

Sex Practice Correlates of Human Immunodeficiency Virus Transmission and Acquired Immunodeficiency Syndrome Incidence in Heterosexual Partners and Offspring of U.S. Hemophilic Men

Dale N. Lawrence, Janine M. Jason, Robert C. Holman, Peggy Heine, Bruce L. Evatt, and the Hemophilia Study Group

Division of Host Factors, Center for Infectious Diseases, Centers for Disease Control, Public Health Service, U.S. Department of Health and Human Services, Atlanta (D.N.L., J.M.J., R.C.H., B.L.E.); National Resource and Consultation Center for AIDS and HIV Infection, National Hemophilia Foundation, New York (P.H.)

We assessed the risk of human immunodeficiency virus (HIV) transmission from heterosexual seropositive hemophilic men to their female sex partners through an HIV serosurvey and questionnaire study conducted during 1984-1987. Five percent of 21 female partners of asymptomatic men and 11% of 35 partners of HIV-symptomatic (acquired immunodeficiency syndrome [AIDS], AIDS-related complex [ARC], peripheral generalized lymphadenopathy [PGL]) hemophilic men had been infected when first tested. One of 19 seronegative women tested about 1 year later reportedly seroconverted. Only 18% of a sample of the serosurvey women responding to sex practices questions said their partners used condoms "nearly always." Over 60% engaged in oral/genital sex in addition to vaginal intercourse. Only 12% of still-seronegative women followed the preventive strategy of consistent avoidance of oral/genital sex, together with consistent condom use by the male partner.

Further evidence for heterosexual transmission comes from the CDC national AIDS surveillance reports showing 25 women who acquired HIV infection through heterosexual contact with U.S. hemophilic men (September 6, 1988). Seven (28%) were diagnosed and reported in the first 6 months of 1988. Their ages range from 20 years to more than 70 years. The dates of infection for the women are unknown but must have been at least 5 years before AIDS diagnosis for at least one. Only approximately 30% of their male partners had already manifested any HIV-associated illness.

Through May 18, 1988, six cases of AIDS have occurred in children whose infection was acquired through exposure of the mother to a hemophilic partner. Four were diagnosed in latter 1987. The median age at diagnosis was 4.5 months. Four had died. None of their mothers is as yet diagnosed.

Key words: human immunodeficiency virus transmission, AIDS incidence, heterosexual AIDS, pediatric AIDS, heterosexual partners, HIV seroprevalence, hemophilia

Received for publication February 15, 1988; accepted October 16, 1988.

Address reprint requests to Dale N. Lawrence, M.D., CDC, Bldg. 1, Room 1407 (Mail Stop D-02), 1600 Clifton Road N.E., Atlanta, GA 30333.

The Hemophilia Study Group includes the following:

Susan Kennedy, Gloria Dixon, Division of Host Factors, Center for Infectious Diseases, CDC; J. Heinrich Joist, John Bouhasin, St. Louis University Medical Center; Margaret Hilgartner, Cornell University Medical Center; Louis Aledort, Mt. Sinai Medical Center, New York City; Carol K Kasper, University of Southern California; Shelby Dietrich, Orthopedic Hospital, Los Angeles; Edward Gomperts, Chil-

dren's Hospital, Los Angeles; W. Abe Andes, Tulane University Medical Center, New Orleans; Margaret Ragni, The Hemophilia Center of Western Pennsylvania, Pittsburgh; Patricia Catalano, Cardeza Foundation Hemophilia Center, Philadelphia; M. Elaine Eyster, Hershey Medical Center, Hershey; Jay Jenkins, private practice, Erie, Pennsylvania; Michael Lederman, Oscar Ratnoff, University Hospitals of Cleveland; Lyman Fisher, Medical College of Virginia, Richmond; Carolyn Chesney, Baptist Memorial Hospital, Memphis; John Rogers II, West Virginia Medical Center, Morgantown; Thomas Amsden, Riverside Medical Center, Minneapolis; Joseph Muscato, private practice, Columbia, Missouri; Susan Saviteer, North Carolina Memorial Hospital, Chapel Hill; Arthur Pitchenik, University of Miami Medical Center; Jeff Stall, private practice, Sarasota, Florida; William Hathaway, University of Colorado Medical Center, Kenneth Matchett, Grand Junction, Colorado.

INTRODUCTION

Documentation of the extent of heterosexual transmission of human immunodeficiency virus (HIV) from hemophilic men to their partners is becoming increasingly available [1-19]. Monitoring the rate of spread of the virus to heterosexual partners and identification of sexual behaviors associated with transmission have emerged as major components of the HIV prevention activities of clinicians and supporting staff who care for hemophilia patients and their families. The Centers for Disease Control (CDC) collaborated in early enrollment of household contacts of HIV-infected hemophilia patients [1-3], including enrollment of spouse/sex partners from many of the hemophilic men initially stricken with acquired immunodeficiency syndrome (AIDS) during the first 5 years of the epidemic.

Indirect measures of heterosexual activity among the adult hemophilic men diagnosed with AIDS are available from ancillary information obtained in association with AIDS surveillance activities of the Division of Host Factors, Center for Infectious Diseases, CDC. For example, approximately 65% of the 364 male hemophilic AIDS patients reported to CDC as of July 6, 1987 who did not belong to another risk group were in the age group 20-49 years, generally associated with higher sexual activity and active parenthood. Of these men, 76% had been sexually active since 1979, 47% were married at the time of their AIDS diagnosis, and 46% had been living with their spouses in the year before their AIDS diagnosis. Thus, a substantial number of women may have been at risk of heterosexual transmission from the several thousand infected U.S. hemophilic men.

We report here the findings of a collaborative longitudinal HIV serosurvey and sexual practices questionnaire study. We compare the HIV serologic status of reportedly asymptomatic women who have been partners of HIV-symptomatic hemophilic men to the serologic status of women whose HIV-infected hemophilic partners were asymptomatic. Their ages, sexual practices, including frequencies and condom usage, are compared; correlations between types of practices and serologic status are made. We have not included results of the many women enrolled in our studies who were recognized as HIV-symptomatic at their enrollment [1-3, 10-11] (unpublished data). Information gained from these serosurvey/sexual practices studies of female partners of typically monogamous hemophilic men are also valuable to public health officials attempting to anticipate the risks associated with male to female heterosexual spread within the "general" adult population in the United States.

In addition, we document here the rapid rate of increase in the incidence of AIDS in 1) women whose infection was attributed to heterosexual contact with an HIV-infected hemophilic man, and in 2) the offspring of

women infected in this way. The description of these cases were drawn from results of our auxiliary investigations correlated with the CDC AIDS surveillance information about these groups of cases.

MATERIALS AND METHODS

Between 1984 and 1987, 56 reportedly asymptomatic female sex partners of HIV-infected hemophilic men were enrolled in a study of sexual transmission of HIV. The women's HIV-antibody status at enrollment was unknown. The concurrent HIV-symptomatic or asymptomatic status of the respective male partner was known, however. The questionnaire and laboratory assessments were the same for each woman, but subsequent analyses were conducted according to the original enrollment category of the women, based on their partner's status.

Category A comprised the 35 women whose male partner had developed AIDS, AIDS-related complex (ARC), or peripheral generalized lymphadenopathy (PGL). The majority (86%) of the women in this group were sex partners of AIDS cases (Table I). At the time of enrollment of the most recent of these women in April 1987, they represented the spouses/steady sex partners of approximately 10% of the hemophilic men with AIDS in the United States. Category B comprised 21 women identified as sex partners of asymptomatic HIV-infected hemophilic men. No preanalysis effort was made to match women in the two categories for any characteristic.

Participants provided written informed consent and blood samples for HIV-antibody testing by Western blot [20]. Serologic reactions were scored as positive if there was reactivity with the 41-kD protein of HIV or reactivity with the 24-kD protein together with any one of several other HIV-associated proteins (18 kD, 31 kD, 51 kD, 55 kD, 65 kD or 110 kD). HIV antigen testing employed antigen capture techniques using a commercial kit (Abbott Labs, North Chicago). A second blood sample was obtained an average of 1 year later from 11 women and sent to CDC for testing. Results were also provided for an additional eight women, initially enrolled in this study, but who are now being followed and tested using comparable methods only by the treatment centers.

Most women (84%) also completed an extensive, self-administered, confidential questionnaire about their health and sex practices. In addition to inquiring about other, nonsexual possible routes of exposure, including assisting the hemophilic sex partner with factor concentrate infusions, questions asked about frequency of sexual relations, type of sexual contacts (vaginal, oral, anal) the number of different sex partners, and the proportion of occasions during the past 3 years in which the partners used condoms and/or various other techniques of "contraception."

Whenever feasible, the male hemophilic partner was

TABLE I. Enrollment Categories for Female Sex Partners of Hemophilic Men in an HIV-Serosurvey and Questionnaire Study

Female partners of symptomatic hemophilic men			
Men's clinical status		Women's clinical status	No.
AIDS	n = 30	All asymptomatic	35
ARC	n = 1	All asymptomatic	
PGL	n = 4 ^a	1 with PGL; 3 asympt.	
Female partners of asymptomatic hemophilic men			
Men's clinical status		Women's clinical status	No.
Asymptomatic		Asymptomatic	21

^aOne woman, enrolled because her spouse had PGL, was found to have PGL also.

asked to complete a questionnaire and submit a blood sample. Analysis of comparable questionnaire responses, available from 30 (54%) of the respective male partners, is not presented here but reveals no important discrepancies in number of sex partners or frequency of sexual relations. Results of analyses are based solely on the women's answers. An absence of sexually transmitted disease history was characteristic of both men and women.

The monthly frequency of sexual encounters for each of the 56 women was obtained from their questionnaires. The proportion of all sexual encounters that did not involve condom use was the sum of the sexual contact frequencies reported by those women whose partners never/rarely used condoms divided by the number of encounters for all women having intercourse.

Personal serologic status and information on the risks of sexual transmission were provided to the participants by collaborating physicians. Additional counseling was provided to the participants. Of the 56 women in the serosurvey, HIV antibody results of 21 had been included in one or more previous reports of a preliminary nature [1-3, 9-11]; these reports were too small for meaningful analysis based on categorization of the women according to the sex partners' clinical status.

Dichotomous factors were analyzed using the method of Thomas and Gart [21,22] to obtain the odds ratio (OR) and the 95% confidence interval (CI). The 95% CI was calculated for single proportions using the method discussed by Fleiss for extremes of a probability distribution [23]. Continuous factors were analyzed using the Wilcoxon rank-sum test [24]. The significance level was $P = .05$.

The description of the 25 women with AIDS who reported a previous heterosexual contact with a hemophilic partner is derived from ancillary investigations correlated with the CDC AIDS surveillance information. Serum, lymphocyte samples, and/or information on sexual practices were collected from six of these women. Preliminary information is provided from similar investigations on the six children with AIDS whose HIV infec-

tion was transmitted from a mother who had been the sex partner of a hemophilic man.

RESULTS

Serosurvey/Sex Practices Study

Seroprevalence. Of the 35 women in category A with HIV-symptomatic partners (Table I), four (11%) were seropositive at initial evaluation (Table II). Three of the four were spouses of AIDS patients; the other, a reportedly asymptomatic partner of a PGL-afflicted hemophilic man, was discovered at her enrollment to have PGL [9]. Of the seven seronegative women retested approximately 1 year later, none had seroconverted.

Of the 21 women in category B, one (5%) was seropositive at enrollment. Of the 12 seronegative women who were re-evaluated, one was reported in 1986 to have seroconverted. No further seroconversions have been noted.

Sex practices. Category A women were similar in age and in several aspects of general sex practices to category B women (Tables III, IV). All had had a sex partner during the preceding 6 months. Although 28% had partners who used condoms at least "sometimes," only 12% used them "nearly always." Of the four seropositive women in category A, three provided sex practices information; all three reported that their partners "never/rarely" used condoms.

Of the spouses in category B (Table IV), one practiced no vaginal sex; she engaged in passive oral/genital sex (cunnilingus) exclusively. She was seronegative. One woman reporting anal sexual contact was seronegative. The only woman found seropositive on first testing for HIV was one of those reporting that her partner sometimes used condoms. The odds ratios in Table IV approximate the fold-increase in (relative) risk for seropositivity given the specified activity. Their associated 95% confidence intervals encompass 1.0 and are statistically nonsignificant. Thus, the two groups did not differ significantly with respect to the activities taken separately.

TABLE II. HIV Status of Female Sex Partners, by Clinical Status of Hemophilic Partner

	Hemophilic partner's status	
	Symptomatic ^a (category A)	Asymptomatic (category B)
	No. women (%)	No. women (%)
No. enrolled	35	21
1983/84	15	10
1985	11	3
1986	5	4
1987	4	4
Initially seropositive [95% confidence limits (%)]	4 (11) [4-28]	1 (5) ^b [0-26]
Initially seronegative HIV antigen tested (% +)	31 30 (0)	20 20 (0)
Seronegative & retested	7	12
At CDC	7	4
At treatment center only	0	8
Seroconverting	0 (0)	1 (8)
Total seropositive	4 (11)	2 (9)

^aSymptomatic category includes 30 hemophilic men with AIDS; one with ARC; and four with PGL.

^bDifferences in seropositivity rate for categories A and B were not statistically significant; the five women (categories A and B, combined) found to be seropositive on initial enrollment were enrolled in 8/84, 3/85, 10/85, 11/85, and 3/87.

TABLE III. Age and General Sex Practices of Female Sex Partners, by Clinical Status of the Hemophilic Partner

Women's	Hemophilic partner's status					
	N ^a	Symptomatic (category A)		N	Asymptomatic (category B)	
		Mean	(±SD)		Mean	(±SD)
Age (years)	35	35.1	(11.4)	21	36.0	(11.1)
Sexual frequency (per month)	29	8	(5)	17	8	(5)
No. different sex partners						
For the preceding 5 years	27	1.4	(1.1)	13	1.6	(1.3)
For the preceding 6 months	27	1.0	(0.7)	13	0.8	(0.4)

^aFor each designated variable, the no. of women from whom information was available was different.

TABLE IV. Specific Sex Practices of Female Sex Partners, by Clinical Status of the Hemophilic Partner

	Hemophilic partner's status					
	Symptomatic (category A)		Asymptomatic (category B)		Odds ratio	(95% CI)
	% yes	N ^a	% yes	N		
Sex practices ^b						
Vaginal sex	96	25	95	19	1.3	(0.0-103.2)
Oral/genital sex	64	25	61	18	1.1	(0.3-4.7)
Anal sex, passive	0	25	6	18	0.0	(0.0-13.7)
Condom use ^{c,d}		25		13		
Never/rarely	72		54			
Sometimes	16		15			
Nearly always	12		31		3.3	(0.4-26.1)
TOTAL	100		100			

^aThe no. of women from whom information was available is provided for each designated variable.

^bSex practice categories not mutually exclusive; oral/genital sex includes both active (fellatio) and passive (cunnilingus) roles for the women.

^cCondom use categories are mutually exclusive; categories are not subdivided further according to use of foam or cervical diaphragm.

^dNever/rarely and sometimes responses were combined for statistical testing and during subsequent correlations (see text).

Since the responses for the women in the two categories were very similar, their results were pooled for summary estimates. Seven (18%) of the 38 women completing questionnaires reported that their partners nearly always used condoms; all were 30–49 years old. Only four of the 38 women had completed a second questionnaire about 1 year later. One had discontinued active oral sex; the other three had not reduced or changed their sex practices. The sex practices information for the enrollees in 1986/1987 were compared to the earlier enrollees (1983–1985); the median number of sexual contacts per month was slightly but not significantly lower.

Whereas 50% of the women having intercourse less than six times per month reported that their partners used condoms sometimes, only 17% of women having sexual contact more than 6 times per month reported their partners used condoms ($P = .07$). Thus, because condom usage was lowest among the most sexually active women, approximately 75% of all sexual encounters by all participating women did not involve condom use.

The initial HIV-seropositivity rates were similar for women whose partners used condoms nearly always (1 of 7), sometimes (1 of 6), or rarely (3 of 25). Since exposure to semen during fellatio (without condoms) might allow HIV infection in spite of condom use during vaginal sex, the seropositivity status was examined according to whether the women used maximal preventive techniques. This was defined as the partner's use of condoms "nearly always" together with avoidance of oral/genital sex. None of five seropositive women used maximal preventive techniques; only four (13%) of 32 seronegative women did ($P = N.S.$).

AIDS Cases in Female Heterosexual Partners and Offspring

As of September 6, 1988, 25 current or former heterosexual partners of U.S. hemophilic men had been reported to CDC as AIDS patients by their respective state health departments (Fig. 1); seven (28%) were diagnosed in the first 6 months of 1988. Their geographic distribution by state is generally similar to that for adult hemophilic AIDS patients. Their age distributions (Fig. 2) are very similar to those found in a hemophilia treatment center population-based survey of sex partners of HIV-infected men (data not shown: Sally Crudder, J. Gross, Sally Stabler, personal communication). Seventy-two percent of the female AIDS cases were 20–39 years old, but two were more than 60 years of age. None of the women reported any other source of HIV infection. One young woman had recently delivered a seronegative child.

In accord with the predominance of hemophilia A patients among the hemophilia AIDS cases, it was noted that only two of 15 women for whom this information was available had a partner with hemophilia B. At diagnosis, most of the women's hemophilic partners were still HIV-asymptomatic (Table V). One woman had developed peripheral generalized lymphadenopathy (PGL) 4 years before her AIDS diagnosis [2].

The dates of infection are not known for either the respective hemophilic partners or for the women. The duration of the sexual liaisons ranged from many months to several decades. The infection of at least one of the women must have occurred at least 5 years prior to the AIDS diagnosis. The great majority of the women with AIDS were married to the hemophilic partner at the time

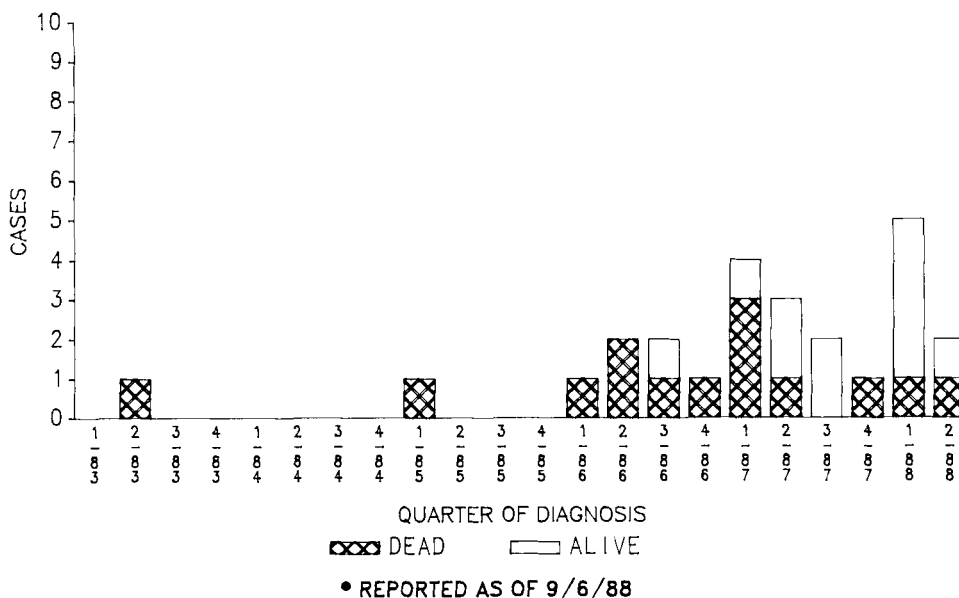


Fig. 1. U.S. cases of AIDS in female heterosexual partners of hemophilic men, by quarter of diagnosis.

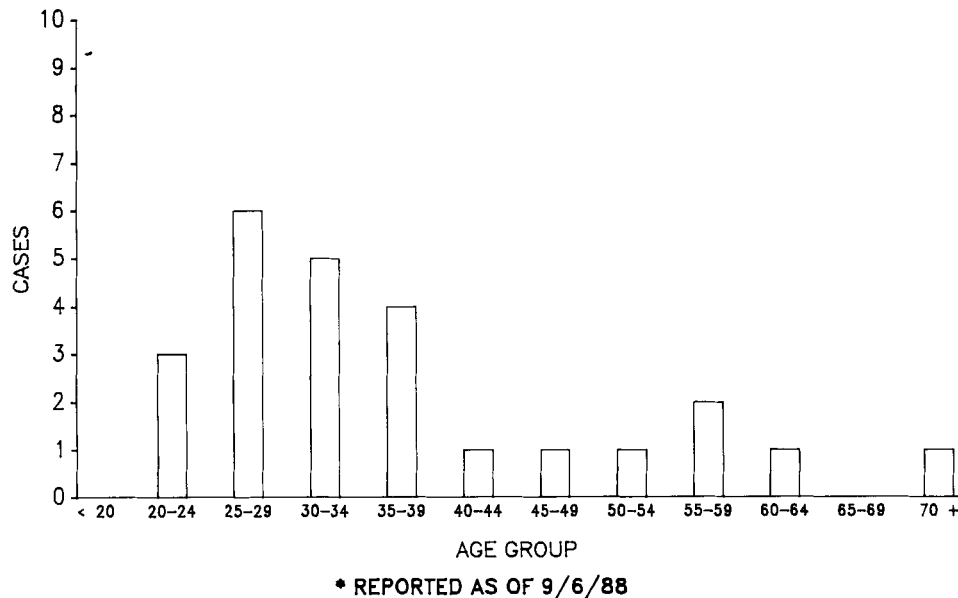


Fig. 2. U.S. cases of AIDS in female heterosexual partners of hemophilic men, by age group.

of her infection and diagnosis. Limited information on sex practices is available at present on only nine of the women. For six from whom responses about anal sex practices were obtained, two admitted occasional use of this method of intercourse; condoms were not used during these occasions.

Through May 18, 1988, six cases of AIDS have occurred in children whose infection was acquired through heterosexual exposure of the mother to a hemophilic partner. Their dates of diagnosis by quarter and year were 3-84, 3-86, 3-87, 3-87, 3-87, 4-87. The median age at diagnosis was 4.5 months. Four had died. None of their mothers was as yet diagnosed although at least two

mothers have lymphadenopathy [3] (unpublished data) and one hemophilic father [3], subsequently diagnosed with AIDS, has died.

DISCUSSION

Reported seroprevalence rates for heterosexual partners of HIV-infected hemophilic men tend to be higher for U.S. than for European studies and for studies based on median year of enrollment in 1986 or later. Rates for U.S. heterosexual partners of HIV-infected hemophilic men range from 0 to 21%; this higher value was associated with a 95% confidence interval of 6-46% [15]. The 95% interval around our observed 11% seroprevalence for partners of symptomatic men includes the 21% value.

Most of the early reports citing seroprevalence values above 10% included a substantial percentage of women whose partners had become clinically HIV-symptomatic; some of these women had drawn the attention of study investigators because they too were having HIV-associated symptoms. To avoid a possible selection bias for enrolling seropositive women, we excluded from this serosurvey women who felt ill or were experiencing HIV-related symptoms.

If, as has been proposed, women whose hemophilic partners are most immunodeficient are more likely to be seropositive [14], then an additional selection bias may have been operating to enhance enrollment of these women. Their attendance with clinically ill spouse/partners may have led to their convenient enrollment and caused some earlier researchers to report higher seroprevalences than were representative for that period.

TABLE V. Female AIDS Patients Who Were Heterosexual Partners of Hemophilic Men, United States, September 6, 1988

Description	No.
Total No. reported to CDC	25
Subtotals	
Dead	14
Pneumocystis pneumonia	21
With antecedent PGL ^a	3
Whose partner had HIV-associated symptoms	
Before her AIDS diagnosis	4 (2 AIDS; 2 PGL)
After her diagnosis	2 (AIDS)
Whose last sexual contact with hemophilic partner was \geq 5 years before her diagnosis	1

^aPeripheral generalized lymphadenopathy.

Unfortunately, we did not have immunologic assessment on enough of the 30 male partners with AIDS, for example, to address the hypothesis directly. However, it would seem that our women with symptomatic partners were probably thereby also exposed to the most immunodeficient partners. Thus, we chose to present the results of the 56 women in our serosurvey study according to the clinical status of their hemophilic partners at enrollment.

Interestingly, the moderately higher (11%) initial seroprevalence rate we observed for these women was not significantly different from the initial rate found in women whose partners were asymptotically infected. Admittedly the difference may have become statistically significant if a larger number of women had been studied. However, we note that a recent assessment of the risk of HIV transmission from heterosexual adults with transfusion-associated HIV infections found seroprevalence rates to be the same for spouses in contact with AIDS patients (15%) or asymptotically infected partners (14%) [25].

The greater concern for the future may be that women with asymptomatic partners, most of whom were continuing to engage in high-risk sexual activities, could seroconvert, as reported from one collaborating center's experience. This latter group of women is considered more typical of sex partners of the majority of HIV-infected hemophilic men who are still asymptomatic. These women may be less conscious of the risks and more likely to become subsequently infected. So too, couples beyond the reproductive years need to be cognizant of HIV and to employ condoms (again) to avoid HIV transmission.

Most of the women enrolled with an AIDS-affected sex partner were being evaluated a few months after the partner's diagnosis. Thus, there is little likelihood that subsequent exposure had occurred; however, the subsequent persistently seronegative status of the seven (23%) of 31 initially seronegative women who were retested is gratifying. Subsequent serologic information on 12 (60%) of the initially seronegative women with an asymptomatic partner reflects a disappointing success rate at present in the follow-up. Attempts to gather information to classify the reasons for these women's later nonparticipation has provided us with poignant descriptions of estrangements, divorces, embitterment at the medical establishment, and grief.

This study, begun officially in 1984, was more than half completed before systematic HIV antibody testing of hemophilia patients or their sex partners became commonplace. Our relatively early study did not contain a formal educational component with appropriate behavioural change assessments. HIV antibody testing and counseling of spouses accelerated in 1987, assisted by government-sponsored research channeled through the

CDC and Health Resources and Services Administration (HRSA) to hemophilia treatment centers.

A source of possible uncertainty on scrutiny from today's perspective is the belated recognition that two questions about sex practices (vaginal, oral, anal sex; frequency of sexual relations) did not specify the time period of interest. We cannot externally validate whether each of the women enrolled because of her exposure to a symptomatic male partner was told (and followed) our instructions to report average coital frequency before the partner's diagnosis or symptoms. We cannot substantiate our impression that sex practices during 1984–1985 did not change markedly for these women even though some of the respective male partners were developing early HIV symptoms.

Another weakness in retrospect was that a question on contraceptive methods pertained to sex practices only during the previous 3 years. For the 17 women enrolled in 1986/1987—53% of whom were partners of AIDS cases—the question about the women's sex practices in the previous 3 years was becoming somewhat removed from the period of their most likely initial opportunity for exposure. However, if the greatest risk was through exposures at a time when the index hemophilic man is most immune deficient as has been proposed [14], then the most recent 3 years would still be most important.

Anal intercourse seems to have been practiced by only one (2%) of the 43 women completing questionnaires. This seronegative woman's partner was asymptomatic. Information specifically about anal intercourse is currently available from only six of the 25 women with AIDS whose HIV infection was transmitted from a heterosexual hemophilic man. Although data are too limited to evaluate the true percentage of the 25 women engaging in the practice, it is noteworthy that two of the six reported doing so, at least briefly.

The number of U.S. women who have already become infected via HIV-infected hemophilic men is unknown, but useful estimates have been under development. Some infected women may already be mildly symptomatic but unaware that a heterosexual exposure to HIV 5 years or more ago may account for their symptoms. This is especially true for women no longer in contact with the hemophilic men. Clinicians taking care of symptomatic women, or children, who do not belong to any recognized risk groups for HIV infection should inquire about possibly distant heterosexual contacts of the women.

As late as 1985–1986, the mid-period of our enrollment period, it appears that many women having sexual contact with an HIV-infected hemophilic man had not consistently adopted the behavior changes encouraged by early published recommendations [26–28], most of which were directed to health care professionals. In late 1986 major federal funding increases became available from

the CDC and the Bureau of Maternal and Child Health, HRSA, to the NHF and to regional hemophilia treatment programs to implement national and regional efforts to reach and motivate couples to discontinue high-risk sex practices. In 1987-1988, therefore, information for health care professionals [29,30] has been supplemented by many recently developed and widely distributed "consumer-oriented" publications [31-34]. It appears from recent publications on AIDS knowledge and attitudes among hemophilia patients [35,36] and the U.S. public [37] that much remains to be done.

We conclude that 1) all at-risk women must recognize the need for abstinence or for sex practices that inhibit the exchange of body fluids; 2) couples should delay conception until more is known about protecting the unborn child and more effective treatment is developed; 3) assessment of the efficacy of the counseling and other efforts currently underway must be used to monitor educational methods and redirect resources. We believe that the bonds of intimacy and the future health of these couples are the common interest of family members, lay leaders of the hemophilia community, and health care professionals.

ACKNOWLEDGMENTS

This project was performed in collaboration with the National Hemophilia Foundation. In addition, the authors specifically thank the following persons for their assistance in this project: M. Mahoney, J Stehr-Green, P. Bozdech, K. Gioia, D. Reier, K. Wulff, and J. Aquino for their assistance in patient enrollment; R. Horton, J. Hall, M. Baker, D. Hemmerlein, M. Simon, and M. Parvin for specimen processing; M. Mays for computer programming/assistance; D. Bush and S. Richardson for data entry; T. Starcher and C. White for AIDS surveillance information; and O. van Assendelft and T. Gyurik for administrative assistance.

REFERENCES

- Pitchenik AE, Shafron RD, Glasser RM, Spira TJ: The acquired immunodeficiency syndrome in the wife of a hemophiliac. *Ann Intern Med* 100:62-65, 1984.
- Ratnoff OD, Lederman MM, Jenkins JJ: Lymphadenopathy in a hemophiliac patient and his sexual partner [Letter]. *Ann Intern Med* 100:915, 1984.
- Ragni MV, Urbach AH, Kiernan S, Stambouli J, Cohen B, Rabin BS, Winkelstein A, Gartner JC, Zitelli BZ, Matatack JJ, Bon-tempo FA, Spero JA, Lewis JH: Acquired immunodeficiency syndrome in the child of a haemophiliac. *Lancet* 1:133-135, 1985.
- Kreiss JR, Kitchen LW, Prince HE, Kasper CK, Essex M: Antibody to human T-lymphotropic virus type III in wives of hemophiliacs: Evidence of heterosexual transmission. *Ann Intern Med* 102:623-626, 1985.
- Jones P, Hamilton PJ, Bird G, Fearn M, Oxley A, Tedder R, Cheingsong-Popov R, Codd A: AIDS and haemophilia: Morbidity and mortality in a well-defined population. *Br Med J [Clin Res]* 291:695-699, 1985.
- Biberfeld G, Böttiger B, Berntorp E, Shulman S, Egberg N, Stigendal L, Blombäck M, Nilsson IM: Transmission of HIV infection to heterosexual partners but not to household contacts of seropositive haemophiliacs. *Scand J Infect Dis* 18:497-500, 1986.
- Allain J-P: Prevalence of HTLV-III/LAV antibodies in patients with hemophilia and in their sexual partners in France [Letter]. *N Engl J Med* 315:517-518, 1986.
- McVerry BA, Machin SJ, Galloway MJ, McCarthy K, Evans P, Barnes RMR, Turner GC, Cheingsong-Popov R, Tedder RS, Winter M: HTLV-III antibody and T-cell subset ratios in haemophiliacs and their spouses. *Br J Haematol* 63:347-352, 1986.
- Andes WA, Lawrence DN, Jason J: Conjugal transmission of HTLV-III and lymphadenopathy in Christmas disease. *Thromb Haemost* 55:129-130, 1986.
- Jason JM, McDougal JS, Dixon G, Lawrence DN, Kennedy MS, Hilgartner M, Aledort L, Evatt BL: HTLV-III/LAV antibody and immune status of household contacts and sexual partners of persons with hemophilia. *JAMA* 255:212-215, 1986.
- McFadden T, Jason JM, Feorino P: HTLV-III/LAV seronegative, virus negative sexual partners and household contacts of hemophiliacs [Letter]. *JAMA* 255:1702, 1986.
- Operskalski E, and the Transfusion Safety Study Group: Transmission of human immunodeficiency virus infection to household contacts of persons with congenital hematologic disorders [Abstract]. Program of the 28th Annual Meeting, American Society of Hematology, Dec 6-9, 1986, San Francisco:131A.
- Centers for Disease Control: HIV infection and pregnancies in sexual partners of HIV-seropositive hemophilic men—United States. *MMWR* 36:593-595, 1987.
- Goedert JJ, Eyster ME, Biggar RJ, Blattner WA: Heterosexual transmission of human immunodeficiency virus: association with severe depletion of T helper lymphocytes in men with hemophilia. *AIDS Res Hum Retroviruses* 3:355-361, 1987.
- Padian N, Marquis L, Francis DP, Anderson RE, Rutherford GW, O'Malley PM, Winkelstein W Jr.: Male-to-female transmission of human immunodeficiency virus. *JAMA* 258:788-790, 1987.
- Ragni MV, Gupta P, Rinaldo CR, Kingsley LA, Spero JA, Lewis JH: Human immunodeficiency virus (HIV) transmission in female sexual partners of HIV antibody positive hemophiliacs. *Public Health Rep* 103:54-58, 1988.
- Brettler DB, Forsberg AD, Levine PH, Andrews CA, Baker S, Sullivan JL: HIV isolation studies and antibody testing in household contacts and sexual partners of persons with hemophilia. *Arch Intern Med* 148:1299-1301, 1988.
- Smiley ML, White GC, Becherer P, Macic G, Matthews TJ, Weinhold KJ, McMillan C, Bolognesi D: Transmission of human immunodeficiency virus to sexual partners of hemophiliacs. *Am J Hematol* 28:27-32, 1988.
- Kamradt T, Niese D, Schneweis KE, Brackmann HH, Kamps BS: Heterosexual transmission of HIV in hemophiliacs. *Abstr 4008 IV International Conference on AIDS, June 12-16, 1988, Stockholm.*
- Tsang VCW, Hancock K, Wilson M, Palmer DF, Whaley SD, McDougal JS, Kennedy S: "Enzyme-Linked Immuno-electro-transfer Blot Technique (Western blot) for Human T-Lymphotropic Virus Type III/Lymphadenopathy-Associated Virus (HTLV-III/LAV) Antibodies." Atlanta: Centers for Disease Control, 1986 (Immunology series no. 15, procedural guide).
- Thomas DG: Exact and asymptotic methods for the combination of 2×2 tables. *Comput Biomed Res* 8:423-446, 1975.
- Thomas DG, Gart JJ: A table of exact confidence limits for differences and ratios of two proportions and their odds ratios. *J*

- Am Stat Assoc 72:73-76, 1977.
23. Fleiss JL: "Statistical Methods for Rates and Proportions." New York: John Wiley & Sons, 1981, pp 13-15.
 24. Lehmann EL: "Nonparametrics--Statistical Methods Based on Ranks." San Francisco: Holden-Day Inc, 1975, pp 23-31.
 25. Peterman TA, Stoneburner RL, Allen JR, Jaffe HW, Curran JW: Risk of human immunodeficiency virus transmission from heterosexual adults with transfusion-associated infections. *JAMA* 259:55-58, 1988.
 26. Centers for Disease Control: Prevention of acquired immune deficiency syndrome (AIDS). *MMWR* 32:101-104, 1983.
 27. National Hemophilia Foundation: "AIDS Update: Hemophilia and Acquired Immune Deficiency Syndrome (AIDS): Intimacy and Sexual Behavior." New York: National Hemophilia Foundation, 1985.
 28. Centers for Disease Control: Recommendations for assisting in the prevention of perinatal transmission of human T-lymphotropic virus type III/lymphadenopathy-associated virus and acquired immunodeficiency syndrome. *MMWR* 34:721-726, 731-732, 1985.
 29. Centers for Disease Control: Condoms for prevention of sexually transmitted diseases. *MMWR* 37:133-137, 1988.
 30. Centers for Disease Control: Additional recommendations to reduce sexual and drug abuse-related transmission of human T-lymphotropic virus type III/lymphadenopathy-associated virus. *MMWR* 35:152-155, 1986.
 31. National Hemophilia Foundation: "Hemophilia Information Exchange: Intimacy, Sexuality and Hemophilia." New York: National Hemophilia Foundation, 1987.
 32. Waterbury, MGray GL, Scott J, Kessler CM, Sachse K: "Safer Sex: Guidelines for the Prevention of Transmission of the AIDS Virus." Washington, DC: Children's Hospital National Medical Center, 1987.
 33. Nimorwicz P: "What Women Should Know About HIV Infection AIDS and Hemophilia." New York: National Hemophilia Foundation, 1988.
 34. Levine SB: "Let's Talk About Sex." New York: National Hemophilia Foundation, 1988.
 35. Hargraves MA, Jason JM, Chorba TL, Holman RC, Dixon GR, Eastham CJ, Brownstein AP, Heine P, Agle DP, Evatt BL, Hemophilia/AIDS Collaborative Study Group: Hemophiliac patients knowledge and educational needs concerning acquired immunodeficiency syndrome. *Am J Hematol* 26:115-134, 1987.
 36. Wasserman K, Wilson PA. Psychosocial impact of AIDS. 19A, Abstracts of the 39th Annual meeting of the National Hemophilia Foundation, Omaha, NE, October 9-10, 1987.
 37. National Center for Health Statistics, Dawson DA, Cynamon M, Fitti JE: AIDS knowledge and attitudes for October 1987. Provisional data from the National Health Interview Survey. Advance Data from Vital and Health Statistics. No. 150. DHHS Pub. No. (PHS) 88-1250. Public Health Service. Hyattsville, MD.