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Comparison of Antimicrobial Susceptibility of Urogenital *Neisseria gonorrhoeae* Isolates Obtained from Women and Men

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Abstract

Background—The United States' (US) system for gonococcal antimicrobial susceptibility surveillance monitors trends exclusively among men with urethral infection, the population from whom the yield of gonococcal culture is highest. Little is known about the susceptibility of female urogenital isolates, and it is unclear whether gonococcal susceptibility among men who report sex exclusively with women (MSW) is representative of susceptibility among women.

Methods—Using isolates collected during a recent treatment trial in five US cities, we performed a secondary analysis to compare antimicrobial susceptibilities of *N. gonorrhoeae* urogenital isolates obtained from women, MSW, and men who have sex with men (MSM). Pre-treatment isolates were collected from trial participants; minimum inhibitory concentrations (MICs) were determined by agar dilution. Geometric mean MICs were adjusted for geographic location using general linear models.

Results—Susceptibility data for urogenital isolates from 56 women, 252 MSW, and 170 MSM were studied. The adjusted geometric mean ceftriaxone MIC was similar among women (0.0067 µg/ml, 95% CI 0.0049–0.0092 µg/ml) and MSW (0.0060 µg/ml, 95% CI 0.0053–0.0066 µg/ml). In

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contrast, the adjusted geometric mean ceftriaxone MIC was higher among MSM (0.0098 µg/ml, 95% CI 0.0082–0.0119 µg/ml) than MSW. This same pattern was observed for other antimicrobials, including cefixime and azithromycin

Conclusions—Ceftriaxone, cefixime, and azithromycin MICs were higher among MSM than MSW, but were similar among women and MSW. These findings suggest that gonococcal antimicrobial susceptibility surveillance based on urethral isolates from MSW may adequately represent susceptibility of urogenital *N. gonorrhoeae* in women.

Keywords

Neisseria gonorrhoeae; antimicrobial susceptibility; antimicrobial resistance surveillance; male; female

Introduction

Gonorrhea treatment is complicated by *Neisseria gonorrhoeae*'s ability to develop antimicrobial resistance. Since the introduction of antimicrobials to treat *N. gonorrhoeae* infection 70–80 years ago, *N. gonorrhoeae* has progressively developed resistance to every antimicrobial previously recommended for treatment, including sulfonamides, penicillins, tetracyclines, and fluoroquinolone antibiotics.(1) Most recently, a decline in susceptibility to third generation cephalosporins and reports of cephalosporin treatment failures internationally have raised concern about the dwindling number of effective treatment options for gonorrhea and the potential impact of multi-drug resistant gonorrhea on gonorrhea control programs worldwide.(2–5)

Gonorrhea is the second most commonly reported notifiable disease in the United States (US), with 333,004 cases reported to the Centers for Disease Control and Prevention (CDC) in 2013.(6, 7) Owing to under-detection and under-reporting, the true number of cases is likely much higher than the number reported, and it is estimated that over 800,000 new infections occur in the US each year.(8) Approximately half of reported gonorrhea cases occur in women, and *N. gonorrhoeae* infection is associated with health sequelae in women, including pelvic inflammatory disease (PID), chronic pelvic pain, tubal infertility, and ectopic pregnancy. Prompt treatment with an effective antimicrobial regimen, ideally as a single dose, limits sequelae of infection within individual patients and minimizes further transmission within the population by shortening duration of infection. However, effective treatment regimens for gonorrhea have become increasingly scarce, as *N. gonorrhoeae* has developed and maintained an unacceptable prevalence of resistance to previously recommended antimicrobials, and few new antimicrobial options are in development.(7, 9) At present, there is just one CDC-recommended first line regimen for gonorrhea treatment: dual therapy with single doses of ceftriaxone and azithromycin.(10)

CDC gonorrhea treatment guidelines are informed by national gonococcal antimicrobial susceptibility data obtained from the Gonococcal Isolate Surveillance Project (GISP).(2, 10, 11) GISP is a sentinel surveillance system, located in 25–30 cities throughout the US, that monitors gonococcal antimicrobial susceptibility among urethral isolates obtained from men with urethritis.(12) Little is known about gonococcal susceptibility among women in the US,

and it is not clear whether gonococcal susceptibility among men who have sex exclusively with women (MSW) is representative of gonococcal susceptibility among women. The primary objective of this analysis was to compare antimicrobial susceptibility of urogenital gonococcal isolates obtained from women to that of urethral isolates obtained from MSW. Secondary objectives were to compare antimicrobial susceptibility of urogenital gonococcal isolates obtained from men who have sex with men (MSM) to that of isolates obtained from women and MSW, and to compare the antimicrobial susceptibility of paired isolates from participants with concurrent urogenital and extra-genital infection.

Materials and Methods

We performed a secondary analysis of data collected during a recent gonorrhea treatment trial (13). Participants were enrolled in STD clinics in five US cities (Baltimore, Maryland; Birmingham, Alabama; Los Angeles, California; Pittsburgh, Pennsylvania; and San Francisco, California) from May 2010 through November 2012. Untreated patients with suspected urogenital *N. gonorrhoeae* infection were eligible for enrollment if (1) Gram stain of urethral (male) or endocervical (female) specimens at the current visit or previous visit revealed gram-negative diplococci and leukocytes, or (2) they reported anal, oral, or vaginal sexual contact with someone diagnosed with gonorrhea within the last 60 days. Patients were excluded from enrollment if they were younger than 15 or older than 60 years; were pregnant or lactating; were diagnosed with abdominal pain related to PID, testicular pain, epididymitis, disseminated gonococcal infection, or genital ulcer disease; or had received antimicrobials within 30 days of study enrollment. Patients were also excluded if they reported an allergy or adverse reaction to macrolides, aminoglycosides, or fluoroquinolones, or if they had certain medical conditions (see (13) for full exclusion criteria).

At enrollment, demographic, behavioral, and clinical information, and culture specimens were collected. For this evaluation, MSW were defined as men who reported having sex with only female partners during the past 3 months, or men who reported no partners in the past 3 months but who self-identified as heterosexual. Men who reported having sex with at least one male partner in the past 3 months or who self-identified as gay or bisexual were classified as MSM. All eligible women were included as a single category, regardless of reported sexual history or sexual orientation.

Laboratory procedures

Specimens for *N. gonorrhoeae* culture were collected from the urethra or cervix using polyester swabs. Pharyngeal and/or rectal specimens were collected if the participant reported exposure at the relevant anatomic site(s). Swabs were immediately smeared onto modified Thayer-Martin medium plates and placed into a candle jar or whirl bags with CO₂ tablets. Cultures were either transferred to the local laboratory within four hours for incubation in 4–7% CO₂ at 37°C ±1°C, or were stored at the clinic in a 4–7% CO₂ incubator at 37°C ±1°C and transferred to the local laboratory within 24 hours. Media were examined for growth of presumptive *N. gonorrhoeae* at 24, 48, and 72 hours.

N. gonorrhoeae isolates were frozen and shipped to CDC Division of STD Prevention Laboratory Reference and Research Branch for confirmatory culture and antimicrobial

susceptibility testing using the agar dilution method. Antimicrobials tested included azithromycin (range 0.03 µg/ml to 16 µg/ml), cefixime (range 0.001 µg/ml to 4 µg/ml), ceftriaxone (range 0.001 µg/ml to 4 µg/ml), ciprofloxacin (range 0.002 µg/ml to 64 µg/ml), penicillin (range 0.004 µg/ml to 64 µg/ml), and tetracycline (range 0.03 µg/ml to 32 µg/ml). Isolates were tested for β-lactamase activity using the Nitrocefin test.

Interpretation of susceptibility results

Minimum inhibitory concentrations (MICs) were interpreted according to criteria recommended by the Clinical and Laboratory Standards Institute (CLSI) when available (14). CLSI definitions of resistance were used for ciprofloxacin (MIC ≥ 1 µg/ml), penicillin (MIC ≥ 2 µg/ml or β-lactamase-positive), and tetracycline (MIC ≥ 2 µg/ml). Because CLSI has not established criteria for resistance to azithromycin, cefixime, or ceftriaxone, we used breakpoints described in the GISP protocol (12) (azithromycin MIC ≥ 2 µg/ml, cefixime MIC ≥ 0.25 µg/ml, ceftriaxone MIC ≥ 0.125 µg/ml) as the definitions of “elevated MICs” for these antimicrobials.

Statistical analyses

We used the chi-square statistic to compare frequency distributions of enrollment location for women, MSW, and MSM. To explore potential differences in antimicrobial susceptibility among women, MSW, and MSM, we compared (1) the proportion of isolates with elevated MICs or resistance and (2) geometric mean MICs for each antimicrobial. Differences between groups were considered statistically significant if 95% confidence intervals of the proportions or geometric mean MICs did not overlap. Because geographic location is associated with differences in antimicrobial susceptibility (15, 16) and was a potential confounder, geometric mean MICs were adjusted for geographic location (West coast location vs. other location) using general linear models. Other demographic variables (i.e., age, race/ethnicity) were not included in the models because of multicollinearity between these variables and geographic location.

Analysis of paired isolates from participants with concurrent urogenital and extra-genital infection

In addition, we identified paired isolates obtained from study participants with concurrent urogenital and extra-genital infection (pharyngeal infection or rectal infection). For these pairs, we compared MICs of the urogenital isolate with those of the extra-genital isolate and described the proportion of pairs with discordant MICs. “Discordant MICs” was defined as MICs that differed by ≥ 2 doubling dilutions. Among those with discordant MICs, we assessed the proportion of pairs that had a higher urethral MIC than extra-genital MIC, and proportion with a higher extra-genital MIC than urethral MIC.

Results

Urogenital isolates from 170 MSM, 252 MSW, and 56 women were tested for antimicrobial susceptibility and included in this analysis. The geographic distribution of enrollment locations varied by sex and sex of sex partner (Table 1). While most (83.5%) MSM were enrolled in San Francisco, most (66.1%) women were enrolled in Birmingham, and most

MSW were enrolled in one of three locations: Birmingham (41.3%), San Francisco (31.0%), and Pittsburgh (24.2%). MSM who were enrolled in the study tended to be older than MSW and women; and most MSM were either non-Hispanic white or Hispanic, while most MSW and women were non-Hispanic black.

Data on the distribution of MICs for azithromycin, cefixime, ceftriaxone, ciprofloxacin, penicillin, and tetracycline for MSM, MSW, and women are summarized in Table 2. Across antimicrobials, the proportion of isolates with elevated MICs or resistance was similar among isolates collected from women and MSW. In contrast, with the exception of penicillin, the proportion of isolates with elevated MICs or resistance was higher among MSM than either MSW or women. However, none of these differences between MSM and MSW or women were statistically significant. For ceftriaxone, 1.8% (95% CI 0.1%–9.6%) of isolates collected from women and 0% (95% CI 0%–2.2%) of isolates collected from MSW had an elevated MIC, compared with 2.4% (95% CI 0.6%–5.9%) of isolates collected from MSM. This same pattern of elevated MICs among MSM was observed for most antimicrobials tested, including azithromycin (women: 0%, 95% CI 0%–6.4%; MSW: 0.4%, 95% CI 0%–2.2%; MSM: 0.6%, 95% CI 0%–3.2%) and cefixime (women: 1.8%, 95% CI 0.1%–9.6%; MSW: 0.4%, 95% CI 0%–2.2%; MSM: 3.5%, 95% CI 1.3%–7.5%).

Likewise, crude and adjusted geometric mean MICs were similar among women and MSW, but higher among MSM. For ceftriaxone, the adjusted geometric mean MIC among women (0.0067 µg/ml; 95% CI 0.0049–0.0092 µg/ml) did not differ from MSW (0.0060 µg/ml; 95% CI 0.0053–0.0066 µg/ml), but was statistically significantly higher among MSM (0.0098 µg/ml; 95% CI 0.0082–0.0119 µg/ml) than MSW. This same pattern was seen for azithromycin (women: 0.1567 µg/ml, 95% CI 0.1076–0.2281 µg/ml; MSW: 0.1740 µg/ml, 95% CI 0.1551–0.1953 µg/ml; MSM: 0.2797 µg/ml, 95% CI 0.2410–0.3247 µg/ml), cefixime (women: 0.0161 µg/ml, 95% CI 0.0109–0.0237 µg/ml; MSW: 0.0173 µg/ml, 95% CI 0.0156–0.0192 µg/ml; MSM: 0.0235 µg/ml, 95% CI 0.0197–0.0280 µg/ml), and tetracycline (women: 0.6020 µg/ml, 95% CI 0.3095–1.1707 µg/ml; MSW: 0.7308 µg/ml, 95% CI 0.5911–0.9035 µg/ml; MSM: 1.7699 µg/ml, 95% CI 1.3155–2.3812 µg/ml). Adjusted geometric mean MICs were also higher among MSM than MSW for ciprofloxacin and penicillin, but these differences were not statistically significant.

Analysis of paired isolates obtained from patients with concurrent urogenital and extra-genital infection

Paired pharyngeal and urogenital isolates were obtained from 11 MSM, 3 MSW, and 13 women with concurrent pharyngeal and urogenital gonococcal infection (Table 3a). Paired rectal and urogenital isolates were obtained from 5 MSM and 2 women with concurrent rectal and urogenital infection (Table 3b). The majority of pharyngeal/urogenital and rectal/urogenital pairs had concordant MICs (identical MICs or within one dilution of each other). Few pairs had discordant MICs (≥ 2 dilution difference), but when discordance was observed, there was no trend towards either pharyngeal or rectal isolates having higher MICs than urogenital MICs.

Discussion

In this analysis of urogenital gonococcal isolates contemporaneously collected from women, MSW, and MSM, gonococcal MICs were higher among MSM than MSW, but were similar among women and MSW. Among women, we identified a high prevalence of resistance to the antimicrobials previously recommended for gonorrhea treatment (19.6% resistant to ciprofloxacin, 21.4% resistant to penicillin, and 17.9% resistant to tetracycline), and lower prevalences of elevated azithromycin MICs (0%), elevated cefixime MICs (1.8%, n=1), and elevated ceftriaxone MICs (1.8%, n=1). These prevalences were similar to those of MSW in our sample and are consistent with GISP data on gonococcal susceptibility among MSW during the same time period, 2010–2012.(15) These results also support the current CDC gonorrhea treatment recommendation, dual therapy with ceftriaxone and azithromycin, and highlight the need for additional treatment options given the potential threat of cephalosporin resistance.

To adjust for the potential confounding effect of geographic location, this study compared geometric mean MICs that were adjusted for geographic region. Region-adjusted geometric mean MICs for azithromycin, cefixime, and ceftriaxone were higher among MSM than MSW. In contrast, region-adjusted geometric mean MICs among MSW did not differ from those among women. The higher prevalence of gonococcal resistance and elevated MICs among MSM compared with MSW has previously been documented (16–18), but there are few published comparisons of gonococcal MICs among women and MSW. Studies comparing all male urethral isolates to female urogenital isolates have generally reported a higher prevalence of resistance or elevated MICs among men.(19–21) However, because these studies were not able to stratify men by sex of sex partner, it is likely that the higher prevalence observed among men was largely attributable to MSM in the sample. The few studies that have stratified men by gender of sex partner and compared MSW to women have demonstrated either no difference between women and MSW or a slightly lower prevalence of resistance or elevated MICs among women compared with MSW.(17, 18, 22) While limited by the relatively small sample size of women, our findings are consistent with these studies and suggest that US gonococcal antimicrobial susceptibility among urogenital isolates from women is similar to antimicrobial susceptibility among urethral isolates from MSW.

These findings have important implications for the surveillance of antimicrobial susceptibility in *N. gonorrhoeae*. The US surveillance system for *N. gonorrhoeae* antimicrobial susceptibility, GISP, provides crucial data that inform CDC gonorrhea treatment recommendations, including treatment recommendations for female urogenital infection. However, GISP monitors gonococcal susceptibility exclusively among male urethral isolates.(12) This approach to surveillance has several advantages in settings that do not routinely collect specimens for gonococcal culture when testing for gonorrhea. Male urethral infections are frequently symptomatic, and are therefore easier to identify than female urogenital infections, which are typically asymptomatic. In addition, the sensitivity of gonococcal culture is higher for male urethral infections than female urogenital infections, likely owing to a higher *N. gonorrhoeae* bacterial load and lower concentrations of other bacteria at the urethral site.(23, 24) Men with urethral symptoms also tend to seek

out evaluation and treatment, and therefore represent a consistent population that is less likely to be affected by changes in screening practices, which is beneficial when monitoring susceptibility trends over time. The results of this analysis suggest that surveillance of gonococcal antimicrobial susceptibility among MSW may adequately represent the susceptibility of *N. gonorrhoeae* circulating among heterosexuals, including the susceptibility of urogenital *N. gonorrhoeae* among women, and provide evidence in support of the GISP sampling strategy.

Our study also provides reassuring, albeit limited, data regarding the antimicrobial susceptibilities of co-existent extra-genital (i.e. pharyngeal and rectal) gonorrhea. Among the small numbers of paired genital/extra-genital isolates we collected from study participants, no immediate tendency for isolates from one site to be more, or less, resistant to currently used antibiotics was noted. The numbers of paired isolates in this study however was quite small. Given the suggested importance of extra-genital infection as a contributor to the emergence of gonococcal antimicrobial resistance (25, 26), additional studies should expand upon our investigations.

The main limitation of this study was the relatively small number of isolates collected from women. It is possible that this study was not sufficiently powered to detect differences between women and MSW. However, particularly for the antimicrobials most recently used to treat gonorrhea (azithromycin, cefixime, ceftriaxone, and ciprofloxacin), the point estimates for prevalence of elevated MICs or resistance and the adjusted geometric mean MICs were similar, and there was no consistent trend towards women having higher or lower MICs than MSW. A second limitation, and a potential limitation for all studies that stratify based on sex of sex partner, is possible misclassification of men as MSM or MSW. Some men might have been reluctant to disclose that they had a male sex partner, and might have been misclassified as MSW. Given the higher prevalence of resistance and elevated MICs among MSM, this would lead to overestimates of the prevalence of resistance or elevated MICs and overestimates of geometric mean MICs among MSW. Our data were also limited to a small number of geographic locations, and point estimates of the geometric mean MICs or prevalence of elevated MICs in this study may not be representative of all *N. gonorrhoeae* infections in the US.

In summary, we found that US gonococcal MICs for azithromycin, cefixime, and ceftriaxone were higher among MSM than MSW. In contrast, gonococcal MICs were similar among women and MSW. These findings suggest that surveillance for gonococcal antimicrobial susceptibility among urethral isolates from MSW are likely to adequately represent susceptibility of *N. gonorrhoeae* among urogenital infections among women. Given the potential threat of cephalosporin resistance, and as the number of effective treatment options for gonorrhea becomes more limited, local surveillance for *N. gonorrhoeae* antimicrobial susceptibility will become increasingly important to inform local and regional treatment guidelines. As settings that do not routinely collect gonococcal culture specimens for the diagnosis of gonorrhea consider establishing surveillance for *N. gonorrhoeae* antimicrobial susceptibility, it will be important to select a sampling strategy that is both efficient and representative of *N. gonorrhoeae* circulating in local sexual

networks. The findings from this study support the GISP sampling strategy of monitoring gonococcal susceptibility using urethral isolates from males.

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Table 1

Characteristics of patients from whom urogenital gonococcal isolates were collected, by sex and sex of sex partner.

	MSM ^a (N=170) n (%)	MSW ^a (N=252) n (%)	Women (N=56) n (%)
Enrollment location^b			
Baltimore	0	3 (1.2)	0
Birmingham	8 (4.7)	104 (41.3)	37 (66.1)
Los Angeles	0	6 (2.4)	4 (7.1)
Pittsburgh	20 (11.8)	61 (24.2)	11 (19.6)
San Francisco	142 (83.5)	78 (31.0)	4 (7.1)
Age in years (median [IQR])^a	30 (25–39)	25 (21–34)	22.5 (20–26.5)
Race/ethnicity			
Asian/Hawaiian/Pacific Islander	7 (4.1)	4 (1.6)	0
Black, Non-Hispanic	33 (19.4)	199 (79.0)	48 (85.7)
Hispanic or Latino	35 (20.6)	16 (6.4)	3 (5.4)
White, Non-Hispanic	83 (48.8)	14 (5.6)	3 (5.4)
Multiracial	9 (5.3)	14 (5.6)	2 (3.6)
Other	3 (1.8)	5 (2.0)	0

^a Abbreviations: MSM = men who have sex with men; MSW = men who have sex with women only; IQR = interquartile range.

^b p<0.0001

Table 2
Comparison of minimum inhibitory concentrations (MICs) of urogenital gonococcal isolates by sex and sex of sex partner.

	MSM ^a (N=170)	MSW ^a (N=252)	Women (N=56)
Azithromycin			
MIC50 ^d , in µg/ml	0.25	0.25	0.1875
MIC90 ^d , in µg/ml	0.5	0.5	0.5
MIC range, in µg/ml	0.03 – 2	0.03 – 16	0.03 – 1
Percent (95% CI) ^d with elevated MIC (≥ 2 µg/ml)	0.6 (0–3.2)	0.4 (0–2.2)	0 (0–6.4)
Geometric mean MIC (95% CI), in µg/ml	0.2831 (0.2535–0.3161) *	0.1669 (0.1495–0.1862)	0.1279 (0.0981–0.1669)
Adjusted geometric mean MIC (95% CI), in µg/ml ^b	0.2797 (0.2410–0.3247) *	0.1740 (0.1551–0.1953)	0.1567 (0.1076–0.2281)
Cefixime			
MIC50, in µg/ml	0.03	0.015	0.015
MIC90, in µg/ml	0.06	0.03	0.03
MIC range, in µg/ml	0.004 – 1	0.001 – 0.25	0.001 – 0.25
Percent (95% CI) with elevated MIC (≥ 0.25 µg/ml)	3.5 (1.3–7.5)	0.4 (0–2.2)	1.8 (0.1–9.6)
Geometric mean MIC (95% CI), in µg/ml	0.0232 (0.0203–0.0264) *	0.0167 (0.0152–0.0184)	0.0115 (0.0087–0.0152)
Adjusted geometric mean MIC (95% CI), in µg/ml	0.0235 (0.0197–0.0280) *	0.0173 (0.0156–0.0192)	0.0161 (0.0109–0.0237)
Ceftriaxone			
MIC50, in µg/ml	0.008	0.004	0.004
MIC90, in µg/ml	0.03	0.015	0.015
MIC range, in µg/ml	0.001 – 0.125	0.001 – 0.06	0.001 – 0.125
Percent (95% CI) with elevated MIC (≥ 0.125 µg/ml)	2.4 (0.6–5.9)	0 (0–2.2)	1.8 (0.1–9.6)
Geometric mean MIC (95% CI), in µg/ml	0.0100 (0.0087–0.0115) *	0.0055 (0.0049–0.0061)	0.0050 (0.0040–0.0063)
Adjusted geometric mean MIC (95% CI), in µg/ml	0.0098 (0.0082–0.0119) *	0.0060 (0.0053–0.0066)	0.0067 (0.0049–0.0092)
Ciprofloxacin			
MIC50, in µg/ml	0.004	0.004	0.004
MIC90, in µg/ml	12	4	4
MIC range, in µg/ml	0.002 – 32	0.002 – 32	0.002 – 32
Percent (95% CI) resistant (MIC ≥ 1 µg/ml)	30.0 (23.2–37.5)	19.4 (14.8–24.9)	19.6 (10.2–32.4)
Geometric mean MIC (95% CI), in µg/ml	0.0417 (0.0245–0.0709) *	0.0153 (0.0107–0.0219)	0.0155 (0.0069–0.0347)

	MSM ^a (N=170)	MSW ^a (N=252)	Women (N=56)
Adjusted geometric mean MIC (95% CI), in µg/ml	0.0412 (0.0201–0.0847)	0.0167 (0.0115–0.0244)	0.0188 (0.0059–0.0598)
Penicillin			
MIC50, in µg/ml	0.5	0.5	0.5
MIC90, in µg/ml	4	4	2
MIC range, in µg/ml	0.004 – 32	0.004 – 64	0.004 – 8
Percent (95% CI) resistant (MIC ≥ 2 µg/ml or β-lactamase-positive)	28.2 (21.4–35.0)	31.7 (26.0–37.4)	21.4 (10.7–32.1)
Geometric mean MIC (95% CI), in µg/ml	0.6355 (0.5282–0.7647)	0.5967 (0.5006–0.7111)	0.3803 (0.2439–0.5931)
Adjusted geometric mean MIC (95% CI), in µg/ml	0.7700 (0.6018–0.9851)	0.6187 (0.5136–0.7452)	0.4750 (0.2517–0.8966)
Tetracycline^c			
MIC50, in µg/ml	1	0.5	0.25
MIC90, in µg/ml	32	16	16
MIC range, in µg/ml	0.06 – 32	0.03 – 32	0.06 – 32
Percent (95% CI) resistant (MIC ≥ 2 µg/ml)	30.0 (23.2–37.5)	21.4 (16.5–27.0)	17.9 (8.9–30.4)
Geometric mean MIC (95% CI), in µg/ml	1.4052 (1.1239–1.7570) [*]	0.6336 (0.5158–0.7784)	0.5044 (0.3173–0.8017)
Adjusted geometric mean MIC (95% CI), in µg/ml	1.7699 (1.3155–2.3812) [*]	0.7308 (0.5911–0.9035)	0.6020 (0.3095–1.1707)

^a Abbreviations: MSM = men who have sex with men; MSW = men who have sex with women only; MIC50 = minimum concentration needed to inhibit 50% of isolates; MIC90 = minimum concentration needed to inhibit 90% of isolates; 95% CI = 95% confidence interval.

^b Geometric mean MIC adjusted for geographic region (West coast vs. non-West coast).

^c Denominator of 169 for MSM (tetracycline MIC not available for one isolate).

^{*} Geometric mean MIC or adjusted geometric mean MIC significantly higher among MSM than MSW (p < 0.05).

Table 3a

Paired isolates obtained from patients with concurrent pharyngeal and urethral infection: number and proportion with discordant^a minimum inhibitory concentration (MIC) results by sex and sex of sex partner.

	Paired pharyngeal and urethral isolates		
	MSM ^b (N=11) n (%)	MSW ^b (N=3) n (%)	Women (N=13) n (%)
Discordant azithromycin MIC results			
Urogenital MIC higher than pharyngeal MIC	0	1 (33.3)	2 (15.4)
Pharyngeal MIC higher than urogenital MIC	2 (18.2)	0	2 (15.4)
Discordant cefixime MIC results			
Urogenital MIC higher than pharyngeal MIC	1 (9.1)	0	0
Pharyngeal MIC higher than urogenital MIC	0	1 (33.3)	1 (7.7)
Discordant ceftriaxone MIC results			
Urogenital MIC higher than pharyngeal MIC	2 (18.2)	0	0
Pharyngeal MIC higher than urogenital MIC	1 (9.1)	1 (33.3)	2 (15.4)
Discordant ciprofloxacin MIC results			
Urogenital MIC higher than pharyngeal MIC	0	0	0
Pharyngeal MIC higher than urogenital MIC	0	1 (33.3)	2 (15.4)
Discordant penicillin MIC results			
Urogenital MIC higher than pharyngeal MIC	0	0	0
Pharyngeal MIC higher than urogenital MIC	0	2 (66.7)	2 (15.4)
Discordant tetracycline MIC results			
Urogenital MIC higher than pharyngeal MIC	0	0	1 (7.7)
Pharyngeal MIC higher than urogenital MIC	0	1 (33.3)	1 (7.7)

^aDiscordant = the difference between the pharyngeal MIC and urogenital MIC was ≥ 2 doubling dilutions.

^bAbbreviations: MSM = men who have sex with men; MSW = men who have sex with women only.

Table 3b

Paired isolates obtained from patients with concurrent rectal and urethral infection: number and proportion with discordant^a minimum inhibitory concentration (MIC) results by sex and sex of sex partner.

	Paired rectal and urethral isolates		
	MSM ^b (N=5) n (%)	MSW ^b (N=0) n (%)	Women (N=2) n (%)
Discordant azithromycin MIC results			
Urogenital MIC higher than rectal MIC	0	-	0
Rectal MIC higher than urogenital MIC	1 (20.0)	-	0
Discordant cefixime MIC results			
Urogenital MIC higher than rectal MIC	0	-	0
Rectal MIC higher than urogenital MIC	1 (20.0)	-	0
Discordant ceftriaxone MIC results			
Urogenital MIC higher than rectal MIC	1 (20.0)	-	0
Rectal MIC higher than urogenital MIC	1 (20.0)	-	0
Discordant ciprofloxacin MIC results			
Urogenital MIC higher than rectal MIC	1 (20.0)	-	0
Rectal MIC higher than urogenital MIC	1 (20.0)	-	0
Discordant penicillin MIC results			
Urogenital MIC higher than rectal MIC	1 (20.0)	-	0
Rectal MIC higher than urogenital MIC	2 (40.0)	-	0
Discordant tetracycline MIC results			
Urogenital MIC higher than rectal MIC	1 (20.0)	-	0
Rectal MIC higher than urogenital MIC	0	-	0

^aDiscordant = the difference between the rectal MIC and urogenital MIC was ≥ 2 doubling dilutions.

^bAbbreviations: MSM = men who have sex with men; MSW = men who have sex with women only.