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Human Immunodeficiency Virus Infection in Mexico City

Rectal Bleeding and Anal Warts as Risk Factors among Men Reporting Sex with Men

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The objectives of this study were to evaluate the frequency and determinants of rectal bleeding and the association between rectal bleeding and risk of human immunodeficiency virus (HIV) infection among homosexual/bisexual men in Mexico City. Men who requested anonymous HIV testing at a public clinic in Mexico City and who reported engaging in any homosexual behavior were eligible to participate in this study. Trained staff collected information on demographic factors, sexual behavior, psychological states, and HIV serostatus from all consenting, eligible clients. Logistic regression modeling was used to investigate the independent effect of risk factors among 2,758 men who were tested between June 1991 and December 1992. Bleeding during anal intercourse was a common occurrence: More than one third of the men in the study reported some bleeding, and 8% reported bleeding in half or more of their intercourse episodes. The prevalence of HIV infection among bleeders was 42% as compared with 28% in nonbleeders ($p < 0.0001$), and the adjusted odds ratio was 1.8 (95% confidence interval (CI) 1.1–2.8) for men who bled in more than half of their anal intercourse episodes relative to nonbleeders. There was a trend of increasing HIV seroprevalence with increasing frequency of rectal bleeding ($p = 0.001$). Nine percent of all HIV infections and 42% of infections among frequent bleeders were attributable to rectal bleeding. Men who reported both rectal bleeding and anal warts were 3.5 (95% CI 2.1–5.8) times more likely to be HIV-infected in multivariate analysis than men reporting neither rectal bleeding nor anal warts. Determinants of rectal bleeding included older age, more education, more receptive anal intercourse than insertive intercourse, receptive digital-anal contact, anal warts, and genital ulcers. Among men reporting sex with men in Mexico City, rectal bleeding is common. It is an independent risk factor for HIV infection, and warrants attention in acquired immunodeficiency syndrome prevention efforts. Rectal bleeding that results from rupture of anal warts may be an especially effective portal of HIV transmission. *Am J Epidemiol* 1996;144:817–27.

acquired immunodeficiency syndrome; anus; health promotion; HIV infections; homosexuality; rectum; sex behavior; warts

The epidemic of human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) is spreading in Mexico, with a national incidence rate of AIDS that has risen from 0.07 per million population in 1984 to 58.4 per million in 1993 (1). The cumulative total number of AIDS cases as of February 1994 was 17,919, the third highest absolute number and the seventh highest incidence rate in the Americas (1). The epidemic in Mexico has a unique pattern in which male homosexual (25.8 percent) and male bisexual (18.0 percent) behavior has accounted for the majority of reported AIDS cases as of February 1994. Intravenous drug use is rare, accounting for less than 1 percent of AIDS cases, and heterosexual transmission accounts for a small (19 percent) albeit growing proportion of AIDS cases.

Much remains unknown about HIV transmission via sexual behavior. Some individuals become HIV-infected after a single or a few sexual encounters with an HIV-infected partner, whereas others remain uninfected despite hundreds of unprotected sexual contacts

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Abbreviations: AIDS, acquired immunodeficiency syndrome; CI, confidence interval; HIV, human immunodeficiency virus; OR, odds ratio; STD, sexually transmitted disease.

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(2, 3). Knowledge of risk factors for transmission is essential for the design and evaluation of prevention programs (4).

Higher levels of infectiousness have been found during the development of symptoms of AIDS (5–10) and very soon after HIV infection (11–13). The presence of other sexually transmitted diseases (STDs), particularly ulcerative STDs, increases the infectiousness of the infected partner and the susceptibility of the noninfected partner by facilitating the transit of the virus across mucous membrane or epithelial surfaces (14, 15). Among types of sexual intercourse, receptive anal intercourse is a more effective route of HIV transmission than insertive anal intercourse (16), receptive vaginal intercourse among women (17, 18), and oral intercourse (19).

One of the factors that has been found to increase the probability of male-to-female HIV transmission is bleeding during vaginal intercourse (5, 18). Although it is commonly assumed that lacerations in the mucosal lining of the anus and rectum are responsible for the increased effectiveness of HIV transmission in anal intercourse relative to vaginal intercourse, there is inconclusive scientific evidence for this assumption. Two prospective studies conducted in 1986 in the United States (20–22) tested the hypothesis that rectal bleeding increases the risk of HIV transmission. One prospective study reported a positive association (20). In contrast, the other prospective study of over 3,000 men reported a null association in the longitudinal study (21) but a positive association in the baseline, cross-sectional study (22). In addition, to our knowledge, no research has evaluated whether rectal bleeding during anal intercourse has decreased over calendar time with the adoption of safer sex practices among homosexual/bisexual men. Furthermore, a review of US and Mexican safe-sex educational materials for gay men indicated that none specifically mention or discuss rectal bleeding during anal intercourse (J. A. Izazola, CONASIDA, personal communication, 1993). If rectal bleeding does facilitate HIV transmission during anal intercourse, prevention programs need to emphasize the importance of avoiding this phenomenon.

The objectives of this study were to evaluate the reported frequency of rectal bleeding, the determinants of rectal bleeding, and the interactions between rectal bleeding and other risk factors with HIV infection among homosexual/bisexual men in Mexico City, and to investigate whether rectal bleeding is an independent risk factor for HIV transmission. This study follows up on an earlier study conducted at the same national HIV testing center, in which a significant association between reported rectal bleeding and HIV infection was found, with an adjusted odds ratio of 3.5 (16).

MATERIALS AND METHODS

Study population

Men who visited a center in Mexico City (the CONASIDA-Flora testing center) to obtain an anonymous, free test for HIV infection between June 1991 and December 1992 were eligible to participate in the study. Informed consent for HIV testing and participation in the study was obtained, and the men were then asked to complete a structured questionnaire before being tested. The study protocol was approved by the Harvard School of Public Health Institutional Review Board and the Mexican Ministry of Health. All participants received pretest counseling, and HIV test results were communicated by specially trained personnel, always maintaining confidentiality. The testing center at this site provides free, confidential testing, counseling, education, and condom distribution for HIV/AIDS prevention, and is one of the few sites in Mexico City that provide these services free of charge.

Of the 4,327 men for whom HIV test and questionnaire data were available, 2,978 men (68.8 percent) reported ever having had sex with men. Of those 2,978 men, 2.4 percent had missing data on their HIV test results, 1.3 percent had missing data on rectal bleeding, and 4.3 percent did not have reported data on the lifetime number of partners with whom they had engaged in receptive anal intercourse. The size of the final sample for analysis was 2,758.

Outcome measurement

HIV infection prevalence was assessed by second generation enzyme-linked immunosorbent assay, and positive results were confirmed by Western immunoblotting (Organon Teknika, Durham, North Carolina). Only serum samples that tested positive in both assays were considered positive (23).

Exposure measurement

A pretested, structured questionnaire was initially self-administered, after which a trained psychologist reviewed the questionnaire with the interviewee, paying special attention to missing answers. The questionnaire collected information about sexual behaviors, history of STDs, HIV disease-related symptoms, and psychological variables.

The exposure of interest for this research, the occurrence of rectal bleeding during receptive anal intercourse, was assessed by a question regarding how often during his sexual activities the subject had no-

ticed blood coming out of his anus. ("Durante sus contactos sexuales, han notado sangrado proveniente de su ano?") The answer had five levels (1 = always, 5 = never). Other sexual behaviors were assessed in a similar manner.

History of STDs was assessed by questions regarding whether or not the respondent had been diagnosed with an STD in his lifetime and during the previous 6 months. Attitude toward condom use, safe-sex self-efficacy, and knowledge of HIV/AIDS were assessed by a series of questions concerning each construct of interest. The reliability of these scales was measured by internal consistency using Cronbach's alpha; the alpha values for these scales were 0.64, 0.59, and 0.57 respectively, suggesting a fair to good level of internal consistency for the scales. The Center for Epidemiologic Studies Depression Scale (24) was used to assess levels of depressive symptoms.

Statistical analysis

Univariate relations between potential predictors of rectal bleeding and HIV serostatus were assessed using χ^2 tests and odds ratios. Multiple logistic regression models were fitted to control for multiple confounders. In determining confounders of the association between rectal bleeding and HIV infection, model selection kept a priori important variables in the model and included other variables that changed the estimated exposure effect by 10 percent or more (25).

Interaction effects of rectal bleeding with unprotected receptive anal intercourse and anal warts were assessed in logistic regression models where terms for both the independent effects and the interaction were included. Estimates of 95 percent confidence intervals for independent and interaction effects were obtained from these models, and the statistical significance of the interaction effects was assessed by likelihood ratio test.

The predictors of rectal bleeding, which was an ordinal variable ranging from "never" to "always," were determined using binary logistic regression with a dichotomous outcome (any vs. none) and by ordinal logistic regression with an ordinal outcome (frequently or sometimes vs. none) (26). The results did not differ significantly using these two methods, so the simpler binary logistic regression analysis was used.

RESULTS

Characteristics of the study population

Table 1 gives the characteristics of the study population, as well as the univariate differences between HIV-positive and HIV-negative men. Men who were infected with HIV differed significantly in terms of demographic factors from noninfected men in that infected men were more likely to be older and less educated than noninfected men. HIV-positive men were significantly more likely to report rectal bleeding during sex, but not blood or cuts on the penis. In terms of sexual behavior, HIV-positive men reported significantly more lifetime numbers of male partners, more receptive anal intercourse partners (i.e., partners with whom the subject was receptive), and fewer female partners. They were more likely to be exclusively homosexual rather than bisexual, were more likely to engage in receptive anal intercourse, were more likely to be both receptive and insertive in a given sexual encounter versus only receptive or only insertive, and were more likely to meet their partners in places of anonymous sex, such as bathhouses and gay cinemas. HIV-infected men were more likely to report condom use during receptive anal intercourse, possibly because they had already developed symptoms of HIV-related disease and thus suspected that they were HIV-positive (men who reported having symptoms were more likely to use condoms than nonsymptomatic men). HIV-infected men reported less frequently receiving a sexual partner's fist ("fisting") or hand in their anus. HIV-infected men reported a significantly greater experience of STDs than noninfected men.

In terms of psychological characteristics, HIV-positive men had a significantly less positive attitude toward condom use. They reported more depressive symptoms than noninfected men in univariate analysis but not in multivariate analysis. There were no significant differences with regard to knowledge of HIV/AIDS, sense of self-efficacy in initiating and maintaining safe sex, or alcohol's influencing the initiation of sex. However, 80 percent (2,213/2,758) of men reported that alcohol influenced them to initiate sex in more than half of their sexual contacts.

Predictors of rectal bleeding

Table 2 shows the predictors of rectal bleeding in univariate and multivariate analysis. Men reporting rectal bleeding were significantly older and more educated. Sexual behaviors associated with increased rectal bleeding were number of receptive anal intercourse partners (i.e., partners with whom the subject was receptive) and the practice of "fisting." Men who reported always using condoms during receptive anal intercourse had significantly less rectal bleeding than men who never or almost never used condoms. A lifetime history of anal warts and genital ulcers was reported significantly more frequently by rectal bleeders than by nonbleeders. There were, however, no significant differences in syphilis, gonorrhea, or herpes simplex virus infection.

TABLE 1. Self-reported characteristics of homosexual and bisexual men tested for human immunodeficiency virus (HIV) in Mexico City between June 1991 and December 1992, by HIV serostatus (n = 2,758)

Characteristic (mean or %)	HIV+ (n = 939)	HIV− (n = 1,819)	p value for difference*
Demographic factors			
Age (years)	29.8	27.2	<0.001
University education (%)	37.9	42.3	0.025
Married (%)	5.4	7.3	0.056
Rectal bleeding during sex (%)			
Never	51.2	65.9	<0.001
Sometimes	37.9	26.3	<0.001
From half the time to always	10.8	7.4	0.003
Blood or cuts on the penis during sex (%)			
Never	73.0	75.1	0.248
Sometimes	22.1	20.0	0.212
From half the time to always	4.9	4.9	0.993
Sexual behavior			
Lifetime no. of male partners	47.0	29.2	<0.001
Lifetime no. of RAI† partners	27.4	15.1	<0.001
Lifetime no. of female partners	4.7	7.5	<0.001
Unprotected RAI during sex (%)	51.0	39.1	<0.001
Both insertive and receptive intercourse versus only one or neither (%)	41.9	28.0	<0.001
Anonymous partner score‡	17.1	13.2	<0.001
Condom use (% of receptive anal intercourse episodes)	41.4	38.3	0.038
Receiving partner's fist or hand in anus (% ever)	15.7	19.2	0.022
Bisexual (ever having a male partner versus never) (%)	54.2	59.9	0.004
History of sexually transmitted diseases (lifetime) (%)			
Any sexually transmitted disease in lifetime	33.1	20.3	<0.001
Anal warts	7.8	3.6	<0.001
Syphilis	9.2	3.5	<0.001
Gonorrhea	23.3	15.1	<0.001
Genital ulcers	4.8	2.9	0.009
Herpes simplex	2.2	1.8	0.387
Psychological factors			
Positive attitude toward condom use§	70.0	71.5	0.015
Depressive symptoms score (CES-D‖)	17.2	14.8	<0.001
Knowledge of HIV/acquired immunodeficiency syndrome¶	51.5	49.9	0.290
Safe-sex self-efficacy score#	74.2	75.3	0.155
Alcohol influencing initiation of sex half or more times (%)	81.0	79.9	0.466

* p values for difference were determined by χ^2 test for categorical variables and Kruskal-Wallis test for ordinal and continuous variables.
† RAI, receptive anal intercourse. (Refers to partners with whom the subject was receptive).
‡ Based on six questions on where partners were met. Scores ranged from 0 to 100. High score = more anonymous.
§ Based on six questions on attitudes toward condom use. Scores ranged from 0 to 100. High score = more positive.
‖ CES-D, Center for Epidemiologic Studies Depression Scale. Possible scores ranged from 0 to 60. High score = more depressed.
¶ Based on 10 questions. Possible scores ranged from 0 to 100. High score = more knowledge.
# Based on six questions on perceived ability to adopt and maintain safe-sex practices. Score ranged from 0 to 100. High score = greater ability.

Association of rectal bleeding and other risk factors with HIV infection

Table 3 lists the significant predictors of HIV infection. The overall prevalence of HIV infection was 32.8 percent. Rectal bleeding was significantly associated with HIV serostatus. Men reporting rectal bleeding were significantly more likely to be HIV-infected than nonbleeders (42 percent vs. 28 percent, $p < 0.0001$).

TABLE 2. Determinants of rectal bleeding among homosexual and bisexual men in Mexico City, June 1991–December 1992 (n = 2,758)

Characteristic	Rectal bleeding (%)	Total no.	Crude OR†	Adjusted OR‡	95% CI†
Demographic factors					
Age (years)					
<20	27.2	221	1.0	1.0	
20–24	38.0	792	1.6	1.5	1.08–2.2*
25–29	39.1	727	1.7	1.4	0.96–2.0
≥30	41.7	1,018	1.9	1.5	1.05–2.1*
Total	38.8	2,758			
Education					
None/primary	31.8	494	1.0	1.0	
Secondary	37.1	399	1.3	1.4	1.01–1.9*
Tertiary	39.7	739	1.4	1.5	1.13–1.9**
University	41.8	1,126	1.5	1.5	1.17–1.9***
Sexual behavior					
No. of RAI† partners§ (lifetime)					
0	6.9	520	1.0	1.0	
1–2	29.9	615	5.7	5.3	3.59–7.73***
3–7	46.5	606	11.7	10.8	7.41–15.8***
8–29	54.7	530	16.2	14.9	10.1–21.8***
≥30	56.9	487	17.7	16.1	10.9–23.7***
Partner's fist or hand in anus					
No	36.0	2,262	1.0	1.0	
Yes (ever)	51.4	496	2.0	1.6	1.27–1.9***
Condom use during RAI					
Never/almost never	40.3	1,339	1.0	1.0	
Half the time	48.0	252	1.4	0.84	0.60–1.2
Almost always	51.0	396	1.5	1.2	0.89–1.6
Always	40.0	433	1.0	0.61	0.48–0.78***
History of STDs† (lifetime)					
Anal warts					
No	38.0	2,619	1.0	1.0	
Yes	54.0	139	1.9	1.6	1.13–2.4**
Genital ulcer					
No	38.1	2,661	1.0	1.0	
Yes	55.7	97	2.0	1.8	1.15–2.9**
Syphilis					
No	37.9	2,608	1.0	1.0	
Yes	54.0	150	1.9	1.2	0.85–1.7
Gonorrhea					
No	37.7	2,265	1.0	1.0	
Yes	43.6	493	1.3	1.1	0.89–1.4

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.
† OR, odds ratio; CI, confidence interval; RAI, receptive anal intercourse; STD, sexually transmitted disease.
‡ Adjusted for lifetime number of receptive anal intercourse partners, age, education, receptive "fisting," symptoms of human immunodeficiency virus disease, and history of STDs. See "Materials and Methods" for model selection procedures.
§ Refers to partners with whom the subject was receptive.

The adjusted odds ratios were 1.3 (95 percent confidence interval (CI) 1.1–1.6, $p = 0.003$) for men who "sometimes" bled and 1.8 (95 percent CI 1.1–2.8, $p = 0.017$) for men who bled in more than half to all of their anal intercourse episodes, relative to nonbleeders. A trend of increasing odds ratios with increasing frequency of reported rectal bleeding was statistically significant ($p = 0.001$). The association between rectal bleeding and HIV infection was not modified by level of reported condom use during receptive anal intercourse.

Other predictors of HIV infection status were older age, less education, more lifetime receptive anal intercourse partners, the practice of both receptive and insertive anal intercourse in any given sexual encounter (versus only receptive or only insertive inter-

TABLE 3. Risk factors for human immunodeficiency virus (HIV) infection status, including rectal bleeding, in multivariate analysis among homosexual and bisexual men in Mexico City, June 1991–December 1992 (n = 2,758)

Characteristic	HIV+ (%)	No.	Crude OR†	Adjusted OR‡	95% CI†
Rectal bleeding during sex					
Never	28.5	1,689	1.0	1.0	
Almost never	42.7	834	1.8	1.3	1.11–1.62**
Half the time	42.2	147	1.8	1.3	0.91–1.88
Almost always/always	44.3	88	2.0	1.8	1.11–2.82**
Total	34.1	2,758			
Demographic factors					
Age (years)					
<20	12.2	221	1.0	1.0	
20–24	24.9	792	2.4	2.4	1.55–3.77***
25–29	35.8	727	4.0	4.1	2.62–6.83***
≥30	44.7	1,018	5.8	5.9	3.81–9.15***
Education					
None/primary	39.5	494	1.0	1.0	
Secondary	36.8	399	0.89	0.98	0.73–1.31
Tertiary	32.6	739	0.74	0.75	0.58–0.97*
University	31.6	1,126	0.71	0.56	0.44–0.71***
Sexual behavior					
No. of RAI† partners§ (lifetime)					
0	15.4	520	1.0	1.0	
1–2	28.6	615	2.2	2.3	1.68–3.12***
3–7	34.7	606	2.9	2.6	1.90–3.59***
8–29	43.6	530	4.2	3.3	2.40–4.67***
≥30	49.7	487	5.4	3.8	2.73–5.26***
Receiving partner's fist or hand in anus					
Never	35.0	2,262	1.0	1.0	
Ever	29.6	496	0.78	0.70	0.56–0.88***
Anal intercourse role					
Entirely or mostly receptive	38.0	597	1.0	1.0	
Both receptive and insertive	43.6	901	1.3	1.5	1.18–1.87***
Entirely or mostly insertive	28.4	762	0.64	1.1	0.83–1.43
No/almost no anal intercourse	20.7	489	0.42	0.94	0.67–1.31
Sexually transmitted diseases (ever)					
Anal warts					
No	33.1	2,619	1.0	1.0	
Yes	52.5	139	2.2	1.8	1.22–2.52**
Syphilis					
No	32.7	2,608	1.0	1.0	
Yes	57.3	150	2.8	1.7	1.16–2.34**

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

† OR, odds ratio; CI, confidence interval; RAI, receptive anal intercourse.

‡ Obtained from multiple logistic regression analysis, controlling for the following confounders: age, education, lifetime number of receptive anal intercourse partners, condom use, "fisting" practice, usual anal intercourse role (insertive/receptive), and lifetime history of syphilis or condyloma. See "Materials and Methods" for model selection procedures.

§ Refers to partners with whom the subject was receptive.

course), less fisting or digital-anal contact, and a reported history of syphilis and anal warts.

Variables that were not associated with HIV serostatus in univariate and multivariate analyses were condom use, circumcision, penile bleeding, knowledge of HIV/AIDS, perceived safe-sex self-efficacy, lifetime number of insertive anal intercourse partners, lifetime number of oral intercourse partners, and all measures of recent sexual behavior (in the previous 3 months). Variables that were associated with HIV infection prevalence in univariate analysis but not multivariate analysis were anonymous partner score, meeting part-

ners in bathhouses, having a positive attitude toward condom use, having depressive symptoms, and homosexual or bisexual orientation.

Modification of the relation between unprotected receptive anal intercourse and risk of HIV infection by rectal bleeding

When examined separately and in combination (figure 1), rectal bleeding alone in the absence of receptive anal intercourse was not a significant predictor of HIV serostatus (OR = 1.2, 95 percent CI 0.38–3.9); receptive anal intercourse (any) alone was a significant predictor of HIV serostatus (OR = 3.0, 95 percent CI 2.1–4.3); and rectal bleeding in combination with receptive anal intercourse had more than a multiplicative effect over the individual effects combined (OR = 4.4, 95 percent CI 3.0–6.3). Thirty-six individuals (1.3 percent) reported rectal bleeding in the absence of receptive anal intercourse, possibly caused by internal hemorrhoids.

Effect modification of the relation between rectal bleeding and HIV infection by anal warts

A reported history of anal warts was a strong modifier of the effect of rectal bleeding (figure 2). The individual association of rectal bleeding (any) with HIV infection had an odds ratio of 1.3 (95 percent CI 1.1–1.6). The individual association of reported lifetime history of anal warts in the absence of rectal bleeding was null (OR = 1.2, 95 percent CI 0.69–2.1). However, in multivariate analysis, men who reported both rectal bleeding and anal warts were 3.5 times (95 percent CI 2.1–5.8) more likely to be HIV-infected than men who reported neither risk factor. No multiplicative association between rectal bleeding and syphilis or herpes simplex infection was seen, but a weak multiplicative effect between rectal bleeding and gonorrhea was found. Since anal warts may be more florid in HIV-infected individuals (27), HIV-related disease may increase the symptoms of anal warts, which may in turn exacerbate rectal bleeding, leading to a false association of anal warts and rectal bleeding with HIV infection. However, the estimates of interaction between rectal bleeding, anal warts, and HIV were almost identical among men with (OR = 3.6, 95 percent CI 1.0–13.2) and without (OR = 3.4, 95 percent CI 1.9–6.2) HIV-related symptoms.

Rectal Bleeding	Receptive anal intercourse: No		Receptive anal intercourse: Yes	
No	1.0	{13.8%}	3.0 (2.1-4.3)	{32.8%}
Yes	1.2 (0.38-3.9)	{14.8%}	4.4 (3.0-6.3)	{42.6%}

FIGURE 1. Modification of the association between rectal bleeding and human immunodeficiency virus (HIV) infection by receptive anal intercourse, Mexico City, Mexico, June 1991–December 1992. Adjusted odds ratios* are shown. Numbers in parentheses, 95% confidence interval; numbers in braces, percentage HIV-positive. (*Estimate of odds ratios obtained from the sum of coefficients for independent effects and the interaction term obtained from multiple logistic regression, controlling for age, education, lifetime number of receptive anal intercourse partners, condom use, digital-anal activity, usual anal intercourse role (insertive/receptive), and history of syphilis or condyloma. See "Materials and Methods" for model selection procedures.)

Rectal Bleeding	Anal Warts: No		Anal Warts: Yes	
No	1.0	{27.2%}	1.2 (0.69-2.1)	{34.1%}
Yes	1.3 (1.1-1.6)	{39.7%}	3.5 (2.1-5.8)	{67.9%}

FIGURE 2. Modification of the association between rectal bleeding and human immunodeficiency virus (HIV) infection by anal warts, Mexico City, Mexico, June 1991–December 1992. Adjusted odds ratios* are shown. Numbers in parentheses, 95% confidence interval; numbers in braces, percentage HIV-positive. (*Estimate of odds ratios obtained from the sum of coefficients for independent effects and the interaction term obtained from multiple logistic regression, controlling for age, education, lifetime number of receptive anal intercourse partners, condom use, digital-anal activity, usual anal intercourse role (insertive/receptive), and history of syphilis. See "Materials and Methods" for model selection procedures.)

DISCUSSION

The findings of this study support the hypothesis that rectal bleeding during receptive anal intercourse has an independent effect on increasing the risk of HIV infection. Men who reported bleeding during most of their sexual contacts had an 80 percent higher risk of HIV infection after data were controlled for confounders. There was a dose-response relation in the rectal bleeding-HIV association, and the test for trend was highly significant. Nine percent of all HIV infections in the population studied were attributable to rectal bleeding, and 42 percent of HIV infections among bleeders were attributable to rectal bleeding. No similar effect of increasing risk with blood on the penis of the insertive partner was found, which suggests that the risk of infection associated with bleeding is to the receptive partner rather than the insertive partner. However, the results of this study indicate that any unprotected anal intercourse is potentially dangerous for acquiring HIV infection.

Other factors associated with higher HIV seroprevalence were older age, a greater number of receptive anal intercourse partners, less education, practicing

both receptive and insertive anal intercourse as opposed to only receptive or only insertive intercourse, and never practicing "fisting" or digital-anal contact. Condom use during receptive anal intercourse and all of the psychological constructs examined were not associated with HIV seroprevalence. Determinants of rectal bleeding were: multiple receptive anal intercourse partners, fisting or digital-anal contact, a history of anal warts or genital ulcers, older age, more education, and never use of condoms.

The mechanism by which rectal bleeding during receptive anal intercourse increases the risk of HIV infection is not clear; however, it is probably by providing a lesion on the mucocutaneous surface of the anus or rectum which acts as a portal of entry for the virus into the new host. The strong relations between rectal bleeding and lifetime number of receptive anal intercourse partners and fisting suggest that rectal bleeding occurs when the anal sphincteric muscles adapt and loosen from frequent sexual activity and thus more stretching and friction during intercourse are necessary to produce the same amount of sexual stimulation. We hypothesize that modification of the effect of rectal bleeding on HIV infection risk by anal warts occurs because the protrusions formed on the anal mucosa by anal warts are susceptible to rupture during the friction of anal intercourse. These ruptures may cause bleeding and the formation of large lacerations which may act as effective portals for virus entry across the mucous membrane of the receptive partner. Reopening of a previous rupture may provide an abundance of target cells for HIV that resulted from an earlier immune response with activated CD4 cells at the site of the wound (28, 29).

The observed association between rectal bleeding and HIV infection risk could be due to confounding, bias, or chance, or it could be a true effect. Confounding is unlikely, however, because we controlled for number of receptive anal intercourse partners and lifetime history of STDs, as well as other confounders. Residual confounding is unlikely because self-reports of high risk behavior for HIV transmission have been found to be accurate and correlated with HIV seroconversion rates (4, 30), and the crude and adjusted odds ratios were quite similar among frequent bleeders in this study. However, because our measures of number of sexual partners and prevalence of HIV infection in a sexual network were only approximate, these results must still be interpreted with caution.

Misclassification of rectal bleeding and history of STDs due to self-reporting is improbable, since there is no apparent motivation for incorrectly overreporting rectal bleeding when it does not occur. In contrast, it is likely that misclassification of rectal bleeding may occur among men who report no rectal bleeding, because they are unaware of or do not notice their rectal bleeding or are embarrassed to report it. The effect of this differential misclassification would be to underestimate the true effect, since rectal bleeding was parameterized as a dichotomous or polytomous variable and not as a continuous variable. Differential misclassification away from the null could occur if HIV-negative men were more likely to underreport rectal bleeding than HIV-positive men. However, most of these men did not know their HIV serostatus at the time of interview, and the association between bleeding and HIV was similar among men with (OR = 1.5, 95 percent CI 1.01–2.3) and without (OR = 1.3, 95 percent CI 1.03–1.60) symptoms of HIV-related disease. A similar argument applies to misclassification of STDs.

In this cross-sectional study, the causal sequence of events is unclear; thus, ulcerative STDs may cause rectal bleeding and enhance HIV transmission, or rectal bleeding may facilitate acquisition of HIV and other STDs. To clarify this issue, we compared the measure of association between rectal bleeding and HIV among people who reported no STDs versus those who reported a history of STDs, excluding anal warts. The odds ratio was essentially unchanged, suggesting that ulcerative STDs are not likely to be the cause of both rectal bleeding and increased HIV infection risk; this supports the hypothesis that rectal bleeding is an independent determinant of HIV risk.

HIV-related immunodeficiency may increase the prevalence of intestinal amebiasis, which is found fairly commonly among men engaging in sex with men in Mexico (31). However, amebiasis rarely causes bleeding, and the bleeding is usually accompanied by diarrhea. In addition, it appears that HIV infection does not increase the incidence of amebiasis or its complications (32).

Chance is an unlikely explanation for these findings, because these results are consistent with those from earlier analysis (16) of a separate sample of men who visited the same testing center in Mexico City during the period immediately preceding this study (1990–1991). In this earlier analysis of 731 homosexual and bisexual men, HIV seroprevalence among men who reported that they bled one half to all of the time when they had anal sex was 54 percent, compared with 26 percent in those reporting no bleeding (OR = 3.26, $p < 0.0001$) (16). In multivariate analysis controlling for 15 variables, this odds ratio increased to 3.45. In addition, the increase in the adjusted odds ratio relative to the unadjusted odds ratio indicates that residual confounding is unlikely.

The high prevalence of HIV infection among men visiting the testing site indicates that this is a sample of men at high risk for HIV infection. A population-based study of HIV infection among men reporting sex with men in Mexico City estimated the prevalence of HIV infection to be 4 percent (33). To our knowledge, no population-based estimates of the frequency of rectal bleeding during anal intercourse among homosexual/bisexual men are available for Mexico or the United States. This indicates a need for further data collection on this behavior.

No protective effect of condom use was observed in this study, although condoms have been shown to be effective in limiting the transmission of STDs, including HIV (4, 34–36). However, condoms may be used more frequently by individuals who engage in higher risk sexual activity or by individuals who develop symptoms of HIV-related disease because they suspect they are HIV-infected. Reported condom use was associated with more receptive anal intercourse, and was higher among men with HIV-related symptoms.

The higher prevalence of HIV infection among men practicing both insertive and receptive anal intercourse during a given sexual encounter, compared with men who were uniquely receptive or insertive, confirms a similar finding of an earlier study of men who visited the same center in Mexico City between 1990 and 1991 (22) and a study of men in six Mexican cities (37). Trichopoulos et al. (38) have argued that role separation during homosexual intercourse is protective against HIV infection, for several reasons: 1) uniquely insertive men are less likely to acquire HIV infection than men practicing mixed behavior, because insertive anal intercourse is a less efficient transmission route for HIV than receptive anal intercourse, and 2) uniquely receptive men are likely to choose sexual partners who have a low prevalence of HIV infection because these partners are more likely to be uniquely insertive.

The sixfold higher HIV seroprevalence in older men compared with younger men, regardless of number of sexual partners, may result from sexual activity that took place before AIDS prevention and education messages were widespread, and reflects HIV infection rates several years prior to the study interview, when high risk sexual practices were more frequent and condom use was lower.

The finding in this study that anal warts are independently associated with HIV infection among gay men has been reported previously (39, 40). Other investigators have hypothesized that the association is caused by increased expression of human papilloma virus as a sequela of early immune deficiency associated with HIV-related disease (40, 41). However, our findings suggest that the association between anal warts and HIV is mediated by rectal bleeding. There was no association between anal warts and HIV infection in men who reported no rectal bleeding (OR = 1.0, 95 percent CI 0.48–2.0). In addition, the estimates of interaction between rectal bleeding, anal warts, and HIV were almost identical among men with (OR = 3.6, 95 percent CI 1.0–13.2) and without (OR = 3.4, 95 percent CI 1.9–6.2) HIV-related symptoms. The similarity of these interaction estimates suggests that the interaction between rectal bleeding and anal warts is not caused by HIV infection's increasing the expression of human papilloma virus, and suggests that anal warts are associated with HIV infection because they are likely to bleed during the friction of anal intercourse. In contrast, herpes simplex virus infection, syphilis, and gonorrhea do not form protrusions that bleed upon friction. The ulceration or inflammation caused by syphilis or gonorrhea can be quickly and effectively treated with antibiotics, and therefore the disturbance to the integrity of the rectal mucosa usually has a short half-life.

The public health message from these results is to completely avoid unprotected anal intercourse in order to prevent HIV transmission or acquisition. However, 39 percent of the men in this study reported some rectal bleeding during anal intercourse; therefore, a harm reduction approach to limiting HIV infection is to promote avoidance of rectal bleeding. A potential public health intervention would be the provision of water-based lubricants (since oil-based lubricants may affect the integrity of latex condoms), social marketing to increase their use, and education regarding the risk of rectal bleeding to homosexual and bisexual men in Mexico City. Only 25 percent of these men reported using lubrication with condoms, and they were not asked any questions about use of lubrication when condoms were not used. There is a surprising dearth of information in the literature on practices used by homosexual/bisexual men to avoid rectal bleeding during anal intercourse.

Other potential interventions would be wider treatment of anal warts or vaccination against the types of human papilloma virus that cause anal warts. Vaccines against human papilloma virus are currently in phases I and II of development. Available treatments for exophytic warts include podofilox (Oclassen Pharmaceuticals, Inc., San Rafael, California), podophyllin (Paddock Laboratories, Inc., Minneapolis, Minnesota), cryotherapy, topical 5-fluorouracil (Roche Laboratories, Inc., Nutley, New Jersey), intralesional interferon, systemic interferon, and laser surgery (41). However, recurrence rates associated with all treatment options are high (41). In addition, scarring re-

sulting from laser surgical treatment may also pose a risk for bleeding.

In conclusion, rectal bleeding occurs commonly and is independently associated with HIV infection among men reporting sex with men in Mexico City. It is unlikely that this association is due to confounding, bias, or chance. The dose-response effect, the effect modification by receptive anal intercourse and anal warts, and the clear and very feasible biologic mechanism add support to the hypothesis that rectal bleeding is an independent determinant of the risk of acquiring HIV infection. Rectal bleeding that results from rupture of anal warts may be an effective portal of HIV transmission, and warrants further study. Further research on behavioral practices that cause rectal bleeding during anal intercourse is needed. Reduction of the frequency of rectal bleeding through education and intervention programs and providing easy access to water-based lubricants may be effective additions to AIDS prevention activities.

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