CONCISE COMMUNICATION

Characterization of Sexually Transmitted Disease Clinic Patients with Recent Human Immunodeficiency Virus Infection

Sandra K. Schwarcz,[1] Timothy A. Kellogg,[1] Willi McFarland,[1] Brian Louie,[1] Jeffrey Klausner,[1] David G. Withum,[2] and Mitchell H. Katz[1]

[1]San Francisco Department of Public Health, San Francisco, California; [2]Division of HIV/AIDS Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia

The serologic testing algorithm for recent human immunodeficiency virus (HIV) seroconversion (STARHS) distinguishes between recent acquisition of HIV infection (seroconversion, on average, in the past 129 days) or long-standing infection. STARHS was offered to sexually transmitted disease clinic patients to estimate HIV incidence and determine correlates of recent infection from October 1998 through December 1999. Of the 5227 patients tested, 116 (2.1%) were HIV infected, and 28 had recent infections. The incidence was highest among homosexual men (5.3%/year; 95% confidence interval [CI], 2.6%–10.0%), those who had HIV-infected partners (8.6%/year; 95% CI, 2.9%–21.1%), and those who had gonorrhea (6.7%/year; 95% CI, 1.5%–20.3%). Among homosexual men, African American (odds ratio [OR], 3.61; 95% CI, 1.13–11.55) or Latino (OR, 3.08; 95% CI, 1.11–8.55) race/ethnicity, and having unprotected anal intercourse (OR, 2.98; 95% CL, 1.20–7.45) or gonorrhea (OR, 3.03 95% CI, 1.07–8.63) predicted the predominance of a recent seroconversion. HIV infections in San Francisco may be shifting from white men who have sex with men to men of color who have sex with men.

A recent report by the Institute of Medicine [1] calls for increased efforts to identify and characterize persons with new human immunodeficiency virus (HIV) infections as a method of evaluating the effectiveness of prevention efforts. Sexually transmitted disease (STD) clinics are sites where persons with recent HIV infection are particularly likely to be seen. Such persons can be identified using the serologic testing algorithm for recent HIV seroconversion (STARHS), a newly developed testing strategy that distinguishes persons with recent infections (seroconversion, on average, in the past 129 days) from those with long-standing infections [2]. We prospectively offered STARHS to patients who received voluntary HIV testing at the municipal STD clinic from October 1998 through December 1999 to determine HIV incidence and the demographic, HIV risk, and STD diagnostic correlates of recent HIV infections among STD clinic patients.

Subjects and Methods

Subjects. Subjects were clients at the only municipal STD clinic in San Francisco which offers free and low-cost medical examinations and treatment for STDs. Patients seeking care for a new or suspected STD routinely undergo a physical examination and testing for *Neisseria gonorrhoeae, Chlamydia trachomatis,* syphilis, and other STDs, as indicated by symptoms or clinical protocol. Patients who are at risk for HIV infection are routinely offered HIV counseling and testing. Clients who consent to HIV testing are asked to complete a standardized demographic and risk-assessment questionnaire. During the study period, patients who agreed to HIV testing were also asked to consent to participate in a study using STARHS. Patients provided verbal informed consent for STARHS testing in the event that the standard HIV test (EIA, followed by confirmation with an immunofluorescent antibody [IFA] test) was positive. HIV and STARHS test results were provided during a face-to-face counseling session 1 week after specimen collection.

Laboratory methods. Serum samples were tested for HIV antibodies by use of EIA (Organon Teknika), and positive specimens were confirmed by use of IFA (Waldheim Neufield). HIV-positive specimens were tested using an HIV-1 antibody EIA (3A11-LS) in which the sample dilution, as well as sample and conjugate incubation times, were modified from the conventional method (HIV-1 EIA [3A11]; Abbott Laboratories) to render the test less sensitive [2]. Specimens with a calculated standard optical density (OD) (sample OD − negative control OD/positive control OD) <1.500 were retested in triplicate. Retested specimens that had a mean

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Informed consent was obtained from participants, and the human experimentation guidelines of the US Department of Health and Human Services and the University of California, San Francisco, were followed in conducting this research.

Study protocols were approved by the institutional review boards of the University of California, San Francisco, and the Centers for Disease Control and Prevention.

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Reprints and correspondence: Dr. Sandra Schwarcz, AIDS Office, San Francisco Department of Public Health, 25 Van Ness, Ste. 500 San Francisco, CA 94102 (sandy.schwarcz@sfdph.org).

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Table 1. Characteristics of persons with recent human immunodeficiency virus (HIV) infection and HIV incidence among sexually transmitted disease (STD) clinic patients, San Francisco, October 1998–December 1999.

Characteristic	No. (%) of subjects			HIV incidence, %/year (95% CI)
	Recent HIV positive	Long-standing HIV positive	HIV negative	
All patients	28	83	5116	1.5 (0.8–2.8)
Sex				
Male	27 (96.4)[a]	76 (92.7)[a]	3769 (74.0)	2.0 (1.0–3.7)
Female	0	4 (4.9)	1302 (25.6)	0 (0.0–1.0)
Transgender	1 (3.6)	2 (2.4)	21 (0.4)	12.9 (0.1–98.0)
Unknown	0	1 (1.2)	24 (0.5)	0 (0.0–61.7)
Race/ethnicity				
White	13 (46.4)	28 (33.7)[a]	2599 (50.8)	1.4 (0.6–3.1)
African American	8 (28.6)	23 (27.7)	838 (16.4)	2.7 (0.9–6.8)
Latino	6 (21.4)	21 (25.3)	983 (19.2)	1.7 (0.5–4.9)
Asian/other	0(	4 (4.8)	424 (8.3)	0 (0.0–10.1)
Unknown	1 (3.6)	7 (8.4)	272 (5.3)	1.0 (0.0–7.9)
Age group, years				
<25	3 (10.7)	11 (13.2)[a]	1509 (29.5)	0.56 (<0.01–2.2)
25–35	10 (35.7)	46 (55.4)	2227 (43.5)	1.27 (0.5–3.0)
⩾36	15 (53.6)[a]	25 (30.1)	1359 (26.6)	3.12 (1.3–6.5)
Unknown	0 (0.0)	1 (1.2)	49 (0.96)	0 (0.0–3.5)
Risk behaviors (in the past 12 months)[b]				
MSM	23 (82.1)[a]	64 (77.1)[a]	1208 (23.6)	5.3 (2.6–10.0)
Injection drug use	8 (28.6)	25 (30.1)[a]	1060 (20.7)	2.1 (0.7–5.4)
HIV-positive partner	9 (32.1)[a]	17 (20.5)[a]	286 (5.6)	8.6 (2.9–21.1)
Injection drug–using sex partner	4 (14.3)[a]	5 (6.0)	196 (3.8)	5.7 (1.0–19.1)
⩾10 sex partners	12 (44.4)[a]	24 (30.4)[a]	774 (15.5)	4.3 (1.7–9.6)
Unprotected anal sex, insertive/receptive	16 (57.1)[a]	42 (50.6)[a]	845 (16.5)	5.3 (2.3–10.8)
Unprotected oral sex	23 (82.1)[a]	57 (68.7)	3137 (61.3)	2.1 (1.0–3.9)
Unprotected vaginal sex	4 (14.3)[a]	17 (20.5)[a]	2978 (58.2)	0.4 (0.1–1.3)
STD diagnosis[b]				
Gonorrhea	5 (17.9)[a]	17 (20.5)[a]	207 (4.1)	6.7 (1.5–20.3)
Chlamydia	1 (3.6)	6 (7.2)	294 (5.8)	1.0 (0.1–7.3)
Nongonococcal urethritis	2 (7.1)	2 (2.4)	165 (3.2)	3.4 (0.2–16.4)

NOTE. CI, confidence interval; MSM, men who have sex with men.
[a] χ^2 test, $P < .05$.
[b] Categories are not mutually exclusive.

standard OD <0.750 were defined as "nonreactive," and those that had a mean standard OD ⩾0.750 were defined as "reactive" [2]. STARHS testing was performed under the Investigational New Drug program through the Food and Drug Administration and included a quality-assurance protocol.

Persons who tested positive on the standard HIV tests and were nonreactive with the less sensitive test (3A11-LS) were presumed to have seroconverted within the past 129 days (95% confidence interval [CI], 109–149 days) and were classified as having recent infections. Persons who tested reactive on both the sensitive assay and the less sensitive assay were considered to have seroconverted sometime before the past 129 days and were classified as having long-standing infections.

N. gonorrhea and *C. trachomatis* were diagnosed using standard culture and ligase chain reaction (Abbott Laboratories LCX), respectively. A diagnosis of nongonococcal urethritis was made in men whose diagnostic tests for *N. gonorrhea* and *C. trachomatis* were negative, if microscopic examination of urethral discharge revealed ⩾5 white blood cells per high-power field or examination of urine sediment identified ⩾10 white blood cells per high-power field.

Statistical methods. The characteristics of persons with recent HIV infections were compared with those of uninfected patients, using the χ^2 test for differences in proportions. The independent predictors of recent infections were assessed using multiple logistic regression models with best-subset selection of variables. The best-subset selection finds a specified number of models with the highest likelihood score (χ^2) statistic for all possible model sizes from ⩾1 explanatory variable [3]. The variables that were eligible for inclusion in the model were age group, race/ethnicity, risk behaviors in the past year, and STD diagnosis at time of test (gonorrhea, chlamydia, and nongonococcal urethritis).

The incidence rate of HIV infection (crude incidence) was estimated by dividing the number of persons with recent infections by the total number of infected persons and persons with recent infections. HIV incidence was annualized used the following formula: crude incidence × ([365 days/129 days] × 100). Ninety-five percent CIs for estimated HIV incidence were constructed using a Bonferroni procedure that assumes a Poisson distribution, an α of 0.025 and adjusts for the variability around the ~129-day interval [2]. The lower and upper confidence limits were adjusted using the following formulas: for the lower limit, estimated HIV incidence × (365 days/154 days); for the upper limit, estimated HIV incidence × (365 days/108 days) [2]. All statistical tests were conducted using SAS software (SAS Institute) [3].

Results

A total of 5391 STD patients were confidentially tested for HIV at the municipal STD clinic from 1 October 1998 through

31 December 1999. Eighty-nine percent of those tested did not report a prior test during the study period and represent distinct individuals. There were 246 patients who had a prior HIV test during the study period, none of whom reported a prior positive HIV test. The demographic characteristics of the patients who were tested >1 time during the study period did not differ from those of patients who were only tested once ($P > .05$, data not shown).

Of the 5391 patients tested, 116 (2.1%) were HIV infected. Ninety-seven percent ($n = 5227$) of all testers and 96% ($n = 111$) of the 116 HIV infected patients had consented to STARHS at the time of the pretest counseling. Patients who refused STARHS were more likely not to report demographic and risk information than those who accepted STARHS testing ($P < .001$). However, among patients who did report demographic and risk information, race/ethnicity, age, and risk-group of patients who refused STARHS did not significantly differ from those of patients who consented to STARHS. Of the 111 HIV-infected patients who were tested with STARHS, 28 (25%) had recent infections, and 83 (75%) had long-standing infections. Patients who declined STARHS testing were excluded from further analysis.

Table 1 displays the characteristics of patients with recent and patients with long-standing infection and annualized HIV incidence estimates by demographic characteristics, risk behavior, and STD diagnosis. Of particular note, none of the 1302 female patients had been recently infected with HIV. There were 22 transgender patients, of whom 20 were male–to-female; for the other 2, no further description regarding their transgender status was available. One (male-to-female) of 22 transgender persons had been recently infected. The remaining recent infections (27 of 28) were in men, with 23 in men who had sex with a man (MSM) in the past 12 months. The incidence among men overall was 2%/year. African Americans had the highest incidence rate (2.7%/year), followed by Latinos (1.7%/year) and white subjects (1.4%/year); the differences in these incidence estimates were not statistically significant ($P = .15$ for African American vs. white subjects; $P = .69$ for Latinos vs. white subjects). No recent infections were found in Asians, Native Americans, or patients of other race/ethnicity. HIV incidence was highest among patients aged ⩾36 years (3.1%/year). Incidence was high among MSM patients (5.3%/year), patients who had had sex with partner who was HIV infected (8.6%/year) or who was an injection drug user (5.7%/year), and patients who had had, in the past 12 months, sex with ⩾10 partners (4.3%/year) and unprotected anal intercourse (5.3%/year). Incidence was also high among patients with gonorrhea (6.7%/year) and nongonococcal urethritis (3.4%/year).

Patients with long-standing infections were similar to those with recent infections; 93% were male, 34% were white, and 77% reported male homosexual activity in the past 12 months. In contrast to patients with recent infections, those with long-standing infections were older (table 1).

The independent predictors of recent infection were assessed only among MSM, because 85% of recent infections in men occurred in this group (table 2). In the multivariate analysis, age >35 years, African American race, Latino ethnicity, unprotected anal intercourse in the past 12 months, and a diagnosis of gonorrhea were independently associated with recent seroconversion.

Discussion

We found that 2% of patients who voluntarily underwent testing for HIV at the STD clinic in San Francisco were HIV infected, and 25% of the HIV-infected patients, on average, had seroconverted in the previous 129 days. Thus, the STD clinic is a setting in which newly infected persons can be identified and characterized. Consistent with other local studies [4–6], the majority of new HIV infections occurred in MSM.

In our study, African American and Latino subjects had a higher incidence estimate than white subjects, but the incidences were not statistically different in the bivariate analyses. However, in multivariate analysis, we found that African American and Latino MSM had a higher risk of recent infection than did white MSM. Previous local incidence studies have produced inconsistent results. African Americans had the lowest HIV incidence (1.1%/year) and Latinos the highest incidence (3.1%/year) in one study in which STARHS was used to identify recent HIV infections among MSM who voluntarily underwent testing at the anonymous test sites in San Francisco from 1996 through 1998 [4]. In a second study, in which STARHS was applied to stored specimens collected in a blinded manner from patients attending the STD clinic from 1989 through 1998, the pooled incidence was lower among African Americans (0.88%/year) than among whites (2.5%/year) or Latinos (1.1%/year) [6]. In a record-based study of patients who were tested more than once at the local county hospital from 1993 through mid-1999, Latinos had a somewhat higher incidence (1.2/100 person-years) than African Americans (1.0/100 person-years) and a lower incidence than whites (2.2/100 person-years) [7].

These apparent discrepancies may result from differences in the populations sampled. It is also possible that San Francisco may be in the early stages of a shift in the epidemic from white MSM to African American and Latino MSM. This would be consistent with national trends [8].

Table 2. Independent predictors of acquisition of recent human immunodeficiency virus (HIV) infection among men who have sex with men who received voluntary HIV testing at the San Francisco sexually transmitted disease clinic, October 1998–December 1999.

Characteristic	Adjusted odds ratio (95% confidence interval)
Age ⩾36 years	2.50 (1.05–5.97)
African American	3.61 (1.13–11.55)
Latino	3.08 (1.11–8.55)
Unprotected anal sex <12 months	2.98 (1.20–7.45)
Gonorrhea	3.03 (1.07–8.63)

HIV incidence was high among patients with concomitant gonorrhea and nongonococcal urethritis. Studies elsewhere have found increased HIV risk among individuals with suppurative urethritis [9–11]. In the multivariate analysis among MSM, gonorrhea tripled the risk associated with recent seroconversion. This highlights the need to expand services for diagnoses and treatment of STDs among MSM.

Our study has several limitations. Patients attending the STD clinic are at high risk for STDs, including HIV. Thus our findings may not be representative of the wider populations at risk. However, it is the higher risk among STD clinic patients that results in this population serving as a sentinel population for emerging trends in the wider community. Rather than measure the current rate of HIV transmission in the community, STD clinic patients serve as a herald of what may come. In addition, the HIV/AIDS epidemic in San Francisco differs from the epidemic in other parts of the United States, where groups other than MSM account for a substantial proportion of the persons with AIDS and HIV infection [12]. Although all the STD clinic patients at risk for HIV infection are advised to undergo HIV testing and most accept, there are some who decline testing and are not included in our findings. There are limitations associated with STARHS, as well. STARHS may be falsely negative in persons receiving highly active antiretroviral therapy, in 2% of persons with AIDS, and 0.4% of persons with long-standing infection [2]. These factors are unlikely to significantly affect our results, because HIV testing was voluntary and offered only to persons not known to be infected who would be unlikely to have AIDS or to be receiving antiretroviral therapy. STARHS was originally validated on clade B HIV subtypes [2]. This is unlikely to affect our findings, because evaluation of subtype distributions has demonstrated that >96% of HIV infections in North America are with clade B [13].

Despite these limitations, our study provides useful information on persons with recently acquired HIV infection and illustrates the feasibility of tracking the leading edge of the HIV epidemic through the use of STARHS. Although our study demonstrates the utility of STARHS as an epidemiologic tool, there may be additional benefits to the patient and to public health in general. For example, partner notification may be more effective when targeted to persons with recent HIV infection. Although this has not been proven to be true in San Francisco [14], other jurisdictions may find that STARHS assists in effective partner notification. Our study also underlines the importance of developing new methods of HIV prevention for MSM, especially those of color. Despite >15 years of targeting HIV prevention messages to MSM, the incidence of HIV infection remains high in this group, and the risk factors for transmission remain unchanged. Also, the highest incidence in our study was found among older MSM, a group that is likely to have been exposed to past prevention messages. Data on HIV incidence, risk behavior, and trends in other STDs indicate that a resurgence of HIV infection among MSM in San Francisco began in 1997 [6, 15]. HIV prevention efforts must be modified to address the current issues that place MSM at risk for HIV infection including a decrease in concern about acquisition of HIV infection among MSM due to the availability of highly effective antiretroviral treatment [16]. HIV prevention efforts must include messages that are relevant for MSM of color as well as white MSM.

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