonorrhoeae* isolated in Guangzhou from 1996 to 2001.

## METHODS

## Bacterial isolates

In all, 793 consecutive isolates of *N gonorrhoeae* were collected from outpatients with gonorrhoea attending STD clinics of Guangdong Provincial Centers for STIs and Skin Diseases Control and Prevention, and Guangzhou Center for STD Control and Prevention from 1996 to 2001 in Guangzhou, China.

Isolation of *N gonorrhoeae*

Urethral and endocervical specimens were directly inoculated on Thayer-Martin medium (GC agar base + haemoglobin + growth supplement + VCNT) and GC agar supplemented with 10% defibrinated sheep blood. The plates were incubated at 35°C in a humid candle extinction jar for 36–48 hours. The isolates were identified as *N gonorrhoeae* on the basis of colony morphology, Gram staining, oxidase test, and carbohydrate

**Table 1** Interpretation of susceptibility ( $\mu\text{g/ml}$ )

Antibiotic	Sensitive	Intermediate	Resistant
Penicillin	0.03	0.06–0.5	$\geq 1$
Spectinomycin	$\leq 32$	–	$\geq 64$
Ceftriaxone	$\leq 0.03$	0.06–0.5	$\geq 1$
Ciprofloxacin	$\leq 0.03$	0.06–0.5	$\geq 1$

degradation tests. All stains were preserved in skimmed milk and stored at  $-70^{\circ}\text{C}$  before use.

### Antibiotic susceptibility

All the isolates were examined for susceptibility to penicillin G, ciprofloxacin, ceftriaxone, and spectinomycin by the agar plate dilution method for minimum inhibitory concentrations (MICs).<sup>5</sup> The ranges of concentration of antibiotics were as follows: penicillin G, 0.31–32  $\mu\text{g/ml}$ ; tetracycline, 0.5–32  $\mu\text{g/ml}$ ; spectinomycin, 4–128  $\mu\text{g/ml}$ ; ciprofloxacin, 0.15–32  $\mu\text{g/ml}$  and ceftriaxone, 0.002–1  $\mu\text{g/ml}$ . The sensitivity of isolates was determined according to agar plate dilution methods similar to those in use by the Western Pacific WHO GASP programme as follows. The medium used was GC agar (Oxoid) supplemented with 10% defibrinated sheep blood. Pure subculture from 18 to 24 hours' growth on GC agar was suspended in saline and adjusted to contain approximately  $10^8$  cfu/ml as inoculum. A multi-point inoculator was used to inoculate the suspension onto antibiotic containing media. After overnight incubation at  $35^{\circ}\text{C}$  in a carbon dioxide incubator, the MICs were read.

### Interpretation of susceptibility

Two methods were used in AHPWPR, one is the American method and other the non-American method. We apply the latter method, modified by using sheep blood instead of lysed horse blood. The laboratory obtained satisfactory results in the China GASP QA programme external quality assurance programme conducted by the Nanjing National Reference STD centre. The American method uses MIC  $\geq 2$  mg/l as penicillin resistance, while the non-American method standard is 1 mg/l. The criteria for resistance in this test system are shown in table 1.

WHO *N gonorrhoeae* reference strains A–E, kindly provided by Dr Ye Shunzhang, the National Center for STD control, Nanjing, were used as controls in each antimicrobial assay. Because these reference strains are all quinolone sensitive, we also reference the external QA results as control.

A  $\beta$  lactamase assay was performed by the paper acidometric method.<sup>6</sup> WHO reference strains A and E were used as negative and positive control, respectively.

### Statistics

Geometric MICs were determined using the base<sub>2</sub> logarithms. The Mann-Whitney U test was used for evaluating the trends of the resistant rates.

### RESULTS

Among the 793 gonococcal isolates examined, 55 PPNG strains were identified by the paper acidometric method. The prevalence dramatically increased from 2% to 21.8% in 1996–2001 ( $U = 6.38$ ,  $p < 0.01$ ) (table 2).

The distribution of MIC<sub>50</sub>, MIC<sub>90</sub>, and MICmean of the four antibiotics to 793 consecutive strains collected in Guangzhou during these 6 years is summarised in table 3. Out of the four antibiotics tested, ceftriaxone and spectinomycin appeared to be the most effective agents and the MICs remained stable over the years, while MICs of penicillin G and ciprofloxacin enlarged dramatically. MIC<sub>50</sub>, MIC<sub>90</sub>, and MICmean of penicillin G multiplied by 2, 8, and 3.5 times from 1996 to 2001, respectively; those of ciprofloxacin by 33, 16, and 18.7 times higher in 1996–9, respectively, and declined slightly in 2000–1.

Antimicrobial susceptibilities of 793 strains, interpreted according to WHO standards, were shown in table 2. It appeared that the strains were more sensitive to ceftriaxone and spectinomycin. Only two spectinomycin resistant gonococcal strains were isolates during the 6 years. The proportion of sensitive strains to penicillin decreased from 8.4% to 0.9%, while the resistant rate increased from 57.2% to 81.8% ( $U = 4.39$ ,  $p < 0.01$ ). A significant trend for increasing resistance to ciprofloxacin developed dramatically from 1996 to 2001. The proportion of sensitive organisms dropped from 18.6% to 1.8%, while the resistant rate rose steeply from 17.6% to 72.7% ( $U = 9.67$ ,  $p < 0.01$ ).

### DISCUSSION

The antibiotic resistant profile changes constantly over time. Since the emergence of PPNG in 1976 and the chromosomally mediated penicillin resistant isolate in 1983, the resistant gonococci have spread worldwide and the prevalence increased rapidly. In south east Asian, very high proportions of penicillin resistance were recorded—Korea (91%), the Philippines (89%), China (80%), Singapore (58%), Hong Kong (54%), and Vietnam (48%) in 2000.<sup>7</sup> We identified 546 penicillin resistant strains out of 793 consecutive isolates in Guangzhou, in which 55 were PPNG and 491 chromosomally mediated penicillin resistant. The prevalence of PPNG were lower during the first 4 years but rose steeply from 5.4% to 21.8% ( $U = 4.2$ ,  $p < 0.01$ ) in the past 2 years, indicating that Guangzhou had become a highly prevalent region. The penicillin resistant rates increased from 57.2% to 72.7% in 1996–2001 and were higher than the report (66.7%) by the National Center for STD Control.<sup>3</sup> The resistant trend was statistically significant ( $U = 4.39$ ,  $p < 0.01$ ). The MIC<sub>50</sub>, MIC<sub>90</sub> and MICmean in 2001 were 2, 8, and 3.5 times higher than those in 1996, respectively. A high

**Table 2** Comparison of susceptibility and PPNG of *N gonorrhoeae* isolated in Guangzhou during 1996–2001

Year	No	Penicillin			Spectinomycin		Ceftriaxone			Ciprofloxacin			PPNG (%)
		S (%)	I (%)	R (%)	S (%)	R (%)	S (%)	I (%)	R (%)	S (%)	I (%)	R (%)	
1996	201*	17 (8.4)	69 (34.3)	115 (57.2)	199 (99)	2 (1)	120 (62.5)	72 (37.5)	0 (0)	37 (18.6)	127 (63.8)	35 (17.6)	4 (2)
1997	51	2 (3.9)	13 (25.5)	36 (70.6)	51 (100)	0 (0)	40 (78.4)	11 (21.6)	0 (0)	2 (3.9)	18 (35.3)	31 (60.8)	1 (2)
1998	203	1 (0.5)	81 (39.9)	121 (59.6)	203 (100)	0 (0)	122 (60.1)	81 (39.9)	0 (0)	16 (7.9)	64 (31.5)	123 (60.6)	7 (3.4)
1999	167	3 (1.6)	24 (14.4)	140 (83.8)	167 (100)	0 (0)	153 (91.6)	14 (8.4)	0 (0)	5 (3.0)	31 (18.6)	131 (78.4)	9 (5.4)
2000	61	0 (0)	17 (27.9)	44 (72.1)	61 (100)	0 (0)	50 (81.9)	11 (18.0)	0 (0)	0 (0)	15 (24.6)	46 (75.4)	10 (16.4)
2001	110	1 (0.9)	19 (17.3)	90 (81.8)	110 (100)	0 (0)	90 (81.8)	20 (18.2)	0 (0)	2 (1.8)	28 (25.5)	80 (72.7)	24 (21.8)

\*192 strains were tested for ceftriaxone and 199 for ciprofloxacin.

**Table 3** Comparison of MIC<sub>50</sub>, MIC<sub>90</sub>, MICmean of the four antibiotics to *N gonorrhoeae* isolated in Guangzhou during 1996–2001 (µg/ml)

Year	No	Penicillin			Spectinomycin			Ceftriaxone			Ciprofloxacin						
		Range	MIC <sub>50</sub>	MIC <sub>90</sub>	MICmean	Range	MIC <sub>50</sub>	MIC <sub>90</sub>	MICmean	Range	MIC <sub>50</sub>	MIC <sub>90</sub>	MICmean				
1996	201*	16–0.016	1	4	0.68	64–1	8	16	6.80	0.5–0.002	0.031	0.25	0.03	2–0.002	0.1	2	0.14
1997	51	16–0.008	1	4	1.01	32–8	16	16	15.36	0.5–0.004	0.031	0.06	0.02	16–0.008	1	8	1.19
1998	203	16–0.125	2	4	1.59	64–4	16	32	16.67	0.25–0.002	0.031	0.06	0.04	16–0.016	4	16	1.30
1999	167	32–0.004	2	16	2.09	32–2	16	16	13.27	0.25–0.002	0.016	0.02	0.02	32–0.002	4	32	2.62
2000	61	>32–0.06	1	32	1.74	16–4	8	16	8.96	0.25–0.002	0.031	0.06	0.021	32–0.06	1	4	1.24
2001	110	>32–0.03	2	32	2.35	16–4	8	16	8.79	0.25–0.002	0.015	0.06	0.018	32–0.03	2	8	1.44

\*192 strains were tested for ceftriaxone and 199 for ciprofloxacin, \*mean = geometric mean MIC.

rate (21.8%) of PPNGs in 2001 might cause the MIC increase. The high prevalence of PPNGs may cause an increase of penicillin MIC and, in addition, the widespread use of penicillin for treatment might also have contributed to the findings of a steep increase in syphilis infection in Guangzhou in recent years.

Quinolones had been recommended by the Centers For Disease Control and Prevention (CDC) for treatment of gonorrhoea since 1989.<sup>8</sup> With widely use of these agents, resistance has sharply increased in many districts of south east Asia and the resistant strains have spread recently. In Hong Kong, quinolone resistant *N gonorrhoeae* (QRNG) increased from 0.5% in 1992 to 10.4% in 1994<sup>9</sup> and from 60% in 1998 to 80% in 2000.<sup>7</sup> Other information identified an increasing number of QRNG in Japan.<sup>10</sup> A report from Sydney, Australia, represented 3% QRNG from 1991 to 1994, and in the first 6 months of 1995, the proportion (8%) of QRNG rose substantially.<sup>11</sup> It was considered that the appearance of QRNG in Sydney has been caused by the continuing importation of resistant strains by travellers entering or returning to Australia from Asian destinations. In Guangzhou, our finding was similar. There had been a significant increase in the rate of ciprofloxacin resistant *N gonorrhoeae* from 17.6% in 1996 to 72.7% (U = 9.67, p < 0.01) in 2001. A WHO document stated that an agent should be withdrawn from treatment regimens if the rate of 5% resistance to the agent occurs.<sup>12</sup> The MIC<sub>50</sub>, MIC<sub>90</sub>, and MICmean multiplied by 33, 16, and 18.7 times in 1996–9, respectively, and then declined slightly in 2000–1. A recent study on the correlation between the in vitro susceptibility to ciprofloxacin and treatment outcome showed that 96% isolates from patients who had treatment failure were MICs 1–32 µg/ml.<sup>13</sup> The emergence and wide spread of the highly ciprofloxacin resistant strains (MIC ≥ 32 µg/ml) might mean no dose of this agent (or other quinolones) would effect a cure.

Spectinomycin and ceftriaxone are highly effective as single dose treatment for gonorrhoea. Susceptibility to ceftriaxone was proved to have risen slightly in recent years.<sup>14</sup> In Guangzhou, the susceptibilities to both of the antibiotics remained unchanged from 1996 to 2001. The MIC<sub>50</sub>, MIC<sub>90</sub>, and MICmean all fell in the sensitive range of the interpretative criteria although two spectinomycin resistant strains were isolated in 1996. The results showed that spectinomycin and ceftriaxone should be the first line treatment for gonorrhoea in Guangzhou, China.

In summary, the results of this study clearly demonstrate that penicillin/ciprofloxacin resistant gonococcal strains are frequently found in Guangzhou. Local susceptibility data of periodic surveillance are useful in guiding clinicians in the use of appropriate antibiotics for the treatment of gonorrhoea.

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# PostScript

## LETTERS

### Perceived transmissibility of STIs: lack of differentiation between HIV and chlamydia

Sexually transmitted infections (STIs), such as HIV and chlamydia, differ widely in their transmissibility. The estimated probability of HIV transmission from an infected heterosexual man to a woman in one act of unprotected vaginal intercourse is 0.1%,<sup>1</sup> whereas the same probability for chlamydia is 35%.<sup>2</sup> This research examines college students' knowledge about the per act transmission probabilities for HIV and chlamydia.

Previous studies reported median perceived transmission probabilities of 50%<sup>3</sup> and 33.4%<sup>4</sup> for HIV for one act of unprotected receptive vaginal intercourse with an infected man. These findings were interpreted as demonstrating "badly overestimated per act transmission probabilities" (Pinkerton *et al.* p 19). However, the distributions of the estimates were not provided. If estimates are widely dispersed across the entire probability range from 0% to 100%, interpretations of averages are meaningless and interpreting the data as indicating a systematic overestimation of the transmission probability would be unfounded. We studied this possibility in a sample of college students.

In all, 234 undergraduate university students (145 women, 85 men, mean age 21.14 years, SD 2.82, four did not report their age and sex) enrolled in a variety of academic programmes were randomly selected and individually approached after classes. Aside from their age and sex, participants were asked in two separate questions: "What do you think is the probability, in percentages, of a woman becoming infected with HIV (chlamydia) from one unprotected act of vaginal intercourse with an infected man?" The order in which people were asked the two questions was counterbalanced.

Figure 1 presents the distribution of the estimates, showing that they are widely and quite equally dispersed across the entire range from 0% to 100%, and that distributions do not differ between the two infections (Kolmogorov-Smirnov  $Z = -0.73$ ,  $p = 0.46$ ).

No age or sex differences were found. Only 3.9% and 5.6% of the estimates for HIV and chlamydia, respectively, come close to the correct probabilities if "correct" is defined as smaller than 0.5% for HIV and between 30% and 40% for chlamydia. In all, 34.8% of the participants falsely estimate that chlamydia has a lower transmission probability than HIV, 39.5% correctly estimate that chlamydia has a higher transmission probability than HIV, and 25.8% provide exactly the same percentage estimate for both STIs.

The data show that a large majority of college students clearly lacks knowledge of the transmission probabilities of HIV and chlamydia and does not know that chlamydia is more infectious than HIV. Previous reports of statistical averages of the perceived transmissibility<sup>3,4</sup> and their interpretation as indicating a systematic overestimation bias may be unfounded. The results highlight the importance of inspecting response distributions and restraining from reporting statistical averages when distributions are widely dispersed. Furthermore, they highlight that information about transmission probabilities should be incorporated into sexual health programmes in order to make people more aware of STIs that are considerably easier to contract than HIV.

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### Contributors

The study was jointly conceptualised and designed by BK and RK; data were collected by RK, with the assistance of Surkhraj Cheema; BK analysed the data and led the writing; both authors jointly interpreted the findings, reviewed drafts of the manuscript, and approved the final version.

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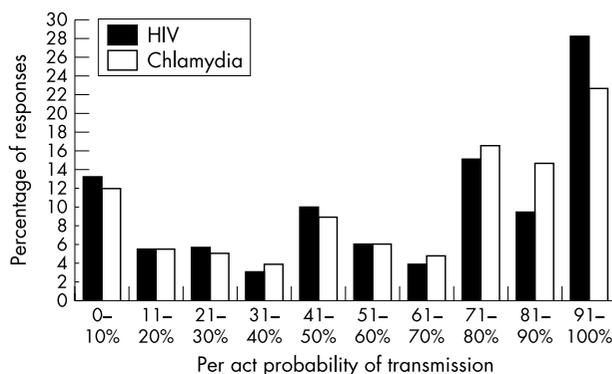


Figure 1 Distribution of estimates for HIV and chlamydia for one act of unprotected vaginal intercourse with an infected man.

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### A new method for extended trichomonad storage

With the introduction of the InPouch test for *Trichomonas vaginalis*,<sup>1</sup> *T. gallinae*, and *T. foetus*, it was desirable to have a procedure available for maintaining extended culture viability. The three trichomonads are viable after 8 days by subculture in the InPouch at 33°C. Extended viable storage of these three trichomonads is the subject of this letter.

We have evaluated various procedures involving freezing 24 hour InPouch cultures at -70°C. We now report a procedure that has demonstrated storage of viable trichomonad cultures for more than 2 years.

The freshly subcultured trichomonads are incubated at 35°C for 24 hours, which should produce a viable count of approximately  $1.0 \times 10^5$ /ml. It is important to note that subsequent subculture will require an adequate nutrient available for growth in the pouch. Then 0.1 ml of pure sterile glycerol is added to the medium in the pouch and thoroughly mixed employing the "shoeshine" technique. It is important to immediately place the pouch in a -70°C freezer.

After freezing most of the trichomonads in the pouch are non-viable, but successful subculture is routinely achieved upon thawing. When the pouch is removed from the freezer, it should be immediately placed in an incubator at 35-37°C. After 3 days a few viable trichomonads will be observed, and after 4 days it may be subcultured.

This procedure has been effective for *T. vaginalis*, *T. gallinae*, and *T. foetus*.

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## “Water can” penis caused by tuberculosis

Tuberculosis of the penis is a very rare condition, clinically manifesting as primary or secondary tuberculosis or tuberculide.<sup>1</sup> Penile involvement secondary to urethral tuberculosis is rare and its presentation with periurethral fistulas leading to “water can” penis is unknown. We report this rather intriguing condition in a patient.

A 40 year old male agricultural labourer presented with a 1 year history of purulent discharge per urethra with multiple discharging sinuses on the tip of the penis. The patient was asymptomatic about a year ago, when he developed multiple nodules on the glans penis that ulcerated to discharge purulent material. These nodules became persistent sinuses and discharged pus. Within a few weeks, he started passing urine through these sinuses in the glans penis. He also experienced difficulty in micturition but it was not associated with pain or strangury. The patient had no systemic complaints. He was married with two children and had no history of extramarital contact or genital ulcers.

On physical examination, the penis shape was like a saxophone. The prepuce and glans penis were oedematous and indurated. The glans penis had multiple sinuses around the urethral meatus (fig 1). On squeezing the penis, pus was expressed from the meatus and the sinuses. The glans penis also showed areas of depigmentation (vitiligo). The distal part of the shaft of the penis showed induration involving corpora cavernosa whereas the proximal part was devoid of any lesion. The testes, bilateral epididymis, and scrotum were normal. The vas deferens was normal on



**Figure 1** Saxophone penis with multiple sinus openings over the glans penis.



**Figure 2** Forearm showing positive Mantoux reaction.

palpation. The prostate was normal on rectal examination.

The routine haemogram revealed an elevated erythrocyte sedimentation rate of 100 mm in the first hour. His liver and renal functions were normal. The discharge smear stained with Gram stain and Zeihl-Neelsen stain. The Gram stained smear revealed numerous pus cells and acid fast stain showed abundant acid fast bacilli. Culture for *Mycobacterium tuberculosis* grew contaminants. A roentgenogram of the chest and penis was unremarkable. An intravenous pyelogram was normal. Voiding cystourethrography revealed glandular urethral stricture with urethrocutaneous fistulas. Ultrasonography of abdomen and prostate was normal. Mantoux skin test was strongly positive (30×30 mm) (fig 2). His venereal disease research laboratory test (VDRL) and HIV serology was non-reactive.

Based on these clinical features, positive Mantoux test and acid fast bacilli in the urethral smear, the diagnosis of urethral tuberculosis with urethrocutaneous fistula was made. The patient was started on anti-tuberculous treatment comprising isoniazid 300 mg, rifampicin 600 mg, pyrazinamide 1500 mg, and ethambutol 800 mg per day. The patient showed marked improvement after 4 weeks of treatment. The sinuses closed and discharge ceased. Patient was referred to urology for management of stricture, which was planned after the anti-tuberculous treatment. The patient tolerated antituberculous treatment and completed 9 months of treatment with remarkable recovery in the swelling of the penis.

Genital involvement occurs in 50% of male patients with urogenital tuberculosis. Penile tuberculosis is rare with less than 1% of patients having penile involvement.<sup>2</sup> Tuberculosis of the penis usually presents as ulcers, tubercular cavernositis, or nodules. In most cases, the lesion appears as a superficial, solitary, painless ulcer on the glans penis. It can be clinically indistinguishable from malignant disease.<sup>3</sup> Rarely, lesions may persist as solid nodule or cavernositis with ulceration.<sup>4,5</sup> Papulonecrotic tuberculide may also present as an ulcer on the penis.<sup>1</sup> Penile

involvement may occur secondary to co-existing urinary tract tuberculosis. The transmission occurs secondary to bacilluria in these patients. Infection of the penis may occur by direct contact at the time of intercourse with a partner having urogenital tuberculosis.<sup>2</sup>

Tuberculosis of male urethra is an uncommon condition and presents as urethral strictures, periurethral abscesses, or fistula formation. Fistulas can occur in the perineum leading on to “water can” perineum.<sup>6</sup> Similar occurrence of fistulas in penis can aptly be designated as “water can” penis. In our case, penile involvement occurred secondary to urethral tuberculosis. Such involvement of the penis by tuberculosis is unique and not reported in the literature. “Water can perineum” is also known to occur with gonorrhoea but our patient had a negative urethral smear for Gram negative diplococci and had features suggestive of urethral tuberculosis. Further, the strictures, fistulas, and lymphoedema had led to “saxophone” deformity of the penis. Such deformity is well known with lymphogranuloma venereum, but is unknown in tuberculosis.

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## South Asians with HIV in London: is it time to rethink sexual health service delivery to meet the needs of heterosexual ethnic minorities?

Recent conservative estimates suggest that at the end of 2002, 4.8 million people were living with HIV/AIDS in south Asia including 4.58 million in India.<sup>1</sup> In the United Kingdom there are estimated to be 1.5 million people of south Asian ethnicity. While the National Strategy for Sexual Health aims to improve health care in those who have HIV through earlier diagnosis,<sup>2</sup> studies have shown that that other ethnic minority groups present with advanced disease and not through routine genitourinary medicine (GUM) screening.<sup>3,4</sup> We studied the case notes of all adults self defining as of Indian, Pakistani, Bangladeshi, or Sri Lankan ethnicity diagnosed HIV positive from

**Table 1** Characteristics of presentation of study population at time of HIV diagnosis (n = 117)

	Heterosexual men (n = 45)	Homosexual men (n = 36)	Heterosexual women (n = 27)	Other risk groups (n = 9)
AIDS illness at presentation	16 (36%)	6 (16%)	2 (7%)	1 (11%)
Median CD4 cell count $\times 10^6/l$ (range)	178 (3–1,023)	381(4–810)	377 (10–1,104)	151(50–795)
Median HIV viral load copies/ml (range)	24 500 (50–1 000 000)	24 636 (425–3 000 000)	7822 (173–489 184)	12 870 (6676–57 530)
Reasons for HIV test				
AIDS/symptomatic	27 (60%)	11 (31%)	7 (26%)	2 (22%)
Known HIV+ sexual partner	3 (7%)	4 (11%)	12 (44%)	0
Routine screen for sexually transmitted infections	1 (2%)	16 (44%)	1 (4%)	0
Patient request	7 (15%)	3 (8%)	2 (8%)	2 (22%)
Child positive	3 (7%)	0	3 (11%)	0
Insurance/visa purposes	3 (7%)	1 (3%)	0	2 (22%)
Antenatal screening	0	0	2 (7%)	0
Other	1 (2%)	1 (3%)	0	3 (34%)

January 1985 to December 2002 attending four HIV treatment centres in London. Information was collected on demography, mode of first presentation, and clinical stage of HIV infection.

In all, 117 patients were identified, 30 women and 87 men. The number of new diagnoses among south Asians increased by more than threefold over the period 1996 to 2002 compared to earlier years (25 diagnoses before 1996, 90 diagnosed from 1996–2002).

The median age at diagnosis was 38 years (range 19–64 years) for men and 28 years (range 20–55 years) for women. Forty five patients (38%) had originated from Africa, 28 (24%) from India, and 18 (15%) from the United Kingdom. The majority were of Indian ethnicity (95/117; 81%) with the next largest ethnic group being Sri Lankan (12/117; 10%).

The primary mode of transmission was heterosexual sex (72/117; 62%) with transmission through sex between men accounting for a further 31% (36/117) of cases. Four infections were acquired through blood transfusion, two through injecting drug use, one from a needle stick injury, and in two cases risk behaviour could not be identified. The majority (39%, 45/117) of patients identified Africa as the probable place of infection with 28% and 15% probably infected in the United Kingdom and India, respectively.

There were substantial differences in the reasons for testing between individuals in the main risk groups. In particular, heterosexual men and women were both significantly less likely than homosexual men to be diagnosed via routine attendance at a GUM clinic (2% and 4%, compared to 44%, respectively,  $p < 0.001$ , Fisher's exact test). Among heterosexuals, the main reason for testing in men was symptomatic HIV infection/AIDS (60% of men but only 26% of women), whereas women were more likely to be tested through partner notification of a known HIV+ sexual contact (44% v 7% in males) (table 1).

The median CD4 count at presentation overall was 300 (range 3–1104) cells  $\times 10^6/l$ . However, male heterosexuals presented with significantly lower CD4 counts (median 178,

range 3–1023 cells  $\times 10^6/l$ ) than either homosexual men (median 381, range 4–810 cells  $\times 10^6/l$ ;  $p = 0.01$ ) or heterosexual women (median 377, range 10–1104;  $p = 0.02$ ).

While there are methodological limitations with retrospective case note reviews and differing reporting categories used for Asian ethnicity, our data confirm national surveillance reports of increasing HIV infection among Britain's south Asian communities.<sup>5</sup> The four centres taking part in this study reported 90 cases from 1996–2002 representing one in three of all HIV positive south Asians reported in this time period. Despite the fact that the majority of these were not diagnosed through routine GUM screening the median CD4 count at presentation of heterosexual and homosexual men was consistent with national trends.<sup>6</sup> Indeed, south Asian women presented higher CD4 counts than seen nationally, primarily attributable to effective partner notification. While south Asians still represent less than 5% of all reported HIV positive diagnoses in UK ethnic minority groups<sup>5</sup> (Asians 334; black Africans 8848; black Caribbeans 844) numbers are likely to continue to increase in the future and methods for encouraging early presentation need to be developed in response to this.

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## Failure to maintain patient access to GUM clinics

We read with interest the article published by Cassell *et al*<sup>1</sup> about the maintenance of patient access to genitourinary medicine (GUM) clinics following a switch to an appointment based system. Their data show no significant change in the age, ethnic mix, symptom status, and disease mix following the change to appointments. In addition, such a system of 35% prebooked appointments produced an increase in the number of patients seen over that time.

A new appointment based system was introduced at the John Hunter genitourinary medicine clinic at the Chelsea and Westminster Hospital in October 2001. This comprised 80% of appointments which were prebooked with a further 20% allocated on the day following triage by a nurse. All patients with symptoms were seen on the day of presentation.

We have analysed the results from two 9 month periods, taken immediately before the change and 3 months after the introduction of an appointment based system. The total number of patients and sex ratio seen

**Table 1** Total number of STI diagnoses

	No (%)		Relative drop (%) (95% CI)
	Jan–Sept 2001	Jan–Sept 2002	
Total no of patients attending	11714	11345	3.2 (2.8 to 3.5)
Patients new to clinic	5191 (44.3)	4669 (41.2)	

**Table 2** Details of STIs diagnosed in men and women

	Male		p Value using $\chi^2$ test	Female		
	Jan–Sept 2001 (n = 6920)	Jan–Sept 2002 (n = 6659)		Jan–Sept 2001 (n = 4794)	Jan–Sept 2002 (n = 4690)	
	No (prevalence per 100 patient)			No (prevalence per 100 patient)	p Value using $\chi^2$ test	
A1	37 (0.5)	53 (0.8)	0.061	0 (0.0)	3 (0.1)	0.121*
B1	262 (3.8)	190 (2.9)	0.002	41 (0.9)	35 (0.7)	0.552
C4a/C4c	244 (3.5)	179 (2.7)	0.005	187 (3.9)	199 (4.2)	0.399
C4h	683 (9.9)	479 (7.2)	<0.001	–	–	–
C10a	89 (1.3)	55 (0.8)	0.009	111 (2.3)	80 (1.7)	0.035
C11a	264 (3.8)	254 (3.8)	0.998	147 (3.1)	164 (3.5)	0.239
Total diagnosed with an STI at this episode	1579 (22.8)	1210 (18.2)	<0.001	486 (10.1)	481 (10.3)	0.849

\*p Value using  $\chi^2$  test with Yates's correction.

(A1) Primary diagnosis of syphilis; (B1) gonorrhoea; (C4a, C4c) uncomplicated chlamydia; (C4h) non-gonococcal urethritis; (C10a) first attack of genital herpes; (C11a) anogenital warts.

over this period did not change. We have shown however a dramatic change in the number of STI diagnoses made over these two periods.

Tables 1 and 2 highlight a significant fall in the total number of STI diagnoses for gonorrhoea (B1), uncomplicated chlamydia (C4a, C4c), non-gonococcal urethritis (C4h), and first attack of genital herpes (C10a) in our male patients. The only significant fall for women was seen in the diagnosis of a first attack of genital herpes. There was no significant change for both sexes in the diagnosis of anogenital warts (C11a) between the two systems. The rise in primary diagnosis of syphilis (A1) reflects the beginning of the current epidemic in London, boosted further by a proactive approach to diagnosis in our HIV positive population.<sup>2</sup>

This fall in acute STI diagnoses in men was approximately twice as marked for men who have sex with men (data not shown).

Our aim in planning the change to a primarily appointment based system was to improve patient experience, by reducing waiting times, and enhance access for symptomatic patients into reserved appointment slots. These data show evidence for an opposite effect which we believe has resulted from asymptomatic individuals requiring sexual health screening booking the majority of clinic appointments well ahead of their appointment, thereby reducing access at convenient times for symptomatic individuals who telephone.

To respond to this we have adjusted the ratio of prebooked versus emergency appointments and significantly amended our approach to triage of symptomatic patients, in an attempt to reverse these trends. Particular attention is now being given to our telephone booking protocol to facilitate symptomatic patients to achieve prompt, immediate appointments. We are publishing these findings to inform others who are implementing changes in clinic appointment schedules, designed to enhance access, to better tailor the booking and triage systems to achieve this goal. We will continue to audit our system to examine the effect of the revised system and to further examine why the change to our appointment system disproportionately affected those men who have sex with men.

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**Prevalence of HSV-1/HSV-2 antibodies in HIV seropositive patients in Coventry, United Kingdom**

The seroprevalence of herpes simplex virus (HSV) antibody among HIV patients within the United Kingdom is unknown. We therefore conducted a HSV seroprevalence study in HIV patients attending our genitourinary medicine clinic from January 2000 to December 2001. Our previous study<sup>1</sup> revealed an overall prevalence of HSV-1 (60%), HSV-2 (20%), and both HSV-1 and HSV-2 (12%) among male and female genitourinary medicine clinic attendees who were either HIV negative or whose HIV status was unknown.

Serum samples from 96 consecutive ethnically diverse HIV patients were collected during routine investigations, and tested for HSV type specific antibodies by monoclonal antibody blocking enzyme linked immunoassay.<sup>2</sup> Out of 96 patients, two HSV-1 and three HSV-2 antibody test results were equivocal in four individuals. These were excluded from the analysis and results are presented here for 92 patients.

There were 56 men and 36 women in the study: 46 (50%) were white, 43 (47%) black African, and three were from other ethnic groups. All the black Africans were heterosexuals and 71% of men were homosexuals. The median age was 35 years (range 21–80).

HSV-1 seroprevalence was 86% among men and 97% among women (p = 0.14). HSV-2 seroprevalence was 50% among men whereas it was 94% among women (p = 0.0001). There was no statistically significant difference between the seroprevalence of HSV-1 between white and black

people. However, seroprevalence of HSV-2 and both serotypes was significantly higher among black than among white people.

This study shows very high seroprevalence of HSV-1 (90%), HSV-2 (67%), and both HSV-1 and HSV-2 (64%) among our HIV positive cohort in Coventry. The high prevalence of HSV-2 in women is possibly because most of them were black African and acquired HIV through sex. These findings may have important public health implications as the high rate of HSV-2 is therefore likely to act as a cofactor in HIV transmission.

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**BOOK REVIEW**

**Effective Sexual Health Interventions: Issues In Experimental Evaluation**

Ed Judith M Stephenson, John Imrie, and Chris Bonell. Pp 232; £55. Oxford: Oxford University Press, 2003. ISBN 0-19-850849-2.

HIV spreads more every day and there are epidemics of other STIs in both the developed and developing world at least in part because the fear of HIV appears to be receding in the population. Our current strategies to contain these problems are meeting with limited success and treatment of people who are already infected, important though that is in controlling bacterial infections, is much less effective with continuing viral infections. There is an urgent need to develop and to test better

methods of helping people to reduce their risky sexual behaviour.

This book is excellent, brief, fairly comprehensive, and very readable. Its focus is designing studies on the effectiveness of sexual health interventions. If we are to get anywhere in improving behavioural interventions it is essential that what is done is carefully evaluated.

The first three chapters of the book are concerned with methodology, particularly whether randomised controlled (RCTs) trials are an appropriate method for evaluating interventions in this area. While this section of the book is well argued on all sides it doesn't really break any new ground. The strengths and weaknesses of RCTs in behaviour change are pretty much what they are in any other area of medicine. Methodologies don't exist as stand alone phenomena, whether an RCT or some other methodology is appropriate depends simply on what question one is seeking to answer.

The second section of the book covers models of behaviour change and the choice of design and outcome measures. It is clear that one of the main problems in intervening in sexual health is the poor quality of the available psychological models and our real lack of understanding about why people behave as they do. Without understanding why people behave as they do it is difficult to help them to change. It is interesting that models of health behaviour never seem to get discarded, even the ones that are known to be weak. There are particularly strong chapters on cluster randomisation, an approach which probably gives rise to more inappropriate statistics than any other and on complex behavioural measures. The latter should be required reading for anyone measuring any aspect of risky sexual behaviour simply because it highlights how weak many studies of sexual behaviour—and not just of behaviour change—are in this respect.

The book ends by looking at generalisability in its broadest sense. Generalisability is an area that tends to get overlooked. Even a highly successful behaviour change programme would be of no use in developing countries if it was labour intensive and dependent on highly skilled staff for its delivery.

I would recommend this book to anyone planning a trial or simply seeking to understand the existing literature. I would however caution that to make sense of it you will have to look at some of the available reviews of the behaviour change literature since the book assumes some knowledge, or willingness to acquire knowledge, of these.

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## NOTICES

### **Australasian Sexual Health Conference 2004: Behind the Mask**

This conference will be held at the Adelaide Convention Centre, South Australia, on 31 March to 3 April 2004. For further details please contact Dart Associates (tel +61 2 9418 9396/97; email [dartconv@mpx.com.au](mailto:dartconv@mpx.com.au); and website <http://www.acshp.org.au>).

### **8th European Society of Contraception Congress**

The 8th European Society of Contraception Congress will be held from 23–26 June 2004 in Edinburgh, Scotland, UK. For further details please contact ESC Central Office, c/o Orga-Med Congress Office, Essenestraat 77,

B-1740 Ternat, Belgium (tel: +32 2 582 08 52; fax: +32 2 582 55 15; email: [orgamed.ann@pandora.be](mailto:orgamed.ann@pandora.be); and website: <http://www.contraception-esc.com/edinburg.htm>).

## CORRECTIONS

In the October issue of *STI* table 2 of the paper by Zheng *et al* (Zheng HP, Cao WL, Wu XZ, Yang LG. Antimicrobial susceptibility of *Neisseria gonorrhoeae* strains isolated in Guangzhou, China, 1996–2001. *Sex Transm Infect* 2003;**79**:399–402) was published with incorrect column headings. Under the heading spectinomycin only “S(%)” and “R(%)” should appear and under ceftriaxone “S(%)”, “I(%)”, and “R(%)” should appear, in that order. Under ciprofloxacin “S(%)”, “I(%)”, and “R(%)” should appear. A corrected version of the table can be found on the website at <http://sti.bmjournals.com/cgi/content/full/79/5/399/DC1>.

The authors of a letter in the December issue of *STI* (Dave SS, Johnson AM, Fenton KA, Mercer CH, Erens B, Wellings K. Male circumcision in Britain: findings from a national probability sample survey. *Sex Transm Infect* 2003;**79**:499–500) were listed in the wrong order. The correct author list should be as follows: Dave SS, Fenton KA, Mercer CH, Erens B, Wellings K, Johnson AM.

In the corresponding author's address of a letter published in the December issue (Bhatia R, Prabhakar S, Shedde D, *et al*. Coexistent cranial tuberculomas and tuberculosis of the cervix in a postmenopausal woman. *Sex Transm Infect* 2003;**79**:496–7) All India Institute of Medical Sciences was incorrectly printed as AU India Institute of Medical Sciences.