HIV Infection, Genital Ulcer Disease, and Crack Cocaine Use among Patients Attending a Clinic for Sexually Transmitted Diseases

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ABSTRACT

Background. Recently there has been a rise in genital ulcer disease (GUD) in urban minority heterosexuals in the United States. The impact of these increased GUD rates on HIV transmission patterns in this population is unknown.

Methods. Sexually transmitted disease (STD) diagnoses were correlated with HIV antibody status and risk factor history in 194 patients who consented to HIV testing at an STD clinic in central Brooklyn.

Results. Of 36 HIV-positive patients, 23 (64%) denied HIV risk factors other than heterosexual contact with persons of unknown HIV status. HIV antibody was associated with GUD (odds radio [OR] = 2.72, 95% confidence interval [CI] = 1.20–6.24), multiple concurrent STDs (OR = 2.51, 95% CI = 1.08–5.81), and a history of crack cocaine use (OR = 2.98, 95% CI = inexact–9.61). Crack use was also associated with GUD (OR = 15.15, 95% CI = 3.27–inexact) and multiple simultaneous STDs (OR = 13.87, 95% CI = 4.62–inexact). In a log-linear model analysis, HIV infection was independently associated with GUD and crack use. HIV infection, genital ulcer disease, and crack cocaine use were more common in women than men.

Conclusions. The association between HIV infection and GUD seen here may be secondary to high-risk sexual behavior, which in turn may be partially attributable to crack cocaine use and drug-related prostitution. The high rate of coinfection with HIV and GUD raises a concern about the increased efficiency of sexual transmission of HIV in this population. (*Am J Public Health.* 1991;81:1576–1579)

Introduction

During the last decade divergent patterns of human immunodeficiency virus (HIV) transmission have been noted in different geographic regions. In North America, HIV transmission has occurred primarily in male homosexuals and intravenous drug users (IVDUs). Studies of heterosexual transmission in the United States have suggested a low efficiency of transmission,[1] while the rate of heterosexual transmission of HIV in Africa appears to be much higher.[2,3] Retrospective and prospective studies suggest that this difference may be related at least in part to the higher prevalence of genital ulcer disease (GUD) in Africa.[3–5] Evidence that GUD may increase the risk of acquiring HIV has also been noted in at least one sexually transmitted disease (STD) clinic population in the United States.[6]

Since 1986 the incidence of primary and secondary syphilis in the United States has been increasing, especially in urban minority heterosexuals.[7] In Brooklyn, this trend has encompassed other etiologies of GUD as well. Between 1986 and 1988, cases of primary and secondary syphilis increased 98% (from 589 to 1165), chancroid cases increased 105% (from 556 to 1140), and herpes simplex genital ulcers increased 78% (from 324 to 577).[8] In the STD clinic at Kings County Hospital in Brooklyn, the number of cases of GUD more than tripled from 1986 to 1988 and by the first half of 1989, 35% of STD clinic visits were for GUD.

The impact of this dramatic rise in GUD on HIV transmission patterns in this population remains to be seen. Because this increase has been relatively recent and the incubation period for symptomatic HIV disease is several years, any resulting shift in the risk factor categories of patients reported with AIDS will not become apparent for several years. In this retrospective study, STD clinic visit diagnoses were correlated with HIV antibody status and HIV risk factor history.

Methods

This study took place at a municipal hospital–based STD clinic serving an urban minority population. Confidential HIV counseling and testing with written informed consent have been offered to STD clinic patients since October 1988. HIV risk behavior history was obtained at the initial visit by trained interviewers using a standard questionnaire and also during the follow-up visit when test results were given to the patient. HIV antibody testing was performed by the New York City Department of Health Retrovirology Laboratory. Positive enzyme immunoassay results were confirmed by Western blot.

STD clinic records of patients who underwent HIV testing from October 1988 through February 1989 were retrospectively reviewed to determine STD diagnoses. Primary and secondary syphilis were diagnosed by darkfield examination

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or direct monoclonal immunofluorescent staining for *T. pallidum* or by serology (rapid plasmin reagin confirmed by fluorescent treponemal antibody-absorbed) with compatible physical findings. Chancroid was diagnosed by culture or characteristic gram stain morphology. Specimens cultured for *Hemophilus ducreyi* were inoculated onto Mueller-Hinton medium with 5% chocolated horse blood and gonococcal agar base with bovine hemoglobin and fetal calf serum.[9] Herpes simplex was diagnosed by viral culture (specimens inoculated into A549 and human neonatal kidney cell lines) or direct immunofluorescent staining.

Except where noted, Cornfield confidence intervals and Mantel-Haenszel χ^2 tests were used in calculations of statistical significance. Log-linear model analysis was performed using SPSS statistical software (SPSS, Chicago, Ill).

Results

During this 5-month period, 513 new patients were seen and records were available for 194 who consented to HIV testing. HIV risk factor and demographic characteristics of HIV seronegatives and seropositives are listed in Table 1. Twenty-three of 36 HIV seropositives (64%) denied risk factors other than heterosexual contact with persons of unknown HIV status.

Twenty-four (67%) of 36 HIV seropositives presented with GUD (Table 2). Conversely, 24 of 91 (26%) patients with GUD were seropositive for HIV. GUD was associated with HIV seropositivity (odds ratio [OR] = 2.72; 95% confidence interval [CI] = 1.20–6.24; $P < .01$).

Herpes simplex was the only genital ulcer pathogen in 5 (21%) of 24 HIV-positive genital ulcer patients and could conceivably have been increased in this group due to HIV-related immunosuppression. When genital ulcers due to herpes simplex were excluded from analysis, the association between HIV infection and GUD persisted (OR = 2.82; 95% CI = 1.14–7.03; $P < .02$). In six patients who presented with genital ulcers, the etiology of the ulcer was not determined. All but one of these individuals were HIV seropositive.

Two or more concurrent STDs (not including HIV) were diagnosed in 46 patients. Fourteen (30%) of 46 patients with multiple STDs were HIV seropositive compared with 22 (15%) of 148 patients with fewer than two STD diagnoses (OR = 2.51; 95% CI = 1.08–5.81; $P < .02$).

TABLE 1—HIV Seroprevalence by Demographic Characteristics and HIV Risk Factor.

Characteristic	HIV Seropositive n = 36 (%)	HIV Seronegative n = 158 (%)
Median age (years)	28	26
Sex		
Female	26 (72)	79 (50)*
Male	10 (28)	79 (50)
Race		
Black	31 (86)	137 (87)
Hispanic	5 (14)	17 (11)
White	0	4 (2)
HIV risk factor		
Intravenous drug use	9 (25)	4 (3)
Male homosexual	2 (6)	1 (1)
Heterosexual partner known to be HIV infected	2 (6)	2 (1)

*$P < .02$.

TABLE 2.—HIV Seroprevalence by Genital Ulcer Diagnosis

Diagnosis	All STD[a] patients N = 513	No. of patients (%) consenting to HIV testing n = 194	HIV antibody positive (%) n = 36
Primary and secondary syphilis	101	45 (23)	9 (25)
Herpes simplex	48	32 (16)[b]	8 (22)
Chancroid	34	26 (13)[c]	3 (8)
Genital ulcers of uncertain etiology	18	6 (3)	5 (14)
All genital ulcers[d]	183	91 (47)	24 (67)*
Nongenital ulcer diagnosis	330	103 (53)	12 (33)

[a]STD = sexually transmitted disease.
[b]Herpes simplex diagnosed by viral culture and direct immunofluorescent staining in 17, by culture alone in 11, by direct immunofluorescent staining alone in 4.
[c]Chancroid diagnosed by culture and gram stain in 14, culture alone in 4, gram stain alone in 8.
[d]In 18 patients more than one etiologic agent for genital ulcer disease was identified; as a result, number of patients with genital ulcer disease is less than number of genital ulcer diagnoses.
*Odds ratio = 2.72, $P < .01$.

A history of using crack cocaine, a freebase form of cocaine which can be smoked, was noted in 23 patients (18 women, 5 men). Twenty-one (23%) of 91 patients with GUD admitted to crack cocaine use compared with 2 (2%) of 103 patients without GUD (OR = 15.15; 95% CI = 3.27–inexact; $P < .001$). Seventeen (37%) of 46 patients with multiple concurrent STDs admitted to crack cocaine use compared with 6 (4%) of 148 patients with less than two STDs (OR = 13.87; 95% CI = 4.62–inexact; $P < .001$). Two or more etiologies of GUD were diagnosed concurrently in 9 (39%) patients admitting to crack use, compared with 9 (5%) patients without a history of crack use (OR = 11.57; 95% CI = 3.51–38.78; $P < .001$, Fisher's exact).

Six (26%) of the 23 patients with a history of crack use were seropositive for HIV (4 women, 2 men). All six patients denied usual HIV risk factors including intravenous (IV) drug use. Five of these six patients presented with genital ulcers, and the sixth with an oral ulcer. The association between HIV infection and crack use was not statistically significant unless patients with recognized risk factors for HIV (e.g., a history of IV drug use, homosexuality, or a sexual partner known to be infected with HIV) were excluded from analysis. When patients with recognized HIV risk factors were excluded, the HIV seroprevalence rates for patients with and without a history of crack use were 26% (6 of 23) and 11% (16 of 151) (OR = 2.98; 95% CI = inexact–9.61; $P < .05$, Fisher's exact). Similarly, when those with recognized HIV risk factors were excluded from analysis there were increases in the association of HIV

TABLE 3—HIV Infection, History of Crack Cocaine Use, Genital Ulcer Disease, and Multiple Concurrent STDs in STD Clinic Patients without Recognized HIV Risk Factors

HIV Serostatus	Crack Cocaine Use	No. of Patients	No. (%) with GUD	No. (%) with >1 STD
Positive	Yes	6	5 (83)	4 (67)
Positive	No	17	11 (65)	6 (35)
Negative	Yes	16	15 (94)	13 (81)
Negative	No	135	48 (36)	17 (13)
Totals		174	79 (45)	40 (23)

Note. GUD = genital ulcer disease; STD = sexually transmitted disease.

with GUD (OR = 3.68; 95% CI = 1.23–11.29; $P < .01$) and with multiple concurrent STDs (OR = 3.10; 95% CI = 1.13–8.49; $P < .02$). Log-linear model analyses were performed with the following variables: HIV infection, GUD, multiple concurrent STDs, and crack cocaine use (Table 3). Those with recognized HIV risk factors were excluded from analysis. In the model, HIV infection remained independently associated with GUD and crack cocaine use. The association between HIV infection and multiple concurrent STDs, however, depended on the association of each with crack use.

The rate of HIV infection in women was more than double that in men (25% vs 11%: OR = 2.60; 95% CI = 1.11–6.22; $P < .02$). Women were more likely than men to have GUD (OR = 2.28; 95% CI = 1.23–4.26; $P < .006$), multiple concurrent STDs (OR = 2.07; 95% CI = 0.98–4.40; $P < .04$), and history of crack use (OR = 3.48; 95% CI = 1.15–inexact; $P < .02$).

Discussion

In this inner-city, predominantly heterosexual STD clinic population the rate of HIV infection among clients tested was 19%. The majority of HIV-infected individuals denied usual risk factors for HIV such as IV drug use, homosexuality, bisexuality, or having sexual partners known to be infected with HIV. HIV infection was associated with female sex, crack cocaine use, GUD, and multiple concurrent STDs. With log-linear regression analysis, HIV infection remained independently associated with GUD and crack cocaine use.

A similar trend of increased HIV seropositivity in those presenting with GUD in New York City has been described by others.[10] In a city-wide study involving approximately 8600 STD clinic patients in 1988, 13% of those presenting with genital ulcers were seropositive for HIV compared with an 8% overall HIV seropositivity rate.[10]

The time interval to seroconversion for HIV exceeds the usual incubation period for most GUD and therefore HIV infection probably preceded the presenting genital ulcer in most of these individuals. One possibility is that immunosuppressed HIV-infected source partners are at increased risk of developing persistent or recurrent genital ulcers. If this is true, someone who acquires GUD may be more likely than someone who acquires another STD to have been exposed to an immunosuppressed partner with HIV infection. Since HIV transmissibility appears to increase with immunosuppression, such source partners may be more likely to have transmitted HIV even prior to the development of GUD. Another possibility is that genital ulcers may be a direct manifestation of HIV disease.[11] Finally, the explanation for the association between HIV infection and GUD seen in these patients may be that both are dependent covariables of sexual behavior that occurs in milieus where both HIV infection and genital ulcers are common. One such setting may be "crack houses," retail distribution points for crack cocaine where drug-related prostitution is reported to be common.

The rising incidence of syphilis in urban minority populations has been ascribed to a variety of factors, including funding cutbacks in STD control programs, increasing use of spectinomycin (which is not active against incubating syphilis) for the treatment of gonorrhea in areas where beta-lactamase–producing gonorrhea are prevalent, and the recent epidemic of crack cocaine use.[12] Crack cocaine use may be associated with high-risk behavior such as decreased selectivity in sexual partner choice and increased participation in unsafe sexual practices.[12–15] Drug-related prostitution, i.e., sex in exchange for drugs or for money to purchase drugs, may play a critical role in this association.[13,14] In one recent study the association of syphilis with cocaine use persisted after adjusting for number of sexual partners and prostitution, suggesting the possibility of an increase in unsafe sexual behavior independent of prostitution or another factor.[15] In this study, crack use was strongly associated with multiple simultaneous STDs, which may be a reflection of multiple partner sexual behavior with greater opportunity for consequent exposure to multiple STDs, including GUD and HIV.

The association of GUD with HIV infection was more pronounced in women than men. This sex-specific association might be attributable to drug-related prostitution, likely a more prevalent behavior in women than men. If female addicts engage in sexual behavior in the context of crack use more frequently than male addicts, then events that depend on such high-risk sexual behavior, such as HIV infection and genital ulcer disease, will also be more common in women.

Polydrug abuse involving both crack cocaine and IV drugs is a potentially confounding variable that might account for the association of HIV infection and crack. Arguing against this proposition is the observation that the association of HIV infection with crack use increased when patients with recognized HIV risk factors (primarily IV drug users) were excluded from analysis. Furthermore, the association of HIV with GUD and multiple concurrent STDs also increased when patients with recognized risk factors for HIV were excluded from analysis. These observations are consistent with the hypothesis that high-risk sexual behavior may have accounted for HIV infection in these heterosexuals without recognized HIV risk factors.

Since voluntary HIV testing was employed in this study, it is possible that selection bias may have influenced these results, although the magnitude and direction of such bias is difficult to ascertain. It is possible that testing was encouraged more aggressively for patients with recognized risk factors for HIV, including those with multiple heterosexual partners and multiple episodes of STDs. On the other hand, many individuals who perceived themselves at high risk, particularly IVDUs, may have been less likely to consent to testing. The net effect of these biases may have been to underrepresent

IVDUs and overrepresent those with heterosexual risk factors who did not perceive themselves at risk. Despite this limitation, these data may provide important clues to the direction of the HIV epidemic in similar urban minority populations. In New York City, the estimated number of IVDUs has remained essentially stable over the last decade, while the estimated number of non-IV drug users, especially of crack cocaine, has continued to rise.[16] If these trends continue, sexual risk behavior associated with crack use may become the dominant mode of HIV transmission in this population.

Crack use history may also have been biased due to the previously reported association between crack use and GUD.[12] It is possible that a history of crack use was more consistently elicited and recorded in the clinic charts of patients presenting with genital ulcers than those with other STDs. This bias by itself would not account for the association seen with HIV and multiple concurrent STDs because in most cases these diagnoses were based on laboratory results that became available after the patient had left the clinic.

The frequent coexistence of HIV with GUD in this population is of concern for several reasons. Genital ulcers may enhance the efficiency of HIV transmission by several mechanisms. The isolation of HIV from the genital ulcers of HIV-infected individuals[17] raises the possibility that genital ulcers may increase the infectiousness of index partners by resulting in increased shedding of HIV. In addition, susceptibility of the contact who acquires GUD from the index partner may be increased. This might occur by disruption of the genital epithelium during ulcer formation as well as by recruitment of HIV-susceptible activated immune cells to the genital tract.[18,19] Thus, the high prevalence of both HIV and GUD in this population may create conditions similar to those in Africa where heterosexual transmission of HIV appears to be common.

The rising incidence of GUD in this population suggests that current efforts to promote reduction in risk behavior are insufficient. Such risk behavior reduction will play an essential role in controlling the parallel epidemics of GUD and HIV. The future of the HIV epidemic in this country may depend largely on the effectiveness of interventions aimed at similar urban minority populations where GUD and HIV infection are on the rise. Increased efforts should focus not only on STD control and risk behavior reduction, but also on prevention and treatment of non-IV drug use associated with sexual risk behavior. □

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