Gonorrhea in the HIV Era: A Reversal in Trends Among Men Who Have Sex With Men

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A B S T R A C T

Objectives. Gonorrhea cases among men who have sex with men (MSM) declined in the early years of the HIV epidemic. We evaluated more recent trends in gonorrhea among MSM through the Centers for Disease Control and Prevention's Gonococcal Isolate Surveillance Project.

Methods. Isolates and case information were collected from 29 US sexually transmitted disease (STD) clinics. Gonococcal urethritis cases among MSM were compared with those among heterosexual men, and cases among MSM in 1995 to 1999 were compared with earlier MSM cases.

Results. Of 34 942 cases, the proportion represented by MSM increased from 4.5% in 1992 to 13.2% in 1999 ($P<$ .001). Compared with heterosexuals, MSM were older, more often White, and more often had had gonorrhea previously, although fewer had had gonorrhea in the past year. MSM with gonorrhea in 1995 to 1999 were slightly older than those with gonorrhea in 1992 to 1994, and a higher proportion had had gonorrhea in the past year.

Conclusions. MSM account for an increasing proportion of gonococcal urethritis cases in STD clinics. Given recent evidence that gonorrhea may facilitate HIV transmission, these trends demand increased attention to safe sexual behaviors and reducing STDs among MSM. (*Am J Public Health.* 2001;91: 959–964)

Reductions in rates of sexually transmitted diseases (STDs) among men who have sex with men (MSM) followed the advent of the HIV epidemic in the United States. Reports from several US cities documented a sharp decline in gonorrhea among MSM during the early 1980s,[1–3] coincident with reports of reductions in unsafe sexual behaviors.[4,5] However, several recent reports suggest a reversal in these trends. Investigators in Seattle reported increases in syphilis, gonorrhea, and chlamydial infection among MSM from 1997 through 1999.[6,7] Cases of rectal gonorrhea among MSM in San Francisco increased as the proportion of MSM practicing unprotected anal intercourse rose.[8]

Through the Gonococcal Isolate Surveillance Project (GISP) of the Centers for Disease Control and Prevention (CDC), we evaluated trends in gonococcal infection among MSM. GISP is a sentinel surveillance project implemented in 1986 to monitor national trends in antimicrobial resistance in *Neisseria gonorrhoeae* through the collection of urethral gonococcal isolates from selected STD clinics nationwide. As a systematic sample of gonococcal isolates from men attending public and military STD clinics in the United States, GISP also provides a unique source of national epidemiologic data on gonorrhea. We analyzed GISP data to assess characteristics of MSM with gonorrhea from 1992 through 1999.

Methods

Project Design

The first 25 urethral isolates of *N gonorrhoeae* from male patients were collected each month at selected public and military STD clinics. GISP was initiated in 1986; however, because significant changes in participating clinics occurred before 1992, the analysis period for this project was limited to 1992 through 1999. The participating clinics were in the following 29 cities and counties: Albuquerque, NM; Anchorage, Alaska; Atlanta, Ga; Baltimore, Md; Birmingham, Ala; Boston, Mass; Chicago, Ill; Cincinnati, Ohio; Cleveland, Ohio; Denver, Colo; Fayetteville, NC; Honolulu, Hawaii; Kansas City, Mo; Long Beach, Calif; Miami, Fla; Minneapolis, Minn; Nassau County, NY; New Orleans, La; Orange County, Calif; Philadelphia, Pa; Phoenix, Ariz; Portland, Ore; San Antonio, Tex; San Diego, Calif; San Francisco, Calif; Seattle, Wash; St Louis, Mo; Tacoma, Wash; and West Palm Beach, Fla. Five clinics did not participate for the entire

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project period. Boston discontinued participation in 1992, and St Louis discontinued in 1993 and rejoined in 1995. Three clinics joined after the beginning of the project period: Chicago in 1996 and Miami and Fayetteville in 1998. Clinics participating for less than 2 full years of the project period were excluded (Boston, Fayetteville, and Miami). Demographic and clinical data were abstracted from patient charts by clinic personnel. Sexual orientation was recorded as reported in the medical record; gay and bisexual categories were combined as MSM. Two clinics (Minneapolis and Tacoma) did not collect information on patients' sexual orientation and were excluded from all analyses. In all, 5 clinics were excluded, leaving 24 clinics for analysis. Analyses were limited to the first 20 viable isolates that met project criteria from each clinic each month. (Further information on GISP can be obtained on the World Wide Web at http://www.cdc.gov/nchstp/dstd/stats_trends/stats_and_trends.htm.)

Laboratory Methods

GISP methods for isolating *N gonorrhoeae* and determining minimum inhibitory concentrations (MICs) by standard agar dilution procedures[9] have been previously described.[10,11] Five regional laboratories (in Atlanta, Ga; Birmingham, Ala; Cleveland, Ohio; Denver, Colo; and Seattle, Wash) performed all laboratory testing. MICs of erythromycin were determined for approximately one half of isolates. Reference strains of *N gonorrhoeae* were tested by all laboratories to ensure interlaboratory consistency in measuring MICs; susceptibilities of selected isolates were confirmed at the CDC.

Statistical Analysis

Data analyses were performed with SAS version 6.12 (SAS Institute, Cary, NC). Estimated total numbers of MSM gonococcal urethritis cases in selected clinics were calculated by multiplying the proportion of GISP cases that involved MSM by the total number of gonorrhea cases among males reported each month in each clinic, and then summing the monthly numbers to produce annual estimates. Estimates were produced for clinics and years in which total numbers of gonorrhea cases among males were reported for at least 11 of 12 months; the year's monthly average was used to interpolate the missing data value. Cases of gonococcal urethritis from MSM were compared with cases from heterosexual men, and MSM cases in 1995 through 1999 were compared with MSM cases in 1992 through 1994. Distributions of demographic and clinical characteristics and resistance phenotypes were compared by the χ^2 test. The Fisher exact test was used when an expected value was less than 5. Medians and geometric means were compared by the Kruskal-Wallis test for 2 groups.

Results

Of 36 509 GISP cases from 1992 through 1999, 34 942 (95.7%) reported sexual orientation data and 8.3% of these (2908 of 34 942) were MSM. The proportion of cases involving MSM increased from 4.5% (219 of 4858) in 1992 to 13.2% (591 of 4465, $P < .001$) in 1999. In 9 clinics (Chicago, Denver, Honolulu, Long Beach, Orange County, Portland, San Diego, Seattle, and San Francisco), more than 5% of cases each year involved MSM; these clinics accounted for more than 80% of MSM cases each year. Among these clinics, the 1999 proportions of cases involving MSM ranged from 11.3% in Chicago to 56.8% in San Francisco (Figure 1). Among the remaining clinics, the proportion of cases involving MSM increased from 1.3% in 1992 to 2.8% in 1999. For 7 clinics, estimated total numbers of MSM gonorrhea cases could be calculated for 5 to 7 years each (Figure 2). In 6 of these clinics, the number was fewer than 150 cases in each year, while San Francisco had more than 500 estimated total cases of gonorrhea among MSM for 1998. Trends in estimated total numbers of MSM cases were similar to the trends in proportions shown in Figure 1.

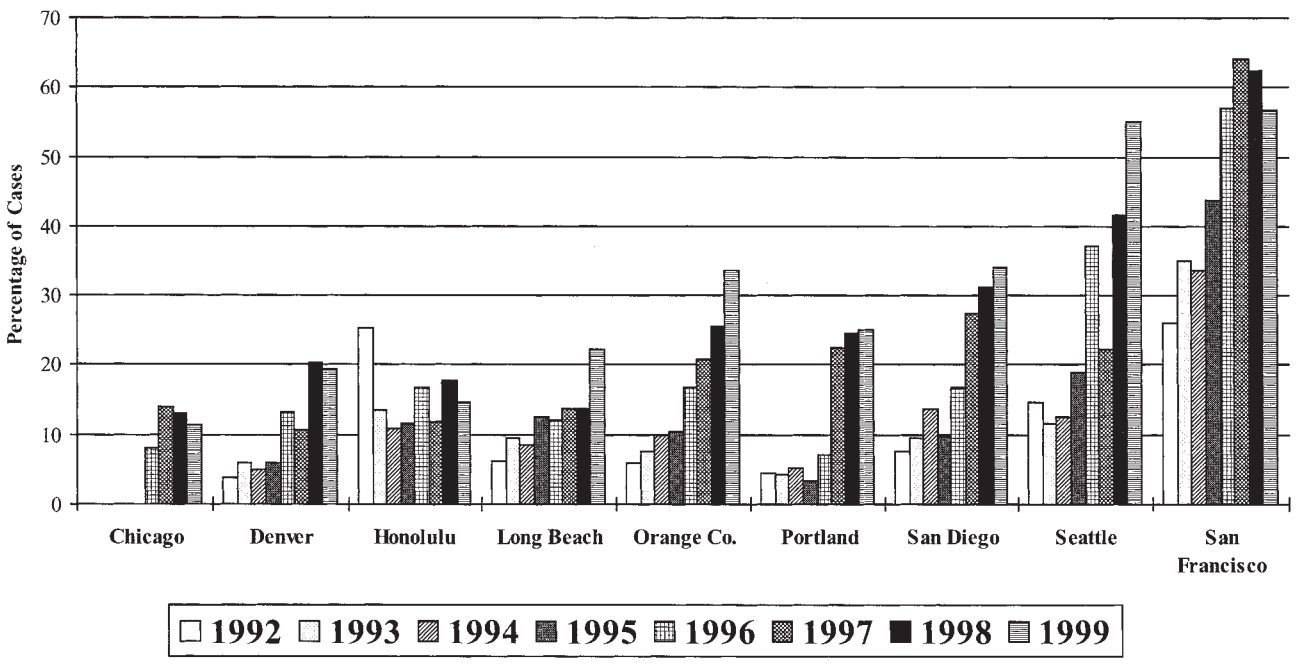

FIGURE 1—Percentages of cases of gonococcal urethritis that occurred among men who have sex with men, from sexually transmitted disease clinics in selected cities from 1992 to 1999.

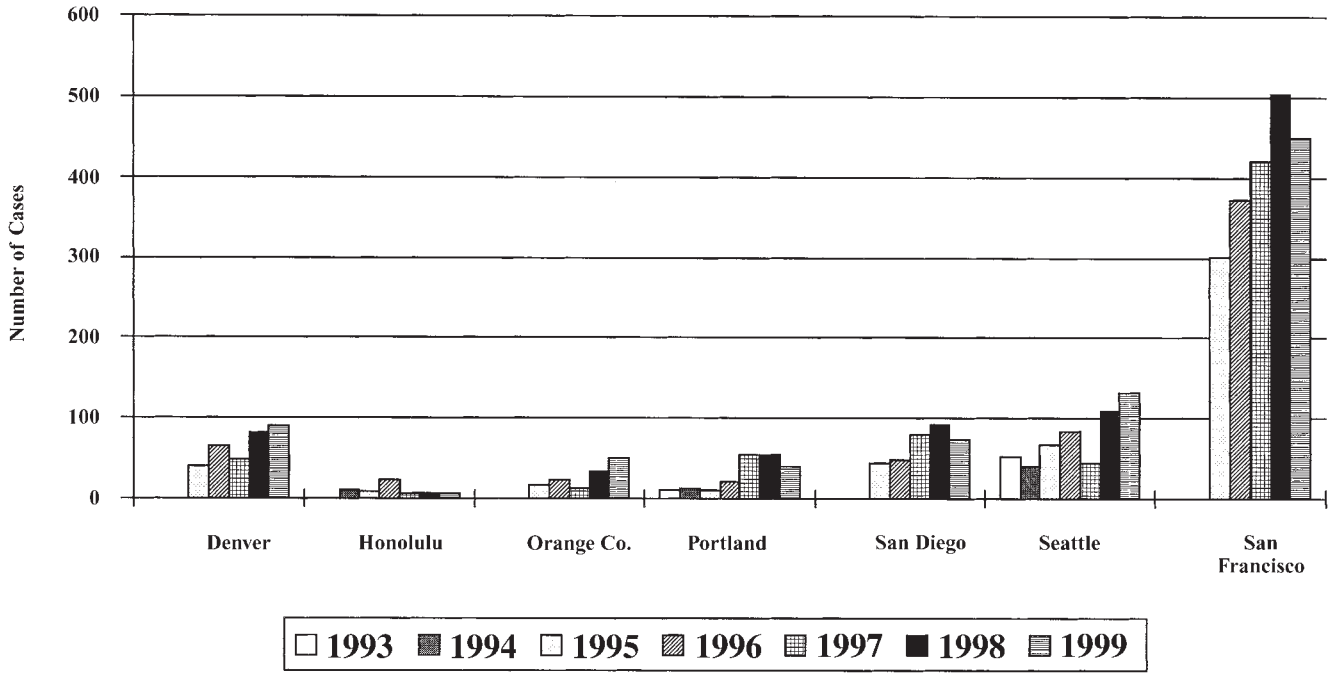

FIGURE 2—Estimated annual numbers of gonorrhea cases that occurred among men who have sex with men, from sexually transmitted disease clinics in selected cities from 1993 to 1999.

TABLE 1—Comparison of Gonococcal Urethritis Cases Among Heterosexual Men and Men Who Have Sex With Men (MSM): 1992–1999

Characteristic	Heterosexual Men[a]	MSM[a]	*P*
No. of cases	32 034	2908	
Race/ethnicity, n (%)			
Black, non-Hispanic	25 042 (78.6)	614 (21.3)	
White, non-Hispanic	2310 (7.3)	1719 (59.5)	
Hispanic	4030 (12.7)	406 (14.1)	
Other	479 (1.5)	151 (5.2)	.001
Median age, y (range)	25 (9–82)	30 (15–66)	<.001
Symptomatic (dysuria or urethral discharge), n (%)	30 878 (96.8)	2819 (97.3)	.16
Reason for attending clinic, n (%)			
Volunteer	30 161 (94.5)	2762 (95.3)	
Contact with an individual with gonorrhea	1338 (4.2)	110 (3.8)	
Other	407 (1.3)	25 (0.9)	.09
Previous episode of gonorrhea (ever), n (%)	13 850 (46.8)	1359 (50.7)	<.001
Previous episode of gonorrhea in past 12 mo, n (%)	5120 (18.9)	439 (16.5)	.003
Isolate with erythromycin MIC ≥ 2.0 μg/mL, n (%)	359 (2.3)	233 (10.5)	<.001
Geometric mean of erythromycin MIC, μg/mL	0.25	0.52	<.001

Note. MIC = minimum inhibitory concentration.
[a]Cases with missing data are excluded from denominators.

Comparison of MSM Cases and Heterosexual Cases

Individuals in MSM cases were older than those in heterosexual cases, with median ages of 30 and 25 years, respectively ($P < .001$) (Table 1). A higher proportion of MSM than of heterosexuals were non-Hispanic Whites (59.5% vs 7.3%), and a lower proportion were non-Hispanic Blacks (21.3% vs 78.6%, $P = .001$). Similar proportions of MSM and heterosexuals were symptomatic (97.3% and 96.8%, respectively) and attended the clinic as volunteers (95.3% and 94.5%, respectively) or as contacts of known gonorrhea cases (3.8% and 4.2%, respectively). MSM were more likely than heterosexuals to have ever had gonorrhea previously (50.7% vs 46.8%, $P < .001$) but were less likely to have had gonorrhea in the past 12 months (16.5% vs 18.9%, $P = .003$). Among those who had had at least 1 episode of gonorrhea in the past 12 months, MSM and heterosexuals alike had a median of 1 episode (range = 1–10) and a mean of 1.4 episodes.

Isolates with high MICs of erythromycin (MIC ≥ 2.0 μg/mL) were far more prevalent among MSM than among heterosexuals

TABLE 2—Comparison of Characteristics of Gonococcal Urethritis Cases Among Men Who Have Sex With Men, Over 2 Time Periods

Characteristic	1992–1994 Cases[a]	1995–1999 Cases[a]	*P*
No. of cases	695	2213	
Race/ethnicity, n (%)			
Black, non-Hispanic	157 (22.7)	457 (20.8)	
White, non-Hispanic	406 (58.7)	1313 (59.7)	
Hispanic	93 (13.4)	313 (14.2)	
Other	36 (5.2)	88 (5.5)	.12
Median age, y (range)	30 (16–57)	31 (15–66)	.005
Symptomatic (dysuria or urethral discharge), n (%)	682 (98.1)	2137 (97.1)	.13
Reason for attending clinic, n (%)			
Volunteer	672 (97.1)	2090 (94.8)	
Contact with an individual with gonorrhea	17 (2.5)	93 (4.2)	
Other	3 (0.4)	22 (1.0)	.04
Previous episode of gonorrhea (ever), n (%)	336 (53.0)	1023 (50.0)	.19
Previous episode of gonorrhea in past 12 mo, n (%)	78 (12.4)	361 (17.8)	.002
Isolate with erythromycin MIC ≥ 2.0 μg/mL, n (%)	7 (2.1)	226 (12.0)	<.001
Geometric mean erythromycin MIC, μg/mL	0.41	0.55	<.001

Note. MIC = minimum inhibitory concentration.
[a]Cases with missing data are excluded from denominators.

(10.5% vs 2.3%, $P<.001$). The geometric mean MIC of erythromycin for isolates from MSM was twice that for isolates from heterosexuals (0.52 μg/mL vs 0.25 μg/mL, $P<.001$).

Comparison of MSM Cases in 1992–1994 and 1995–1999

Of the 2908 MSM cases, 695 (23.9%) occurred during the early part of the project period (1992–1994) and 2213 (76.1%) occurred during the more recent part of the project period (1995–1999). Early MSM cases were similar to recent MSM cases in race/ethnicity distribution and proportion with symptoms (Table 2). MSM in recent cases were slightly older than those in early cases (median age of 31 years vs 30 years, $P=.005$) and were more likely than those in early cases to attend the clinic as a contact of an individual with a known case of gonorrhea (4.2% vs 2.5%, $P=.04$). Similar proportions of MSM in recent and early cases reported that they had ever had gonorrhea previously (50.0% vs 53.0%), but a higher proportion of recent cases involved MSM who had had an episode of gonorrhea during the past 12 months (17.8% vs 12.4%, $P=.002$). Among MSM with at least 1 episode of gonorrhea in the past 12 months, early and recent cases did not differ in the mean (1.4) or median (1) number of episodes during that time.

Isolates with high MICs of erythromycin (MIC ≥ 2.0 μg/mL) were far more prevalent among recent MSM cases than among early MSM cases (12.0% vs 2.1%, $P<.001$). The geometric mean MIC of erythromycin for isolates from recent cases was higher than that for isolates from early cases (0.55 μg/mL vs 0.41 μg/mL, $P<.001$).

When young MSM (aged <30 years) were compared with older MSM, changes in reason for attending clinic, previous episodes of gonorrhea, and erythromycin susceptibilities were similar for the periods 1992 to 1994 and 1995 to 1999 (data not shown).

Comparison of Heterosexual Cases in 1992–1994 and 1995–1999

Heterosexual cases were similar over time in race/ethnicity distribution, proportion with symptoms, reason for attending the clinic, history of ever having had gonorrhea, and number of episodes of gonorrhea in the past year. Individuals in recent heterosexual cases were slightly older than those in early cases (median age of 26 years vs 24 years, $P<.001$). In contrast to the trends seen with MSM cases, a smaller proportion of recent than of early heterosexual cases involved individuals who had had an episode of gonorrhea during the past 12 months (18.0% vs 20.2%, $P<.001$), and the geometric mean MIC of erythromycin for isolates from recent cases was lower than that from early cases (0.25 μg/mL vs 0.27 μg/mL, $P<.001$). The proportion of heterosexual cases with high MICs of erythromycin did not change over time.

Discussion

National gonorrhea rates began to decline during the 1970s and continued to do so through 1997.[12] During the 1990s, however, increases in rates of gonorrhea and other STDs among MSM were documented in 2 US cities.[6–8] Our data demonstrate that increases in gonorrhea among MSM have occurred across a broad geographic area, including many cities on the West Coast. Most MSM affected are White, and they tend to be older than heterosexual gonorrhea patients. Additionally, MSM with gonorrhea are increasingly likely to acquire repeat gonococcal infections and to be infected with strains having high MICs of erythromycin.

These findings highlight the additional knowledge that may be gained from a surveillance system designed for a separate purpose. GISP was established to monitor antimicrobial resistance in *N gonorrhoeae*, but as a long-standing, systematic sample of gonococcal isolates from men through which demographic and clinical data are also collected, GISP provides a unique opportunity to examine epidemiologic trends in gonorrhea as well.

These data have several limitations. First, GISP is a surveillance system and so relies on data gathered during routine public health activities; not all clinics collected information on sexual orientation, and the manner of collecting these data was subject to local variation. In particular, MSM of color may be less likely than White MSM to self-identify as gay or bisexual and so may be underrepresented in our data.[13] However, if biases in reporting of sexual orientation were consistent over time, the overall trends are most likely valid. Second, GISP collects a systematic sample of urethral gonorrhea cases from each site, with the number of cases sampled per month constant over time. This sampling method allows measurement of percentages of urethral cases that involved MSM but does not allow direct measurement of the total number of MSM gonorrhea cases.

When calculations to derive estimates for these totals are made, underestimation of MSM cases may occur: GISP percentages are derived from urethral cases, whereas the total number of cases per month includes rectal and pharyngeal cases, which occur more frequently in MSM. Nonetheless, for the clinics and time periods for which estimates were possible, proportional increases in MSM cases reflected increases in estimated case numbers. In addition, local investigations in 1997 determined that absolute increases in MSM gonorrhea cases had occurred in several GISP clinics.[14] Finally, GISP clinics are a convenience sample of STD clinics in the United States, chosen to enhance the likelihood of detecting antimicrobial-resistant organisms. These locations may not reflect trends among MSM in other geographic areas or among MSM who seek care in other clinical settings. Changes in health care–seeking behaviors among MSM could affect trends measured in GISP. Changes in the participating clinics before 1992 led us to limit analysis to the years 1992 through 1999. Of note, the overall proportion of cases that were from MSM was relatively stable—ranging from 3.9% to 4.6%—before 1992 (CDC, unpublished data, 2000).

MSM were more likely than heterosexuals, and increasingly likely over time, to have isolates with high (≥2.0 μg/mL) MICs of erythromycin. Such isolates frequently carry alterations in the *mtr* locus, which encodes an efflux pump enhancing the organism's ability to resist a variety of hydrophobic molecules, including some antibiotics and the fecal lipids and bile salts present in the rectum.[15,16] Such alterations give these gonococci a survival advantage in the rectum. The increase in urethral isolates with high erythromycin MICs among MSM is therefore consistent with reports of increases in rectal gonorrhea and unprotected anal intercourse. These isolates may have a survival advantage among MSM, and their increasing prevalence may be contributing to the spread of gonorrhea among MSM.

Increases in gonococcal urethritis among MSM occurred in the context of declining overall gonorrhea rates until 1998; in that year, gonorrhea rates increased by more than 10% in 21 states, including 2 (Illinois and Oregon) with notable increases in gonorrhea among MSM in our project.[17] The overall gonorrhea rate increased by an additional 1.2% in 1999.[18] Increases in gonorrhea among MSM may have contributed to overall increases in reported gonorrhea in some states; however, increases among women also occurred, and several states reported changes in screening and reporting practices that could have increased reported numbers of cases.[17] The increasing percentages of urethral gonorrhea cases involving MSM was most striking in the West. This may have 2 explanations. First, there may be a relatively greater persistence of heterosexual transmission of gonorrhea in other geographic areas. Second, absolute increases in the number of cases of gonorrhea among MSM were documented in several West Coast cities.[14]

The MSM with gonorrhea in this project were older and more often White than the heterosexuals with gonorrhea, and these characteristics did not change over time. In particular, gonorrhea occurred as often among MSM older than 30 years as among those in their teens and 20s. Several studies have identified high prevalences of risk behaviors among young MSM.[19–21] However, our data are consistent with the findings, reported in a study of a recent outbreak of syphilis among older MSM in Seattle, that risky practices are not limited to young MSM.[6]

Gonococcal urethritis has a short incubation period and is usually symptomatic in men, making it useful as an indicator of recent unsafe sexual behaviors. The increases in gonococcal infection among MSM documented here suggest increasing rates of unsafe sexual behavior. Indeed, local investigations of the increases in gonorrhea among MSM in Portland, San Francisco, and Seattle in 1997 found that many cases were linked to attendance at selected nightclubs and bathhouses and to sexual activity with anonymous partners.[14] Other recent studies have found increases in recruitment of anonymous partners[22] and increases in unprotected anal intercourse.[8,23]

Possible explanations for increases in risky sexual behaviors among MSM have been recently outlined.[6] Fatigue with safe sex messages and practice may lead to relapses in behaviors,[22] while optimism about new therapies may reduce fear of acquiring and transmitting HIV infection.[24,25] Risky sexual behaviors may directly increase the potential for infection with HIV and *N gonorrhoeae*. Additionally, prospective epidemiologic studies showing that gonorrhea in women[26] and men[27] is temporally associated with increased risk of acquiring HIV infection, and virologic studies showing that gonococcal urethritis is associated with increased urethral shedding of cell-associated HIV DNA in urethral secretions and with increased concentrations of HIV RNA in semen,[28] strongly suggest that gonorrhea facilitates HIV transmission. Efforts to identify appropriate and effective interventions to promote safe sex and reduce STDs among MSM are critical as the HIV epidemic continues. □

Contributors

K.K. Fox drafted the manuscript, and all authors contributed to manuscript revision. All authors contributed to the analysis and interpretation of the data.

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The GISP is a surveillance activity and has been determined not to require human subjects review by the associate director for science of the National Center for HIV, STD, and TB Prevention.

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