Heterosexual Transmission of HIV in Haiti

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Background: Despite the importance of human immunodeficiency virus (HIV) transmission through heterosexual contact, the incidence of HIV infection in heterosexual cohorts has not been well studied, particularly in the developing world.

Objective: To 1) determine the incidence of HIV infection in discordant heterosexual couples (couples in which one partner had HIV infection and the other did not) in Haiti and 2) assess risk factors for and methods of preventing HIV infection.

Design: Prospective study.

Setting: National Institute for Laboratory Research, Port-au-Prince, Haiti.

Participants: 475 HIV-infected patients and their noninfected regular sex partners.

Measurements: Patients and their partners were evaluated at 3- to 6-month intervals for HIV infection, sexually transmitted diseases, and sexual practices. The efficacy of counseling and provision of free condoms was also evaluated.

Results: Among the 177 couples who remained sexually active during the prospective study period, 20 seroconversions to HIV positivity occurred, for an incidence rate of 5.4 per 100 person-years (95% CI, 5.16 to 5.64 per 100 person-years). Thirty-eight couples (21.5%) discontinued sexual activity during the study. Only 1 seroconversion occurred among the 42 sexually active couples (23.7% of the 177 sexually active couples) who always used condoms. In contrast, the incidence in sexually active couples who infrequently used or did not use condoms was 6.8 per 100 person-years (CI, 6.49 to 7.14 per 100 person-years).

Transmission of HIV was associated with genital ulcer disease, syphilis, and vaginal or penile discharge in the HIV-negative partner and with syphilis in the HIV-infected partner.

Conclusion: Counseling and the provision of free condoms contributed to the institution of safe sex practices or abstinence in 45% of discordant heterosexual couples. However, 55% of couples reported that they continued to have unprotected sex, resulting in an incidence of HIV infection of 6.8 per 100 person-years.

Ann Intern Med. 1996;125:324-330.

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Heterosexual intercourse is the predominant mode of human immunodeficiency virus (HIV) transmission worldwide (1, 2). In Haiti, more than 90% of patients with the acquired immunodeficiency syndrome (AIDS) were infected with HIV by this route (3). Despite the importance of heterosexual transmission, studies done to assess the incidence of HIV infection in heterosexual cohorts, particularly in developing countries, have been limited (4–7). Most of the available data on seroconversion to HIV positivity have been obtained from high-risk groups, such as prostitutes and their clients. We did this study to determine the incidence of HIV infection in discordant couples (couples in which one partner was HIV infected and the other was not) in Haiti. All couples were given professional counseling and free condoms. Co-factors that increased the risk for HIV transmission were also sought.

Methods

Study Group

The Group Haitien d'Etude du Sarcome de Kaposi et des Infections Opportunistes (GHESKIO) at the National Institute for Laboratory Research in Port-au-Prince, Haiti, is the sole source of free testing for HIV in Haiti. From January 1988 to July 1992, 52% of the persons tested by GHESKIO (3800 of 7302) were HIV positive. Patients were referred to GHESKIO for testing by more than 40 public and private health care facilities and by private physicians; as many as one fourth were self-referred. All HIV-positive persons were informed of their HIV status by a physician. Individual counseling was given to HIV-positive persons who returned to obtain their test results (n = 2687). Patients who were HIV positive were asked to bring their regular sex partners to the clinic for HIV testing. The term "HIV positive" refers to persons who had HIV infection at baseline. Persons who were HIV posi-

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tive had positive results on enzyme-linked immunosorbent assay (ELISA) and confirmation on Western blot assay (8). More than 44% of the index patients (1201 of 2687) provided a regular sex partner for HIV testing; 49% of these partners (n = 583) were HIV-negative. Discordant couples were invited to participate in the study. Eligibility criteria were 1) the provision of informed consent by both the HIV-infected patient and the noninfected partner, 2) ambulatory status at the time of study enrollment, and 3) residence within 30 kilometers of the clinic. More than 81% of invited couples agreed to participate (n = 475).

Study Design

Counseling

All participants received counseling and free latex condoms after their initial HIV test, at the time of study enrollment, and throughout the study period. At study entry, a physician advised the HIV-infected patients about the importance of informing their seronegative partners about their HIV status. Subsequently, a session was held with both partners to emphasize the risks of unprotected sexual intercourse and to alleviate fears that HIV could be transmitted through casual contact.

Medical History and Physical Examination

Couples were evaluated every 3 months if they were sexually active and every 6 months if they were not. Sexually active women were tested for pregnancy every 3 months and if they missed menses. At each of these regular visits, a medical history was taken and a physical evaluation and laboratory tests (ELISA and rapid plasma reagin assays) were done. Genital examinations were done whenever patients reported potential symptoms or signs of a sexually transmitted disease. The HIV-infected patients were evaluated for the development of signs or symptoms of HIV infection and AIDS. We used the revised 1987 Centers for Disease Control and Prevention case definition for AIDS (9). A standardized questionnaire was administered in Creole by the same physician who counseled the HIV-infected patient and his or her partner. Pertinent questions included information on sexual activity and habits with the participating partner, sexually transmitted diseases, intravenous drug use, number of sexual partners, sexual contact with prostitutes, previous or current partners with HIV infection or AIDS, and history of blood transfusion within the previous 5 years. Condom use was stratified as "always used" (used for every sexual act during the prospective study period), "never used," and "occasionally used." Sexually transmitted diseases were identified; particular attention was paid to genital ulcerations and abnormal vaginal or urethral discharge. The cause of genital ulcers was classified as trauma, disease (caused by *Treponema pallidum*, *Haemophilus ducreyi*, or Herpes simplex virus), or unknown. An abnormal genital discharge was defined by a change in color, odor, or quantity of discharge, regardless of an association with pain or pruritus. The abnormal discharge and the presence of genital ulcers were identified by the patient and confirmed by physical examination.

At every visit, HIV-positive patients and their HIV-negative partners were asked about other sexual partners. A social worker also administered a standardized demographic questionnaire in Creole and reinforced the physician's counseling on HIV transmission and use of condoms. Social workers were essential for obtaining the cooperation of participants and for visiting the homes of patients who missed scheduled appointments. Frequency of sexual contact was defined as the number of episodes of sexual intercourse each month as reported, independently, by each partner. When the numbers of sexual contacts reported by the partners differed, the median of the reported numbers was used. After an HIV-infected patient died, his or her HIV-negative partner was evaluated annually to determine whether he or she had resumed sexual activity with another partner. No study participants received antiretroviral therapy.

Laboratory Tests

Laboratory tests done at study entry included complete blood count, rapid plasma reagin assay, and HIV serologic assay (ELISA; Abbott Diagnostic, Chicago, Illinois) with confirmation by Western blot assay (DuPont Medical Products, Wilmington, Delaware), according to the Centers for Disease Control and Prevention criteria (8). Positive results of a rapid plasma reagin serologic assay were confirmed by using fluorescent *Treponema* antibody absorption tests. Seroconversion to HIV positivity was defined as a positive result on each of two ELISA tests with confirmation by Western blot assay (8).

Statistical Analysis

The data collected on the questionnaires were entered into a dBASE file (dBASE III+, Asthon-Tate, Torrane, California, 1986) and analyzed using SAS software (version 6.04, SAS Institute, Cary, North Carolina) alone or in conjunction with Epi-Info (version 5.1, United States Distribution Inc., Stone Mountain, Georgia). Descriptive statistics were used for baseline characteristics (demographic, clinical, and laboratory data), frequency tables, follow-up time, and duration of sexual relationship with the infected partner. Chi-square statistics with the Yates correction and the Fisher exact test (used

when an expected value in one of the cells was less than 5) were used to compare proportions of different risk factors in persons who had and had not seroconverted and in men and women. Parametric and nonparametric methods were used to assess the significance of differences between persons who had and had not seroconverted in terms of total follow-up time during the study and effective duration of sexual activity. Incidence rates for seroconversion were calculated manually and expressed per 100 person-years. Unadjusted relative risk was determined as the ratio of the incidence of seroconversion among participants with a specific risk factor to the incidence of seroconversion among the participants who lacked the same risk factor. Cox proportional regression (stepwise method) was used to emphasize, if possible, the importance of specific cofactors found to be significant when unadjusted relative risks were calculated. The number of covariates used in each of the models tested was limited to 2 to 3 because of the small number of events (seroconversions).

Results

Characteristics of the Study Group

The prospective study group comprised 475 HIV-infected patients and their 475 HIV-negative regular sex partners. Sexual activity was discontinued by 298 of the 475 discordant couples (63%) within 6 months of study entry. The other 177 couples (37%) were sexually active during all or part of the prospective study period. The sexually active (n = 177) and sexually inactive (n = 298) HIV-infected patients were similar in age, sex, and level of education. Mean ages were 33 ± 8 years for sexually active patients and 35 ± 7 years for sexually inactive patients. Because the HIV epidemic in Haiti predominately affected men in its early stages, most of our HIV-infected patients were male (81%). Sixteen percent of the sexually active patients and 18% of the sexually inactive patients had had no formal education; a similar percentage in both groups reported having had either a primary (30% to 32%) or secondary (50% to 54%) level of education. Median follow-up periods were 11 months for the sexually inactive patients and 20 months for the sexually active patients. The sexually inactive patients had more advanced HIV disease and were more likely to have died during the follow-up period. Indeed, at study entry, 70% of the sexually inactive patients and only 43% of the sexually active patients had class IV AIDS (9). As a result, 83% of the sexually inactive and 49% of the sexually active patients died during the study. Death in all HIV-infected participants was a consequence of AIDS.

It is logical to think that all persons who seroconverted acquired HIV through heterosexual intercourse with their HIV-positive partners. None of the HIV-negative partners were homosexuals, bisexuals, or intravenous drug users, and none had received a blood transfusion in the previous 5 years. Eighty-two percent of HIV-negative male partners stated that they were monogamous. The men who were polygamous brought their additional female sex partners for HIV testing, and all were found to be HIV negative. All of the female HIV-negative partners were monogamous at study entry and remained faithful to their HIV-infected partners, with the exception of five women who became sexually active with other partners 3 months before their original partners died. Three of these five women brought their new male partners for HIV testing, and all of the partners were HIV negative. The two polygamous women who did not bring their partners for testing remained HIV negative.

After HIV counseling, 21% of couples (95% CI, 15% to 23%) discontinued sexual activity during the study period; 55% (CI, 47% to 62%) of them did so during the first 4 months. The percentage of couples that regularly used condoms increased from none to 24% (CI, 18% to 30%). Ultimately, 45% (CI, 37% to 52%) of the couples who had initially been sexually active adopted safe sex practices or were abstinent during the study period. The advanced stage of the HIV disease seen in the index partners was another important factor in the decision to discontinue sexual activity.

Seroincidence of HIV Infection

The incidence of HIV infection varied widely and depended on sexual activity, the presence of associated sexually transmitted diseases, and the use of condoms. The incidence in sexually active couples who used condoms irregularly or not at all was 6.8 per 100 person-years. Overall, 20 of 475 HIV-negative partners of HIV-infected patients seroconverted after a median follow-up of 27 months. The incidence was 1.6 per 100 person-years after 1267 person-years of observation (Table 1). The incidence of HIV infection was 3.0 per 100 person-years when the period after the death of the index case was excluded from the calculation.

Table 1 shows the incidence of HIV infection as a function of sexual activity, condom use, and sex of the infected partner. There were no discrepancies in partners' reports of condom use. For the couples who did not agree about the number of sexual contacts they had had (n = 4), the median of the two numbers given was used. No seroconversions and no pregnancies occurred in the 298 sexually

inactive couples. The incidence in the couples who continued sexual activity during the study period was 5.4 per 100 person-years (374 person-years of observation). The incidence of HIV infection was 1.0 per 100 person-years for persons who always used condoms and 6.8 per 100 person-years for persons who used condoms irregularly or not at all. The seroconversion rate was similar in couples who never used condoms (14.4% [13 of 90 persons]) and couples who used condoms irregularly (13.3% [6 of 45 persons]) ($P > 0.2$; relative risk, 1.08 [CI, 0.44 to 2.66]).

The risk for HIV transmission was also calculated according to the sex of the HIV-infected partner. The rate of female-to-male transmission of HIV was 7.6 per 100 person-years (5 of 34 persons); the rate of male-to-female transmission was 4.8 per 100 person-years (15 of 143 persons) ($P > 0.2$) (Table 1). When the months of sexual inactivity between partners (based on information obtained from both partners) were excluded from the analysis, the incidence rates increased two- to threefold (to 15.4 per 100 person-years for female-to-male transmission and 12.8 per 100 person-years for male-to-female transmission) ($P > 0.2$). Couples in which the HIV-infected partner had had AIDS at study entry or during follow-up had an incidence rate of seroconversion of 13.4 per 100 person-years, whereas HIV-infected partners who did not have AIDS had an incidence rate for seroconversion of 8.5 per 100 person-years ($P > 0.2$). The median number of episodes of sexual intercourse per month shared by HIV-infected index patients and their HIV-negative partners was 0.32 for those who had AIDS and 0.70 for those who did not. In addition, because the patients with AIDS had a higher mortality rate (83% compared with 49%), the at-risk period of their regular sex partners was shorter (median, 5.20 months compared with 8.83 months).

The incidence of HIV infection calculated for the duration of cohabitation was highest during the first year of the study: 5.73 per 100 person-years in the first 4 months and 6.81 per 100 person-years between 4 and 12 months (Table 2). Later incidence rates (per 100 person-years) were 2.04 in the second year, 2.46 in the third year, 0.92 in the fourth year, and 2.70 after the fourth year. This calculation excludes seronegative partners who discontinued sexual activity either because their infected sex partner died or because they decided to practice abstinence. When HIV-negative partners who used condoms during all episodes of sexual intercourse are also excluded, the incidence rates (per 100 person-years) increase to 7.59 during the first 4 months, 9.57 between 4 and 12 months, 2.82 in the second year, 3.63 in the third year, 1.40 in the fourth year, and 2.16 after the fourth year.

Table 1. Incidence of HIV Infection in Discordant Heterosexual Couples*

Variable	Patients with Seroconversions/ Patients at Risk for Seroconversion, *n/n*	Person-Years of Observation	Incidence per 100 Person-Years (95% CI)†
Entire cohort	20/475	1267	1.6 (1.53 to 1.67)
Sexual activity			
Yes	20/177	374	5.4 (5.16 to 5.64)
No	0/298	803	0
Condom use			
Yes	1/42	101	1.0 (0.80 to 1.19)
No	19/135	278	6.8 (6.53 to 7.14)
Sex of the HIV-infected patient‡			
Male	15/143	309	4.8 (4.55 to 5.04)
Female	5/34	66	7.6 (6.93 to 8.27)
Presence of AIDS in the HIV-infected patient‡			
Yes	9/85	67	13.4 (12.5 to 14.3)
No	11/92	130	8.5 (8.0 to 9.0)

* AIDS = the acquired immunodeficiency syndrome; HIV = human immunodeficiency virus.
† The seroconversion date was defined as the date halfway between the date of the last negative result on enzyme-linked immunosorbent assay (ELISA) and the date of the first positive result on ELISA. The incidence rates were calculated considering the time interval between the date of entry and the seroconversion date or the date of the last ELISA, depending on seroconversion status. In addition, when calculating the incidence for persons with AIDS compared with persons without AIDS, we considered the contribution of both stages of disease if the index patient developed AIDS during follow-up at the clinic.
‡ Index patient.

Seroconversion to HIV positivity was more common when a sexually transmitted disease was present in the seronegative sex partner than when it was present in the HIV-infected patient (Table 3). Among the HIV-negative partners, seroconversion was more likely to occur in persons with genital ulcer disease (relative risk, 6.8 [CI, 2.95 to 15.7]), positive results on a serologic test for syphilis (relative risk, 2.9 [CI, 1.36 to 6.16]), and vaginal or

Table 2. Incidence of Human Immunodeficiency Virus Infection Related to Duration of Cohabitation During the Study Period

Duration of Cohabitation	Persons Who Seroconverted/Total Persons at Risk*	Incidence Rate per 100 Person-Years (95% CI)†
mo	*n/n*	
<4	3/177	5.73 (5.23 to 6.22)
4–12	8/135	6.81 (6.55 to 7.07)
12–24	3/86	2.04 (1.93 to 2.15)
24–36	3/44	2.46 (2.31 to 2.61)
36–48	1/29	0.92 (0.85 to 0.99)
>48	2/14	2.70 (2.59 to 2.81)

* Number of persons excludes seronegative partners who discontinued sexual activity because their infected sex partner died or because they decided to practice abstinence.
† If the date of seroconversion or the date of the last negative result on enzyme-linked immunosorbent assay (ELISA) preceded the last date of sexual contact, then the date of seroconversion was defined as the date halfway between the date of the last negative result on ELISA and the date of the first positive result on ELISA. The incidence rates were calculated considering the time interval between the date of study entry and the date of seroconversion or the date of the last ELISA, depending on seroconversion status. Otherwise, the interval between the date of entry and the last date of sexual activity (as reported by both partners) was considered. We also considered the contribution of the participants who remained sexually active in the intervals after a given interval (for example, the participants who were sexually active after 4 months bring their contribution to the interval "<4").

Table 3. Prevalence of Factors Associated with Seroconversion to HIV Positivity*

Factor†	Seroconversion Status of Initially HIV-Negative Partner		
	Seroconverted (n = 19)	Seronegative (n = 116)	Relative Risk (95% CI)
	n/n (%)		
In HIV-negative regular sex partners			
Genital ulcers‡	8/17 (47)	8/116 (7)	6.82 (2.95 to 15.7)
Genital discharge	8/18 (44)	20/116 (17)	2.58 (1.34 to 4.95)
Positive results on a serologic test for syphilis	7/18 (39)	14/104 (13)	2.89 (1.36 to 6.16)
In HIV-infected index patient			
Genital ulcers	4/18 (22)	7/94 (7)	2.89 (0.97 to 9.15)
Genital discharge	1/18 (6)	6/95 (6)	0.88 (0.11 to 6.88)
Positive results on a serologic test for syphilis	7/17 (41)	17/93 (18)	2.25 (1.10 to 4.59)
In both HIV-infected index patient and his or her HIV-negative partner			
Genital ulcers	2/17 (12)	2/94 (2)	5.53 (0.83 to 36.63)
Genital discharge	0/18	1/95 (1)	
Positive results on a serologic test for syphilis	4/17 (24)	5/95 (7)	4.47 (1.33 to 14.98)

* Values are given as number of persons with the factor/number of persons with data (percentage). Denominators in different categories vary because data for some couples are missing. HIV = human immunodeficiency virus.
† Present either at study entry or during the follow-up period before seroconversion in the 135 sexually active couples who did not use condoms during every episode of sexual intercourse.
‡ Unadjusted relative risk.

urethral discharge (relative risk, 2.6 [CI, 1.34 to 4.95]). In all cases, the sexually transmitted disease was documented before seroconversion.

Human immunodeficiency virus infection was more likely to be transmitted by an HIV-infected index patient with positive results on a serologic test for syphilis (relative risk, 2.25 [CI, 1.10 to 4.59]) (Table 3). A concomitant serologic test result for syphilis in both partners further increased the risk for HIV transmission (relative risk, 4.5 [CI, 1.3 to 15.0]). Concomitant genital ulcer disease did not increase the risk for transmission beyond that seen with genital ulcer disease in the HIV-negative partner. The effect of genital ulcer disease on seroconversion in HIV-negative persons who did not use condoms was also confirmed by multivariate analysis (Cox regression, $P = 0.0001$; risk ratio, 6.55 [CI, 2.57 to 16.67]) using presence of wounds in the sex partner, presence of wounds in the index patient, and discharge in the index patient as covariates.

Our experience indicates that the occurrence of oral–genital contact between partners in discordant couples is low. We found no association between the practice of oral sex and transmission of HIV: Oral sex was practiced by 5 of 19 persons (26%) who seroconverted and by 18 of 105 persons (17%) who remained HIV negative (unadjusted relative risk, 1.54 [CI, 0.65 to 3.63]). Because couples who practiced oral sex were found to have been both active and passive during the act, it was not possible to determine whether one form of oral sex was more strongly associated with HIV transmission. Pregnancy was not identified as a risk factor. Thirty-one women were pregnant at study entry, and 11 became pregnant during the follow-up period. All of these women remained HIV negative. Other potential co-factors were not statistically significantly associated with HIV transmission and could have resulted from the small number of seroconversions seen. For instance, no association was seen between sexual contact during menses and HIV transmission: Four of the 16 women (25%) who seroconverted reported having had such contact, as did 13 of 104 persons who did not seroconvert (13%) (unadjusted relative risk, 2.00 [CI, 0.74 to 5.38]).

The duration of the period of sexual contact between couples was shorter (median, 6.4 months) in those who seroconverted than in those who remained seronegative (median, 12.6 months). On the other hand, the frequency of sexual intercourse among partners in discordant couples was higher for those who seroconverted (median, 24 episodes/mo) than for those who did not (median, 7 episodes/mo). The effect of anal intercourse could not be evaluated because only one woman who seroconverted reported that she had engaged in this practice. Similarly, the role of oral contraceptives in HIV transmission could not be determined because these contraceptives were used by only two women.

Patients with AIDS continued to be sexually active until a median of 4 months before death. Seronegative partners in both sexually active and sexually inactive couples frequently resumed sexual activity after the death of their HIV-infected partner. One year after the death of their HIV-infected partners, 49% of the HIV-negative partners from the "sexually active" group and 20% of the HIV-negative partners from the "sexually inactive" group had resumed sexual activity. Twenty-eight of 159 women (18%) who had resumed sexual activity after the death of their HIV-infected partner requested that their new sex partner be tested for HIV; 8 of 28 new partners (29%) were HIV positive.

Discussion

We examined the dynamics of HIV transmission in discordant couples who were followed prospectively while being provided condoms and counseling. The incidence of HIV seroconversion varied widely according to sexual activity, associated sexually transmitted disease, use of condoms, and duration of cohabitation after study entry. The incidence of HIV infection in the 475 discordant couples (37% of which were sexually active and 63% of which stated that they had discontinued sexual activity) was 1.6 per 100 person-years for the entire study period. This low rate is due to the absence of seroconversion in the HIV-negative partners in couples who stated that they were sexually inactive. This low rate, together with the absence of pregnancy, supports the veracity of the information obtained from this group. When the analysis was restricted to the period during which the HIV-infected partner was alive, the incidence doubled to 3.0 per 100 person-years. The rate of seroconversion in couples who were sexually active at study entry was 5.4 per 100 person-years, without correction for the subsequent death of a partner or institution of safe-sex practices. This rate is higher than those reported in 149 married discordant couples in Zaire (3.1 per 100 person-years) and in 343 HIV-negative, monogamous female sex partners of HIV-infected men in Italy (3.6 per 100 person-years) (4, 10). It is also more than twice the rate seen in 256 discordant couples (2.3 per 100 person-years) in a recent European study (8). The percentages of transmission seen during the period of observation are probably low relative to the whole population, because we specifically selected couples whose partners had not transmitted HIV before the study.

Our experience with counseling is similar to that of Kamenga and colleagues (4) and Allen and coworkers (7); in our study, counseling increased the proportion of couples that regularly used condoms from none at study entry to 24% during the study. Condom use was clearly associated with a marked reduction in the incidence of HIV infection, which was 6.8 per 100 person-years in those who did not use condoms and 1 per 100 person-years in those who always used them. Similar incidence rates were found by Saracco and associates (10). A recent collaborative European study (11) reported no seroconversions among persistent users of condoms. We found that condoms had to be used for every sexual contact to provide protection. The rate of HIV infection seen in the European study was lower than that seen in our study. This could be related to the different percentages of persistent users of condoms in their study (48%) and in our sexually active cohort (24%).

Factors other than condom use must also play a role in determining the incidence of HIV infection, because the rate of infection in our sexually active participants who did not use condoms (6.8 [CI, 6.49 to 7.14]) was higher than that in the European cohort (4.8 per 100 person-years) (11). Indeed, our study confirms that sexually transmitted diseases are co-factors for HIV transmission (12, 13). It also establishes the risk for HIV infection that is present when either or both partners have a sexually transmitted disease. Sexually transmitted diseases were more important in the transmission process when they were present in the noninfected partner than when they were present in the infected patient. A positive result on a serologic test for syphilis in either the HIV-negative or the HIV-infected partner was associated with relative risks of 2.9 and 2.25, respectively. A positive result of a test for syphilis in both partners increased the risk to 4.47. Seronegative women with abnormal vaginal discharge were three times more likely to seroconvert. However, the co-factor that carried the highest risk for seroconversion was the presence of genital ulcer disease in the HIV-negative partner (relative risk, 6.8). Concomitant genital ulcer disease in the HIV-positive partner did not further increase the risk for transmission. By multivariate analysis, genital ulcer disease was an important co-factor for the HIV-negative partner, increasing the risk for seroconversion by a factor of 6.55. Unlike other investigators, we found that seroconversion correlated with frequency of sexual intercourse (14–16).

Some studies (10, 17, 18) have found that the rate of HIV transmission is higher from men to women than it is from women to men. However, de Vincenzi (11) reported that rates of female-to-male and male-to-female HIV transmission were similar; we also found this to be true. Our results could be due to the small number of persons studied. As expected, when our data analysis excluded months without sexual activity, the incidence rates increased. However, the rates for female-to-male and male-to-female transmission were still similar. The high incidence resulting from female-to-male transmission in our study could also be related to the high prevalence of sexually transmitted diseases other than HIV infection in the HIV-negative male sex partners of infected female patients.

Other reports (11, 19, 20) document the importance of an advanced stage of HIV infection in HIV transmission. In our study, couples in which the HIV-infected partner had AIDS had a higher incidence of seroconversion than did the couples in which the index partner did not have AIDS. However, the difference (13.4 compared with 8.5 per 100 person-years) was not statistically significant ($P > 0.2$). It is common for AIDS campaigns worldwide

to neglect the counseling of patients with AIDS who are terminally ill, but these patients remain sexually active almost until death.

The decrease that we observed in the incidence of HIV infection over time may be related to the cumulative effect of repeated counseling, increasing acceptance and use of condoms, and treatment of preexisting sexually transmitted diseases.

This observation also has implications for HIV vaccine trials. Sexually active discordant couples are good vaccine candidates, but a threefold higher incidence of seroconversion in the first study year may present a problem in an evaluation of HIV vaccine, because many at-risk partners will seroconvert before completing the full vaccination schedule. Our study also indicates that the lower, but persistent, rate of infection seen after the first study year, coupled with a high retention rate, may be compensatory. Therefore, phase III vaccine trials will not require large numbers of participants.

Acknowledgments: The authors thank Kareen Thermil for data management and analysis; Jacqueline Saintil, Bichara Rivage, Hubert Abner Pierre, and Myrlande Nicolas for assistance with counseling and follow-up; and Drs. Rose Irene Verdier, Sonia Jean, and Richard Hippolite for their contributions to the care of the patients.

Grant Support: In part by grants R37 AI22624 and D43 TW00018 from the U.S. Public Health Service.

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