

Heterosexual transmission of HIV-1 associated with the use of smokable freebase cocaine (crack)

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A study of risk factors for HIV-1 infection was conducted at a sexually transmitted disease clinic in an area of New York City where the cumulative incidence of AIDS in adults through mid-1990 was 9.1 per 1000 of the population and where the use of illicit drugs, including smokable freebase cocaine (crack), is common. The overall seroprevalence among volunteers was 12% (369 out of 3084), with 80% of those who were seropositive reporting risk behavior associated with HIV-1 infection, including male-to-male sexual contact, intravenous drug use and heterosexual contact with an intravenous drug user. The seroprevalence in individuals denying these risks was 3.6% (50 out of 1389) and 4.2% (22 out of 522) in men and women, respectively. Among these individuals, the behaviors significantly associated with infection were use of crack and prostitution in women, and history of syphilis and crack use in men. These results suggest that in areas where the level of HIV-1 infection in heterosexual intravenous drug users is high and the use of crack is common, increased sexual activity (including the exchange of drugs or money for sex) may result in increased heterosexual transmission of HIV-1.

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Introduction

In February 1991, New York City reported 31 845 adult cases of AIDS. This represented 19% of all cases reported in the USA (New York City Department of Health, AIDS Surveillance Report, March 27 1991). The steady increase in the proportion of AIDS cases in heterosexual intravenous drug users (IVDU) in New York City from 18 to 46% of all cases reported in 1982 and 1990, respectively, together with an estimated seroprevalence of 50-60% among IVDU [1,2] provides evidence of a large reservoir of HIV-1-infected heterosexuals in the city. Thus far, New York City AIDS cases attributed to heterosexual transmission (excluding those from countries where heterosexual transmission predominates [3]) have been largely confined to the female partners of male IVDU. While 25% (1113 out of 4519) of AIDS cases in women are at-

tributed to heterosexual transmission, <1% (eight out of 26 573) of the cases in men have been assigned to this transmission category. However, AIDS case surveillance data may not provide an accurate picture of current HIV-1-transmission patterns because of the long and variable incubation period of the disease [4,5]. Seroprevalence studies, conducted in high-risk populations, provide additional information of HIV-1-associated risk factors among individuals who are infected (seropositive) but who have not yet developed the disease.

Although the overall proportion of heterosexually acquired AIDS cases in the USA has shown only a small increase [6], changes in the epidemiology of sexually transmitted diseases in some US cities, with large numbers of AIDS cases, suggest that the potential for increased heterosexual transmission of HIV-1 exists. For

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example, the recent dramatic increase in the incidence of syphilis in some such cities has been linked to greater sexual activity (primarily prostitution) associated with illicit drug use among heterosexuals [7-10]. The epidemic of smokable freebase cocaine (crack) has closely paralleled the syphilis epidemic in New York City [11,12]. Crack first appeared on the streets of New York City in late 1985, and its abuse quickly became widespread because of its low cost, ready availability, and high addictive potential [13-17].

In view of these changing patterns of behavior, monitoring HIV-1 seroprevalence among heterosexual adults reporting multiple sexual partners in areas of New York City where HIV-1 infection in heterosexual IVDU is common is an important adjunct to AIDS case surveillance. We present an analysis of risk factors associated with HIV-1 infection in patients at a sexually transmitted disease (STD) clinic in a high-risk area and specifically examine the association between crack use and HIV infection.

Methods

Study population

The New York City Department of Health operates 12 clinics for the treatment of STD; these clinics provide services to about 140 000 individuals annually. This investigation was conducted at a clinic located in the Bronx, and includes data collected from 1 February 1988 through 31 December 1990. Study participants were selected from individuals being evaluated for treatment of a STD. At the time of clinic registration, patients were given written information sheets that briefly described the AIDS epidemic and the nature of participation in the study. Those who were willing to participate signed an informed consent for interview and HIV-antibody testing. All participants were given return appointments for test results and received pre- and post-test counseling.

All participants in this non-blinded study were interviewed by trained study personnel who administered a structured questionnaire in English or Spanish, as appropriate. In addition to collecting demographic and socioeconomic data, interviewers enquired about male homosexual contact, including age at first contact and number of male partners since 1978; intravenous drug use (including dates of first and last use and needle-sharing behavior) and crack use since 1978 (yes or no); history of transfusion with blood or blood products and history of occupational exposure to blood. Other questions regarding sexual activity included history of STD since 1978, number of sexual partners in four periods (last 3 months, last year, last 3 years, and

since 1978), AIDS-associated risk behavior of sexual partners (intravenous drug use or male-to-male sexual contact), and specific sexual behaviors such as rectal intercourse, prostitution, and condom use during the past year and during a typical year. The questions about risk behavior concentrated on the period from 1978 to study enrollment. Basic medical information, including medical diagnoses made during the clinic visit and pertinent laboratory test results, were obtained from the clinic records. Because of the sensitive nature of questions related to AIDS risk behavior, the questionnaire was designed to repeat certain questions; for example, male homosexual behavior was addressed in five different questions. All participants were again questioned about risk factors for AIDS when they returned for their test results. None of the information collected in this study became part of the patient's clinic record.

Information collected during the structured interviewing was used to determine HIV-1 seroprevalence by hierarchical transmission categories as defined by the Centers for Disease Control [18,19]. Study participants were assigned to transmission categories by the investigators according to behavior reported by the participants. For example, a man was put in the homosexual/bisexual category if he reported even one sexual contact with another man since 1978.

This study was approved by the Institutional Review Board of the New York City Department of Health.

Laboratory methods

HIV-1 antibodies were detected by an HIV-1 enzyme-linked immunosorbent assay (ELISA, Du Pont, Wilmington, Delaware, USA), followed by Western blot analysis of all reactive samples using reagents prepared by the Laboratory of Retrovirology and Immunobiology of the New York City Department of Health. Syphilis serologies were performed using the rapid plasma reagin card test (RPR; Hynson, Westcott and Dunning, Baltimore, Maryland, USA) and the microhemagglutination assay for *Treponema pallidum* (MHA-TP; Fujirebio Inc., Tokyo, Japan; Ames Division, Miles Laboratories, Elkhart, Indiana, USA). Syphilis was diagnosed by the clinic medical staff on the basis of laboratory data and clinical presentation.

Statistical analysis

A precoded questionnaire was used for data collection. Data were analyzed by using the SAS computer software system version 5.08 (SAS Institute, Inc. 1982). The 95% confidence intervals (CI) were set using the binomial probability distribution [20]. In the bivariate analyses, the strength of association between individual categorical variables or continuous variables grouped categorically and seropositivity was evaluated by the odds ratio (OR). Statistical association between HIV seropositivity and categorical variables was tested by the χ^2 test or Fisher's exact test (two-tailed); as-

sociations with continuous variables were analyzed by the t-test (two-tailed) or Wilcoxon's rank-sum test. The SAS LOGIST procedure was used to fit the multiple logistic regression model [21] to the single binary outcome variable (HIV-1 serologic status, positive or negative).

Results

During the study period, 3084 of the 33 997 (9%) patients visiting the clinic agreed to participate in the study. To determine if the study participants differed demographically from the clinic population, the age and sex distributions in the two groups were compared (data on race/ethnicity are not routinely collected by clinic personnel). There were no significant differences in the proportions of men (70%) and women (30%) in the two groups. The age distributions of the study participants and all clinic attendees > 20 years of age were also similar; 20–24 years of age (both 21%), 25–29 years (24 versus 23%), 30–34 years (18 versus 19%), 35–39 years (10 versus 12%), 40–44 years (7 versus 9%), and ≥45 years (both 10%). Significantly fewer study participants were < 20 years of age, 9 versus 13% ($P < 0.001$).

The HIV-1 seroprevalence of the study participants was 12% (369 out of 3084) and was the same for both men and women. Overall, 81 and 80% of the seropositive men and women, respectively, reported behaviors or other risk factors traditionally associated with HIV-1 infection. The most common risk behaviors reported by the 260 seropositive men were intravenous drug use (33.1%), sexual contact with a man (24.6%), both of these behaviors (4%), and sexual contact with a woman at risk (15.8%), primarily an IVDU. Among the 109 seropositive women, the risk behaviors most commonly reported were intravenous drug use (37.6%) and sexual contact with a man at risk (41.3%), primarily an IVDU (Table 1).

Overall, 66% (172 out of 260) and 59% (64 out of 109) of the seropositive men and women, respectively, returned to the clinic. Thirteen men and 11 women who had denied risk behavior were later found, by reviewing medical charts or during intensive post-test counseling, to engage in risk behavior. Among the men, four had had sexual contact with other men, two had used drugs intravenously, one had received a transfusion in 1984, and four reported female intravenous drug-using sexual partners. Ten of the 11 women subsequently reported high-risk sexual partners and one was an IVDU.

Table 1. Number and percentage of HIV-1-seropositive men and women by AIDS transmission category: hierarchical classification.

Transmission category	HIV + (n)	Total	HIV + (%)	95% CI
Men				
Homosexual/bisexual	64	185	34.6	27.9–42.0
Homosexual/bisexual and IVDU	11	29	37.9	21.3–57.6
IVDU	86	177	48.6	41.1–56.2
At risk female SP	41	321	12.8	9.4–17.0
Transfusion recipient	5	30	16.7	6.3–35.5
Other*	3	39	7.7	2.0–22.0
No identified risk	50	1389	3.7	2.7–4.8
Total	260	2170	12.0	10.7–13.4
Women				
IVDU	41	86	47.7	36.9–58.7
At risk male SP	45	277	16.2	12.1–21.2
Transfusion recipient	1	27	3.7	0.1–20.9
Other*	0	2	0	0–0
No identified risk	22	522	4.2	2.7–14.2
Total	109	914	11.9	9.9–14.2
Overall seroprevalence	369	3084	12.0	10.9–13.2

IVDU, intravenous drug user; CI, confidence interval; SP, sexual partner; *individuals who have no other risks but who are residents of countries where heterosexual transmission predominates.

Approximately 70% of both the seronegative men and women returned to obtain their antibody test results. Additional interviews were conducted with seronegative study participants who enrolled in a prospective study of risk factors for seroconversion. During these interviews, 17 out of 908 men reported risk behavior that they had originally denied. One man had had sexual contact with other men, one had used drugs intravenously, and 15 had had sexual contact with a female IVDU. None of 364 women reported risk behavior during re-interview.

Demographic characteristics, sexual and non-intravenous drug using behaviors were examined in more detail for the 50 seropositive men and the 22 seropositive women who denied traditional risk behavior for HIV-1 infection. The women were significantly younger than the men (mean 25 and 35 years, respectively; $P < 0.0001$) and the seropositive men were more likely to be black (70%) than the seropositive women (46%). Syphilis (either self-reported history or current diagnosis) was common in both men (70%) and women (59%). In the 3 years before enrollment, men reported a median of eight sexual partners (range, 1–200) while women reported a median of four sexual partners (range, 1–≥999). Prostitution (defined as the exchange of money or drugs for sex on more than one occasion since 1978) was reported by 50% of the women and sexual contact with a prostitute reported by 60% of the men. Thirteen (59%) of the women were crack users and one woman was the steady sexual partner of a male crack user. Among the men,

24% reported crack use. The overall HIV-1 seroprevalence among the 201 crack users, who denied traditional HIV-associated risk behaviors, was 12% (95% CI, 8–18).

The analyses of associations between sexual and drug-use behaviors and HIV-1 infection in women without risk show that crack use, prostitution, and a self-reported history of syphilis were all significantly associated with HIV-1 infection (Table 2). Women who reported both crack use and prostitution were more likely to be infected than those who reported only one.

Table 2. Bivariate analyses of the association between potential risk factors and HIV infection for 522 women who deny other risk behavior.

Risk factors*	HIV + (%) (n = 22)	HIV - (%) (n = 500)	Odds ratio	P
Crack use	13 (59)	60 (12)	10.6	<0.001
Prostitution**	11 (50)	37 (7)	12.5	<0.001
Crack-using prostitute	9 (41)	23 (5)	14.4	<0.001
History of syphilis	6 (27)	56 (11)	3.0	0.02

*Categories are not mutually exclusive; **accepted money or drugs for sex one or more times since 1978.

In the analyses of the association between potential risk factors and HIV-1 infection among men without risk, self-reported history of syphilis, crack use, and sexual contact with a crack-using prostitute were significantly associated with HIV-1 infection. There were no significant associations between HIV-1 infection and either sexual contact with other prostitutes, reporting more than 10 partners in the past year, or lack of circumcision (Table 3). Since none of the seropositive women or men reported usually or always having sex during menses or having anal intercourse, these behaviors were not included in the analyses. Consistent condom use was reported by <1% of the participants.

Table 3. Bivariate analyses of the association between potential risk factors and HIV infection for 1389 men who denied other risk behavior.

Risk factors*	HIV + (%) (n = 50)	HIV - (%) (n = 1339)	OR	P
Crack use	12 (24)	116 (9)	3.3	<0.001
Contact with prostitute using crack	13 (26)	197 (15)	2.0	0.03
Contact with other prostitute	17 (34)	395 (29)	1.2	0.50
History of syphilis	15 (30)	130 (10)	4.0	<0.001
≥10 sexual partners in last year	12 (24)	287 (21)	1.2	0.66
Circumcised	14 (28)	542 (40)	0.6	0.08

*Categories are not mutually exclusive. OR, odds ratio.

Separate multiple logistic regression models were constructed for women and men not participating in traditional risk behavior (Table 4). Among women, crack

use and prostitution were independently associated with HIV-1 infection, while history of syphilis did not retain statistical significance. Among men, self-reported history of syphilis and crack use were significantly associated with infection controlling for sexual contact with crack-using and non-using prostitutes and >10 sexual partners in the preceding year (yes or no).

Table 4. Multiple logistic regression analyses of risk factors for HIV-1 infection by sex.

Risk factors	Adjusted odds ratio	95% Confidence interval
Women		
Crack use	4.7	1.6–14.2*
Prostitution	4.6	1.5–14.3*
History of syphilis**	1.5	0.5–4.5
Men		
History of syphilis**	3.8	2.0–7.0*
Crack use	2.8	1.3–5.9*
Contact with prostitute using crack	1.7	0.8–3.8
Other prostitute contact	1.5	0.7–2.8
≥10 sexual partners in the last year	0.9	0.5–1.9

*P < 0.05; **self-reported.

Discussion

In this study, conducted at an STD clinic in the South Bronx, a seroprevalence of 3.6% among the 1389 men and 4.2% among the 522 women, who all denied risk behavior for HIV-1 infection, was found. HIV-1 infection in women was independently associated with crack use and prostitution. While in men, infection was associated with a self-reported history of syphilis and crack use. The 3.9% seroprevalence found in the current study is significantly greater ($P < 0.05$) than the 1% seroprevalence found in men and women without known risk enrolled in a similar study conducted at a different New York City STD clinic in 1987 [22]. The recent proliferation of crack use in New York City may explain these disparate findings.

Unlike intravenous drug use, which can result in direct exposure to infected blood through the sharing of drug paraphernalia, the relationship between smoking crack and HIV-1 infection is probably indirect. The most likely route of transmission is through heterosexual contact with an infected individual (most likely an IVU). An important advantage of our study design was the enrollment of a large number of individuals whose only risk for HIV-1 infection was multiple sexual partners. Crack use may be playing a role in heterosexual transmission among IVU, but since most of the IVU in our study were heavy current or former intravenous users, the relative importance of their high-risk behaviors could not be determined.

Other investigators have found that crack use is associated with having multiple sexual partners, exchanging sex for drugs or the money to buy drugs, using condoms infrequently [23–25], prevalence of a history of STD [26–27], and HIV infection [28–29]. In our study, most of the seropositive individuals who denied traditional HIV risk behavior reported multiple, anonymous sexual partners and a history of other STD. In the South Bronx in 1987, HIV-1 prevalence estimates for men and women aged between 25 and 44 years were 9.4–21.6% and 2.4–5.5%, respectively, [30] suggesting that the probability of selecting a sexual partner who is infected is high in this geographic area.

The association between crack-related sexual behavior and STD, like syphilis, which have shorter incubation periods than AIDS, has already been proposed [7,10]. In New York City, coincident with the crack epidemic, reported cases of primary and secondary syphilis have recently more than doubled, increasing from 2111 to 5042 between 1986 and 1988 [31].

The independent association between a self-reported history of syphilis and HIV-1 infection in men strengthens the hypothesis that these men were infected with HIV-1 through sexual contact. However, the absence of an association between a self-reported history of syphilis and HIV-1 infection in women without identified risk in this study suggests that syphilis is either not a true risk factor for sexual transmission of HIV-1, or only a risk factor for men. Although self-reported histories may not be accurate, similar results were obtained in an earlier study in which history of syphilis, evaluated as a risk factor, was confirmed by laboratory testing [22]. Thus, a history of syphilis, like crack use, may actually be a marker for having an HIV-1-infected sexual partner in both men and women; additional studies are needed to clarify the true nature of the relationship between the two.

The relationship between HIV-1 infection and crack use found in our study was striking. However, the number of subjects was small and it is possible that some of these individuals engaged in other undisclosed behavior that also put them at risk. Although the study participation rate was low, the study and clinic groups had a similar distribution by gender and age. The overall HIV-1 seroprevalence of the study participants was similar (12 versus 8.5%) to the seroprevalence found in a concurrent blinded study of a sequential sample of the clinic group (I.B. Weisfuse, personal communication, 1990).

During the early course of the AIDS epidemic in the USA, the transmission of HIV-1 occurred most widely in two distinctly different populations: (1) sexually active homosexual or bisexual men, and (2) IVDU (predominantly heterosexuals) who shared contaminated

injection equipment. Heterosexual transmission beyond these primary groups has been largely confined to the sexual partners of IVDU. Our study suggests, however, that the heterosexual transmission of HIV-1 is now extending to another group — people using crack, and their sexual partners. The emergence of heterosexual HIV-1-transmission in such individuals is not unexpected since their lifestyle is characterized by the exchange of drugs or money for sex with partners who may already be HIV-1-infected. Although crack use was identified in our study as a 'yes or no', an unpublished survey of our clinic patients has found that >60% of those who use crack do so on a daily basis.

The extent to which crack-related behavior will contribute to the epidemic of AIDS in heterosexuals is unknown, but will depend primarily on the acquisition patterns of sexual partners by crack users. Crack-related heterosexual transmission is likely to be limited to areas with large numbers of infected heterosexual IVDU. However, if the data obtained from crack users at a single STD clinic can be generalized to even a small proportion of crack users in New York City, there will be an increase in the heterosexual transmission of HIV-1. There is an urgent need for a comprehensive strategy to provide treatment for addiction and AIDS prevention services to IVDU or crack users.

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