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HIV Transmission to Female Sexual Partners of HIV Antibody-Positive Hemophiliacs

MARGARET V. RAGNI, MD
PHALGUNI GUPTA, PhD
CHARLES R. RINALDO, PhD
LAWRENCE A. KINGSLEY, DrPH
JOEL A. SPERO, MD
JESSICA H. LEWIS, MD

Dr. Ragni is the Director of the Hemophilia Center of Western Pennsylvania and Assistant Professor of Medicine at the University of Pittsburgh School of Medicine. Dr. Gupta is Director of the Retro Virology Laboratory and Associate Professor of Infectious Diseases and Microbiology at the Graduate School of Public Health, University of Pittsburgh. Dr. Rinaldo is principal investigator of the Pittsburgh Multicenter AIDS Cohort Study (MACS) and Associate Professor of Pathology and Microbiology at the School of Medicine and the Graduate School of Public Health. Dr. Kingsley is the Epidemiologist for the MACS and Assistant Professor of Epidemiology, Department of Infectious Diseases and Microbiology at the Graduate School of Public Health. Dr. Spero is Director of the Hepatitis Reference Laboratory at Central Blood Bank and an Associate Professor of Medicine at the University of Pittsburgh. Dr. Lewis is Director of the Coagulation Laboratory at Central Blood Bank and Professor of Medicine at the University of Pittsburgh.

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Tearsheet requests to M. V. Ragni, MD, Central Blood Bank of Pittsburgh, 812 Fifth Avenue, Pittsburgh, PA 15219.

Synopsis

To study heterosexual transmission of the human immunodeficiency virus (HIV), 21 HIV antibody-positive hemophiliacs and their 21 spouses-sexual partners were evaluated. None belonged to other AIDS risk groups. HIV antibody was detected in four (19 percent) of the female partners. HIV was isolated from peripheral blood lymphocytes of one hemophiliac (4.8 percent), and one female partner (4.8) was antibody-positive. None of the couples engaged in anal intercourse. Compared with HIV antibody-negative female partners, HIV antibody-positive female partners were younger ($P < .05$), had younger hemophiliac partners ($P < .05$), and were likely (although not significantly so) to engage in oral sex ($P = .08$) and to have had more than one sexual partner in the previous 5 years ($P = .08$). Condoms were used all the time by only eight couples (40 percent), and pregnancy occurred in two other couples (9.5 percent), despite prior counseling. These data confirm the low frequency of heterosexual transmission of HIV from HIV antibody-positive hemophiliacs to their female sexual partners and suggest, moreover, that this may be due to the low rate of HIV infectivity in HIV seropositive hemophiliacs exposed to HIV. Further, these data document the need to design more effective educational programs to prevent heterosexual transmission of HIV.

HUMAN IMMUNODEFICIENCY VIRUS (HIV), the etiologic agent of the acquired immunodeficiency syndrome (AIDS), is transmitted by sexual contact, with homosexual transmission accounting for a majority and heterosexual transmission a minority (about 2 percent) of cases of AIDS. Heterosexual transmission has been shown to be bidirectional (*1*) and, correspondingly, HIV has been isolated in semen (*2*), vaginal and cervical fluids (*3*), and saliva (*4*).

Most of the persons who have acquired AIDS through heterosexual contact are the female sexual partners of intravenous (IV) drug users (*5,6*), of bisexual men (*6,7*) or, rarely, of hemophiliacs who are HIV antibody-positive (*8*). While some of these women may belong to high-risk groups through

their own lifestyles, for example, prostitution and IV drug use (*7,9*), the female sexual partners of hemophiliacs, in general, are healthy and have no other known AIDS risk factors. These observations are corroborated by the low prevalence of HIV antibody (*10–15*) and rarity of AIDS or ARC (AIDS-related complex) (*8,16*) among these women and by the rarity of AIDS (*17*) or HIV antibody (*18*) in their offspring. Thus, hemophiliacs and their female sexual partners provide an ideal group in which to study heterosexual transmission of HIV infection. In this study, HIV antibody and viral isolation assays were performed on peripheral blood samples obtained from 21 hemophiliacs and their female sexual partners, and each person was asked to complete a short questionnaire to evaluate possible risk factors of HIV transmission.

Methods

Patient population. Twenty-one HIV antibody-positive hemophiliacs cared for at the Hemophilia Center of Western Pennsylvania and their 21 long-term (more than 2 years) female sexual partners agreed to participate in the study. These 21 hemophiliacs represent 52.5 percent of the known 40 HIV antibody-positive, sexually active hemophiliacs at this center. The 21 couples were chosen for study solely on the basis of their willingness to participate. The 21 hemophiliacs included 15 with hemophilia A treated with factor VIII concentrate, 2 with hemophilia A and an inhibitor to factor VIII necessitating treatment with factor IX concentrate, and 6 with hemophilia B treated with factor IX concentrate. Three of these hemophiliacs have AIDS, 5 have ARC, and 13 are asymptomatic. Of the 21 sexual partners, 3 have unexplained, persistent lymphadenopathy in 2 or more extrainguinal areas, unaccompanied by other symptoms. The mean age of the 21 hemophiliacs was 36.2 years (range 23–60 years) and of the 21 female sexual partners, 34.1 years (range 20–54 years) (table 1).

Table 1. Demographic and clinical characteristics of study group

Variable	Hemophiliac[1]		Female partner[1]	
	Number	Percent	Number	Percent
Age (years)	36.2	...	34.1	...
Treatment:				
Factor VIII concentrate	13	61.9	...	...
Factor IX concentrate	8	38.1	...	...
HIV-related symptoms:				
AIDS	3	14.3	0	0
ARC	5	23.8	0	0
LAS	0	0	3	14.3
Asymptomatic	13	61.9	18	85.7
Intercourse:				
Vaginal	21	100	21	100
Anal	0	0	0	0
Frequency of sex (per month):[2]				
4 or more times	9	45	9	45
less than 4 times	11	55	11	55

[1] $N = 21$ unless indicated otherwise.
[2] $N = 20$
NOTE: ARC = AIDS-related complex; LAS = lymphadenopathy syndrome. Age range for hemophiliac participants, 23–60 years; for female partners, 20–54 years.

Laboratory tests. The HIV antibody was measured on plasma samples by an ELISA technique using an inactivated HTLV-III antigen from the H9/HTLV-IIIB cell line (*A*) or using inactivated whole LAV antigen grown in the CEM-F cell line (*B*). All samples with positive HIV antibody tests were subjected to Western blot confirmation, performed at Abbott Laboratories or at Genetic Systems by standard techniques (*19*).

Virus isolation studies were performed on fresh heparinized blood samples, based on detection of reverse transcriptase (RT) activity, by a modification of previously described methods (*2,20*). HIV isolation was confirmed by LAV antigen capture immunoassay (*C*)(*21*). Using these techniques in our laboratory, we have isolated HIV in 80 percent of homosexual men with AIDS and 30 to 40 percent of asymptomatic HIV antibody-positive homosexual men.

Statistics. The data were analyzed with the use of Fisher's exact test, and ages were analyzed with the use of Student's *t* test.

Results

The demographic and clinical characteristics of the 21 hemophiliacs and their 21 female sexual partners are summarized in table 1. All couples engaged in vaginal intercourse—45 percent of them, four or more times per month. None engaged in anal intercourse. Of the 21 female sexual partners of hemophiliacs evaluated, only 4 (19.0 percent) were antibody-positive (table 2). All of those positive by HIV antibody assay were confirmed by Western blot technique. HIV virus

'The lack of anal sexual intercourse between these couples suggests that anal intercourse is not necessary for heterosexual HIV transmission. . . . the low prevalence of HIV transmission from HIV antibody-positive hemophiliacs to their female sexual partners also implies that vaginal intercourse is not a very effective means of HIV transmission.'

Table 2. Human immunodeficiency virus (HIV) isolation results

Variable	Hemophiliac (N = 21)		Female partner (N = 21)	
	Number	Percent	Number	Percent
HIV antibody-positive[1]	21	100	4	19
HIV virus isolation	1	4.8	[2]1	4.8

[1] Tested positive by both ELISA and Western blot assays.
[2] This female was HIV antibody-positive.

was detected in peripheral blood lymphocytes in only 1 of 21 hemophiliacs (4.8 percent) and only 1 of their 21 (4.8 percent) sexual partners. These results were confirmed by antigen capture immunoassay. Repeat viral culture assays were performed on fresh blood samples of the two culture-positive patients and on five of the negative patients with high HIV antibody ELISA titers (more than 1.9). The initial results were reconfirmed by repeat study in each case.

Compared with the 17 HIV antibody-negative female partners, the HIV antibody-positive female partners were younger (27.8 ± 2.8 years versus 36.5 ± 2.4 years) ($P<.05$) and had younger hemophiliac partners (37.7 ± 2.8 years versus 30.0 ± 2.2 years) ($P< .05$). The only other differences that approached statistical significance were the likelihood of seropositive females to engage in oral receptive intercourse (2 of 4 antibody-positive versus 1 of 16 antibody-negative females) ($P = .08$) and the likelihood of having had more than one sexual partner in the past 5 years (2 of 4 antibody-positive versus 1 of 16 antibody-negative females) ($P = .08$). Sexual frequency, condom use, and assistance with blood product infusion did not differ between the HIV antibody-positive and -negative female sexual partners. Consistent use of condoms (sometimes or always) was begun by four couples in 1984 or before, four in 1985, and six in 1986. None of the couples engaged in anal intercourse, and none of the hemophiliacs or their partners admitted to previous sexually transmissible diseases. None of the "other" sexual partners belonged to any known AIDS risk groups.

Despite counseling about HIV transmission and appropriate precautions to prevent transmission—specifically, use of condoms and prevention of pregnancy—condoms were consistently used (all the time) by only 40 percent of the couples, and pregnancies occurred in two couples (9.5 percent). One was terminated in abortion, and the other continued to term—a healthy, antibody-negative newborn. Both couples were using condoms "sometimes," but neither pregnancy was a result of condom failure.

Discussion

The results of this study confirm that the prevalence of heterosexual transmission of HIV from HIV antibody-positive hemophiliacs to their female sexual partners is low but significant, similar to transmission rates reported in other studies of partners of hemophiliacs (*10–15*), partners of bisexual men (*22*), and partners of transfusion recipients (*23*), but slightly lower than partners of intravenous drug users (*24*). It may be that higher rates of seropositivity in female sexual partners of high-risk men may relate, in part, to the presence of other risk factors, for example, multiple sexual contacts.

These data further suggest that the reason for the low prevalence of heterosexual HIV transmission may be related to a very low prevalence of HIV isolation in HIV antibody-positive hemophiliacs. The recovery of virus among only 4.8 percent of the hemophiliacs studied is lower than the 20 to 30 percent recovery among hemophiliacs described by other researchers (*14,25–27*). However, at least four of the culture-negative hemophiliacs had been infectious at some point in the recent past (two seroconverted in 1981 and one each in 1982 and 1984); their wives are HIV antibody-positive. The low frequency of HIV infectivity (isolation of HIV) among hemophiliacs and, particularly, the absence of HIV isolation among persons with AIDS or ARC contrasts to the 50 percent or higher frequency of HIV viral isolation from peripheral blood lymphocytes of homosexual and

bisexual men (*14,25*) (Gupta et al., unpublished data). This difference is a noteworthy observation and suggests that risk factors for infectivity (viremia) may differ between the two groups. Specifically, the absence of sexually transmissible diseases in these hemophiliacs and the presumed lack of repeated exposures to HIV through the use of heat-treated concentrates since mid- to late 1985 may offer an explanation for their low frequency of infectivity. It is important to point out that culture data may vary greatly between laboratories, and thus, as methods are refined, further studies will be needed before any conclusions can be reached regarding HIV isolation and transmission of HIV.

The lack of anal sexual intercourse between these couples suggests that anal intercourse is not necessary for heterosexual HIV transmission. Moreover, the low prevalence of HIV transmission from HIV antibody-positive hemophiliacs to their female sexual partners also implies that vaginal intercourse is not a very effective means of HIV transmission.

This study documents the urgent need to intensify health education for persons with hemophilia. It also reveals the need for the development and implementation of more effective educational and counseling programs to prevent heterosexual as well as perinatal transmission of HIV. Among the population studied—couples whose risk status should have motivated them to reduce the risk of transmission and who had the benefit of comprehensive care, including counseling in risk reduction—only 40 percent complied with the recommendation to use condoms. Clearly, great strides need to be made in public health education if further spread of HIV is to be prevented.

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Supplies

A. Abbott Laboratories, Chicago, IL.
B. Genetic Systems, Seattle, WA.
C. Cellular Products, Buffalo, NY.

HIV-AIDS Transmission Symbols

R.T. RAVENHOLT, MD, MPH

Tearsheet requests to Dr. Ravenholt, Director, World Health Surveys, Inc., 3156 E. Laurelhurst Dr. NE, Seattle, WA 98105.

As THE AIDS PANDEMIC has gained momentum in this and many other lands, and as the principal mechanisms for the transmission of the human immunodeficiency virus (HIV) have been identified (*1-4*), there has come a need for a set of symbols to indicate each mechanism of HIV transmission and track its spread. If soundly devised, such symbols might have utility for HIV-AIDS communications and control programs, somewhat analogous to the utility of international traffic signs.

For this purpose I propose adaptation of the symbols commonly used to denote male ♂ and female ♀, and diverse permutations of same, while adhering to several simple rules: each circle ○ indicates a body (person), designated as male ♂ or female ♀; with the left-hand symbol indicating the source of HIV-AIDS infection, and the right-hand symbol indicating the recipient of HIV-AIDS. Notations within circles indicate the status of individuals: (HIV) — one infected with HIV, (A) one with AIDS, (P) — a prostitute; or they indicate transmission dynamics: ⊖ — one infected by male sexual intercourse, and ⊕ — one infected by female sexual intercourse. Hence, ○—⊖♂ denotes a male infected with HIV by homosexual intercourse; ○—⊕♂ denotes a male infected with HIV by heterosexual intercourse; and ○—⊖—⊖♀ denotes a female infected with HIV by heterosexual intercourse with a bisexual male infected by homosexual intercourse. A square □ denotes nonsexual transmission of HIV-AIDS: [IV] by IV drug abuse, [N] by contaminated needles, [B] by blood transfusion, or [8] by factor 8 injection.

Vertical (in-utero) transmission of HIV is indicated by attachment of a small body to the female symbol and indicating the sex of the offspring ○—♂. Permutations of such symbols or ideograms are presented in figure 1, identifying the percentage of U.S. AIDS cases through January 1, 1987 resulting from each transmission mechanism.

Application of these symbols to the tracking and presentation of a hypothetical epidemic of HIV-AIDS derivative of one male homosexual is presented in figure 2. It does not show the many additional sexual cross-connections which ordinarily obtain among promiscuous homosexual males during the latent years between HIV infection and AIDS onset; these usually frustrate searches for specific sources of infection—especially in New York, San Francisco, and other communities where AIDS is epidemic.

In figure 3, transmission symbols are applied to the tracking and presentation of hypothetical, inter-related outbreaks in an African society—where common use of HIV-contaminated needles for medical injections, frequent transfusions of blood containing HIV, promiscuous sexual intercourse with HIV-infected female prostitutes, marital and extramarital sexual intercourse with HIV-infectees, and vertical transmission of HIV from infected mothers to offspring, combine to produce