High Prevalence of Gonococcal and Chlamydial Infection in Men Who Have Sex With Men With Newly Diagnosed HIV Infection

An Opportunity for Same-Day Presumptive Treatment

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Background: The increasing use of point-of-care HIV tests in sexually transmitted disease (STD) clinics allows for rapid identification of patients with newly diagnosed HIV infection who may also be at risk for more common sexually transmitted infections. Positive point-of-care HIV test results might be used to identify and provide presumptive treatment to patients who are likely to be coinfected with gonorrhea (GC) and chlamydia (CT).

Methods: Data from 6864 STD clinic visits by men who have sex with men (MSM) with no history of HIV infection and an HIV antibody test at that visit were analyzed. Results from rectal, pharyngeal, and urine nucleic acid amplification tests were used to calculate the prevalence of infection with GC and CT.

Results: MSM with newly diagnosed HIV infection were more likely than HIV-uninfected MSM to be infected with GC (25.9% [53 of 205] vs. 10.9% [728 of 6659]; $P < 0.001$) and CT (18.5% [38 of 205] vs. 7.8% [518 of 6659]; $P < 0.001$).

Conclusions: GC and CT are common in MSM with newly diagnosed HIV infection at an STD clinic. In this population, a positive point-of-care HIV test result is a useful risk marker for untreated gonococcal and chlamydial infections and provides a justification for presumptive GC and CT treatment.

Key Words: chlamydia, coinfection, gonorrhea, newly diagnosed HIV infection, presumptive treatment

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Patients who are at risk for acquiring HIV infection through sexual transmission are also at risk for more common sexually transmitted diseases (STDs). STDs cause biologic changes, such as inflammation, disruption of the genital mucosa, and an increase in the availability of activated immune cells, that increase the likelihood of acquiring HIV infection by 2- to 5-fold.[1] The risk of HIV acquisition increases substantially with exposure to ulcerative STDs; however, the greater frequency of curable nonulcerative STDs, such as gonorrhea (GC) and chlamydia (CT), could mean that those infections are responsible for a greater proportion of sexually transmitted HIV infections in the United States.[1–3] Because STDs can facilitate HIV acquisition and transmission, prompt detection and treatment of curable STDs should be a central component of a comprehensive HIV prevention strategy.[3]

STDs in HIV-uninfected men who have sex with men (MSM) likely play an important role in the acquisition of HIV infection through unprotected receptive anal intercourse. Gonococcal and chlamydial infections, particularly rectal infections, are prevalent in MSM attending STD clinics and in MSM with recently acquired HIV infection.[4–6] Because those infections are often asymptomatic, the Centers for Disease Control and Prevention (CDC) recommend at least annual screening for urethral GC and CT, rectal GC and CT, and pharyngeal GC for sexually active MSM as well as at least annual screening for HIV infection.[3,7]

Routine, rapid, point-of care testing for HIV infection is recommended in STD clinics and is becoming more widely available in those settings.[7–11] Use of point-of-care tests for HIV infection decreases the possibility of patients failing to learn their test results, increases the acceptance of testing, and facilitates timely linkages to care for patients with newly diagnosed HIV infection.[8,9] Results from positive point-of-care HIV tests might also be used as a risk marker to identify patients at high risk for coinfection with GC and CT and to provide presumptive same-day cotreatment for those more common curable infections for which highly accurate and reliable point-of-care tests are not available.

Guidelines for providing presumptive cotreatment for CT to patients with treatment indications for GC (from point-of-care Gram stain results or for those who are sexual contacts of patients with GC) are well established.[7,8] A recent multisite study re-examining the frequency of co-occurrence of CT in

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patients with GC found CT coinfection ranges of 10% to 31% in men and 35% to 50% in women and supported the continuation of CT cotreatment as the standard of care.[12] Providing presumptive treatment for infections that frequently co-occur and cannot be diagnosed with point-of-care tests streamlines clinical care for the patient, reduces time to treatment, and makes more efficient use of limited health resources.

To evaluate the potential role for expansion of presumptive cotreatment practices, we examined the frequency of gonococcal and chlamydial coinfection across multiple anatomic sites in MSM being tested for HIV infection at an STD clinic. Our objectives were to (1) compare the prevalence of gonococcal and chlamydial coinfection in MSM with newly diagnosed HIV infection versus that in MSM testing HIV-negative and (2) to evaluate the time to treatment under current clinical protocols for gonococcal and chlamydial coinfections in MSM with newly diagnosed HIV infection.

METHODS

Clinic Population

We examined data from 6997 visits by self-identified gay and bisexual men who were tested for HIV infection by a rapid or standard antibody test at the San Francisco municipal STD clinic between January 2004 and December 2006. On the basis of their current HIV test result and self-reported clinical history, men were categorized as having newly diagnosed HIV infection, having previous HIV infection, or not being infected with HIV. Newly diagnosed HIV infection was defined as a confirmed positive rapid or standard antibody test result and no prior evidence or self-reported history of HIV infection. After excluding visits from MSM (n = 133) with evidence of previous HIV infection, 6864 visits were included in the analysis. MSM were tested for rectal, pharyngeal, and urethral gonococcal and chlamydial infections based on recent sexual behavior, regardless of condom use. Rectal testing was offered to men who reported receptive anal sex in the previous 6 months or who had rectal symptoms, pharyngeal testing was offered to men who reported receptive oral sex in the previous 2 weeks with more than 1 partner, and urine testing was offered to men who reported insertive sex of any type or who had urethral symptoms.

Laboratory Methods

HIV specimens were tested with point-of-care (Oraquick Advance Rapid HIV-1 Antibody Test; Orasure Technologies, Bethlehem, PA) or standard antibody tests (Vironostika HIV-1 EIA; bioMérieux, Marcy l'Etoile, France or Genetics Systems for HIV-1/HIV-2 plus O EIA Antibody Test; Bio-Rad Laboratories, Hercules, CA [since July 2006]). All reactive test results were confirmed by immunofluorescent assay (Fluorognost HIV-1 IFA; Sanochemia, Vienna, Austria). All rectal, pharyngeal, and urine specimens were tested using nucleic acid amplification tests (NAATs) for GC and CT. The laboratory initially tested specimens with ProbeTec (BD Diagnostics, Sparks, MD) and, in March 2005, switched to the APTIMA Combo 2 Assay (Gen-Probe, San Diego, CA). The San Francisco Department of Public Health Laboratory has verified the performance of the ProbeTec and APTIMA assays for detecting GC and CT in rectal and pharyngeal specimens for clinical use in accordance with the Clinical Laboratory Improvement Act of 1988. All specimens were collected and stored according to manufacturer (urine) or standard clinical (rectal and pharyngeal) protocols.

Statistical Analyses

GC and CT prevalence was defined as infection at 1 or more anatomic sites. Persons not tested at a particular anatomic site were considered negative for infection at that site. Overall prevalence and infection status by anatomic site was compared for men with newly diagnosed HIV infection and HIV-uninfected men using χ^2 tests.

Adequate treatment for GC and CT was defined as documentation in the electronic medical record of a corresponding recommended or alternate antibiotic treatment according to the 2002 CDC STD Treatment Guidelines.[13] Time to treatment for GC and CT was calculated as the difference in days between the treatment date and the date of specimen collection.

To evaluate the appropriateness of recommending presumptive GC and CT treatment for MSM with newly diagnosed HIV infection, we compared the observed GC and CT prevalence in MSM with newly diagnosed HIV infection with the observed CT prevalence in patients with treatment indications for GC, for whom presumptive CT treatment is the standard of care. The prevalence of CT in patients with treatment indications for GC was calculated from (1) all patients (including women) reporting sexual contact with a GC-infected partner and (2) male patients diagnosed with urethral GC by Gram stain at the STD clinic between 2004 and 2006.

All analyses were performed using SAS version 9.1 (SAS Institute, Cary, NC).

Human Subjects Protections

We analyzed these data to evaluate a public health program. This activity therefore met the criteria for exemption from the US Department of Health and Human Services policy on protection of human research subjects (Code of Federal Regulations, Title 45, Part 46).

RESULTS

Patient Characteristics

Most of the 6864 MSM tested for HIV infection at the STD clinic self-identified as gay (80.9%), and the mean age was 34 years (SD = 9.5). The most common race was white (58.8%), followed by Hispanic (19.5%), Asian or Pacific Islander (14.2%), African American (7.0%), and unknown or other (0.7%). There were no statistically significant differences in demographic characteristics by HIV status, but MSM with newly diagnosed HIV infection were slightly more likely to be older (mean: 34.5 vs. 33.9 years; $P = 0.35$) and nonwhite (46.3% vs. 41.1%; $P = 0.15$) than HIV-uninfected MSM.

Three percent (205 of 6864) of MSM were classified as having newly diagnosed HIV infection. Between 2004 and 2006, the proportion of patients tested for HIV infection with point-of-care tests increased from 0.7% (5 of 654) during the first quarter of 2004 to 25.2% (142 of 563) during the fourth quarter of 2006. Collection of specimens for GC and CT

testing varied by anatomic site: 61.5% had rectal specimens, 79.3% had pharyngeal specimens, and 86.8% had urine specimens. MSM with newly diagnosed HIV infection were more likely to have been tested for rectal infection (72.2% vs. 61.2%; $P < 0.01$), but there were no differences in pharyngeal or urine testing practices. A total of 11.7% (24 of 205) of MSM with newly diagnosed HIV infection and 11.4% (756 of 6659) of HIV-uninfected MSM had no GC or CT tests at the time of their HIV test visit.

Gonorrhea and Chlamydia Prevalence

MSM with newly diagnosed HIV infection were 2.4 times more likely than HIV-negative MSM to be infected with GC (25.9% [53 of 205] vs. 10.9% [728 of 6659]; $P < 0.001$) or CT (18.5% [38 of 205] vs. 7.8% [518 of 6659]; $P < 0.001$) (Fig. 1). Rectal GC was 3.7 times more common (13.7% [28 of 205] vs. 3.7% [246 of 6659]; $P < 0.001$) and rectal CT was 3.9 times more common (17.1% [35 of 205] vs. 4.3% [289 of 6659]; $P < 0.001$) in MSM with newly diagnosed HIV infection. Significant differences were also found for urethral GC (10.7% [22 of 205] vs. 3.8% [252 of 6659]; $P < 0.001$) and pharyngeal GC (11.2% [23 of 205] vs. 6.9% [458 of 6659]; $P = 0.02$) but not for urethral CT (4.9% [10 of 205] vs. 3.2% [216 of 6659]; $P = 0.20$) or pharyngeal CT (2.0% [4 of 205] vs. 0.9% [60 of 6659]; $P = 0.12$).

Among MSM with newly diagnosed HIV infection, 52.8% (28 of 53) of GC-infected patients and 92.1% of CT-infected patients had a rectal infection. Overall, 37.5% (77 of 205) MSM with newly diagnosed HIV infection had GC or CT at 1 or more anatomic sites compared with 16.6% (1109 of 6659) of HIV-uninfected men ($P < 0.001$).

Time to Treatment

Same-day treatment for STDs was provided to 58.5% (31 of 53) of GC-coinfected and 36.8% (14 of 38) of CT-coinfected MSM with newly diagnosed HIV infection. The median time to treatment for 36 MSM with newly diagnosed HIV infection and coinfection with GC or CT who were treated after their initial visit was 7.0 days (range: 2 to 26 days). There was no documented treatment for 5.7% (3 of 53) of gonococcal infections and 5.3% (2 of 38) of chlamydial infections. MSM with newly diagnosed HIV infection who received same-day GC and CT treatment were significantly more likely to be infected with those organisms, respectively: 62.8% (27 of 43) of those treated for GC versus 16.1% (26 of 162) of those not treated had GC ($P < 0.001$), and 27.1% (16 of 59) of those treated for CT versus 15.1% (22 of 146) of those not treated had CT ($P = 0.04$).

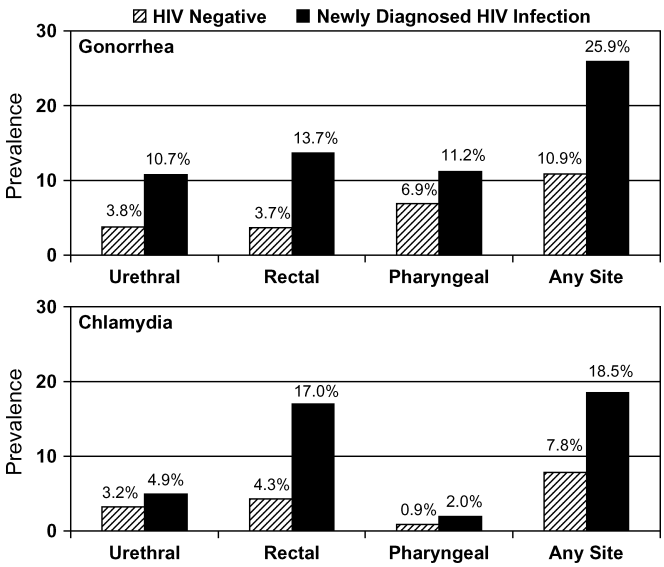

FIGURE 1. GC and CT prevalence among MSM tested for HIV, San Francisco STD clinic, 2004 to 2006.

Evaluation of Current Cotreatment Practices

Between 2004 and 2006, 1331 men with positive Gram stains indicating GC infection and 1996 persons receiving epidemiologic treatment for GC were eligible for presumptive cotreatment for CT. The observed CT prevalence in this population eligible for presumptive CT treatment was 18.3% (243 of 1331) in patients with GC identified by a positive Gram stain and 14.9% (298 of 1996) in sexual contacts of patients with GC. Overall, 16.3% (541 of 3327) of patients with indications for presumptive CT treatment were found to be infected with CT.

DISCUSSION

GC and CT prevalence in MSM with newly diagnosed HIV infection at the San Francisco STD clinic was substantial (25.9% and 18.5%, respectively) and significantly higher than in MSM testing HIV-negative (10.9% and 7.8%, respectively). Prevalence of infection was highest in MSM with newly diagnosed HIV infection receiving same-day treatment for GC (62.8%) and CT (27.1%) because of symptoms or reported contact to disease. Prevalence among those without treatment indications was still high (16.1% for GC and 15.1% for CT) and comparable to the CT prevalence in patients with GC treatment indications (16.3%), for whom presumptive CT cotreatment is the standard of care. Therefore, recommending presumptive treatment for this high-risk population is consistent with existing presumptive treatment guidelines. Also, it is important to note that the true prevalence of GC and CT coinfection is probably underestimated because of categorizing patients as negative for GC and CT if they were not tested at a particular anatomic site. A substantial proportion of patients (11.4%) who were likely tested at a recent STD clinic visit did not have any GC or CT tests, and because of selective testing based on self-reported sexual behaviors, 38.5% were not tested for rectal infections.

The difference in GC and CT prevalence in MSM with newly diagnosed HIV infection was particularly pronounced for rectal infections. Although this might be partially explained by a higher frequency of rectal testing among patients with newly diagnosed HIV infection, it is more likely attributable to the increased risk for HIV and STD acquisition that is associated with unprotected receptive anal intercourse.[5] Rectal infections accounted for a substantial proportion of the overall GC and CT prevalence in this population.

Because gonococcal and chlamydial infections are often asymptomatic, under current clinical protocols, half of those

coinfections in MSM with newly diagnosed HIV infection were not treated until after laboratory results became available. This practice delays time to treatment and, for the HIV-infected patient, might translate into increased viral load.[14] Expanding same-day presumptive treatment for all MSM with newly diagnosed HIV infection would ensure treatment of patients who are currently not being treated, decrease overall time to treatment, and streamline clinic care.

Reducing time to treatment of STDs, however, might have only limited implications for reducing secondary transmission of HIV infection in this population. That is because most patients substantially reduce sexual risk behaviors after first learning that they are infected with HIV.[15] In addition, because of differences in sexual practices and the potential for STDs at multiple anatomic sites, the overall GC and CT prevalence is probably higher in MSM than in other populations. Therefore, these findings may not be generalizable to other populations with newly diagnosed HIV infection who may or may not have acquired HIV through sexual transmission.

The success of implementing a presumptive same-day treatment protocol for MSM with newly diagnosed HIV infection is dependent on the availability of point-of-care testing for HIV infection and medications for STDs. Recent guidance from the CDC encourages the integration of routine HIV testing in medical settings, including STD clinics, and promotes the use of rapid point-of-care testing to ensure that patients are informed of their HIV test results.[8] Additional advantages of point-of-care HIV testing in STD clinics include the ability to provide timely referrals to medical care and initiate partner notification in patients with newly diagnosed HIV infection. Reactive point-of-care HIV test results in MSM can also be used as a risk marker to identify patients at high risk for other STDs.

Based on our findings, we instituted presumptive GC and CT treatment for all MSM at the STD clinic with newly diagnosed HIV infection detected by reactive point-of-care HIV antibody test results. We recommend that other STD programs evaluate the prevalence of STDs in patients with newly diagnosed HIV infection. Confirming our findings in other clinical settings could result in new recommendations to offer presumptive STD treatment to patients newly diagnosed with HIV infection.

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REFERENCES

1. Fleming DT, Wasserheit JN. From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. *Sex Transm Infect*. 1999; 75:3–17.
2. Wasserheit JN. Epidemiological synergy. Interrelationships between human immunodeficiency virus infection and other sexually transmitted diseases. *Sex Transm Dis*. 1992;19:61–77.
3. Centers for Disease Control and Prevention. HIV prevention through early detection and treatment of sexually transmitted diseases. *MMWR Morb Mortal Wkly Rep*. 1998;47(RR-12):1–24.
4. Kent CK, Chaw JK, Wong W, et al. Prevalence of rectal, urethral and pharyngeal chlamydia and gonorrhea detected in 2 clinical settings among men who have sex with men: San Francisco, California, 2003. *Clin Infect Dis*. 2005;41:67–74.
5. Craib KJ, Meddings DR, Strathdee SA, et al. Rectal gonorrhoea as an independent risk factor for HIV infection in a cohort of homosexual men. *Genitourin Med*. 1995;71:150–154.
6. Chin-Hong PV, Hecht FM, Klausner JD. Newly diagnosed HIV infection. *N Engl J Med*. 2006;354:771–772.
7. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2006. *MMWR Morb Mortal Wkly Rep*. 2006; 55(RR-11):1–94.
8. Centers for Disease Control and Prevention. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health care settings. *MMWR Morb Mortal Wkly Rep*. 2006;55(RR-14):1–17.
9. Centers for Disease Control and Prevention. Rapid HIV test distribution—United States, 2003–2005. *MMWR Morb Mortal Wkly Rep*. 2006; 55:673–676.
10. National Alliance of State and Territorial AIDS Directors. Rapid HIV testing assessment, October 2006. Available at: http://www.nastad.org/. Accessed June 27, 2007.
11. Kendrick SR, Kroc KA, Withum D, et al. Outcomes of offering rapid point-of-care HIV testing in a sexually transmitted disease clinic. *J Acquir Immune Defic Syndr*. 2005;38:142–146.
12. Lyss SB, Kamb ML, Peterman TA, et al. *Chlamydia trachomatis* among patients infected with and treated for *Neisseria gonorrhoeae* in sexually transmitted disease clinics in the United States. *Ann Intern Med*. 2003; 139:178–185.
13. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2002. *MMWR Morb Mortal Wkly Rep*. 2002; 51(RR-06):1–80.
14. Sadiq ST, Taylor S, Copas AJ, et al. The effects of urethritis on seminal plasma HIV-1 RNA loads in homosexual men not receiving antiretroviral therapy. *Sex Trans Infect*. 2005;81:120–123.
15. Colfax GN, Buchbinder SP, Cornelisse PG, et al. Sexual risk behaviors and implications for secondary HIV transmission during and after HIV seroconversion. *AIDS*. 2002;16:1529–1535.