



# Risk factors for HIV infection in homosexual men: the Cleveland Men's Study of risks in a low-prevalence area

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■ Detailed questionnaires concerning alcohol and drug use, sexual practices, and medical history were completed by 301 homosexual men living in the Cleveland metropolitan area. Their sera were subsequently tested for antibodies to the human immunodeficiency virus. Fifty-six (18.6%) were seropositive. In a univariate analysis, age, drug use, and four specific sexual practices were associated with seropositivity. In a multiple logistic regression analysis, intravenous drug use and receptive anal-genital sex remained independent predictors of seropositivity.

□ INDEX TERMS: HIV INFECTIONS; RISK FACTORS; HOMOSEXUALITY; SEX BEHAVIOR □ CLEVE CLIN J MED 1992; 59:573-580

**H**OMOSEXUAL ACTIVITY remains a major risk for infection with the human immunodeficiency virus (HIV) in the United States and other developed countries. Several groups have examined the risk factors for HIV infection in homosexual men.<sup>1-10</sup> All have found receptive anal intercourse to be a risk factor for HIV infection. Other sexual practices and epidemiologic factors have been variably associated with HIV infection.

■ See editorial, p. 647

We report here the findings of the Cleveland Men's Study, an epidemiologic assessment of the Cleveland

gay community performed in 1984, at a place and time of low incidence of acquired immunodeficiency syndrome (AIDS). We present our findings and compare them with those in other communities.

## METHODS

From January through March 1984, 320 homosexual men responded to requests to participate in this study. The only criterion for exclusion was known AIDS. The requests were distributed primarily through advertisements in gay publications and via gay organizations. A few individuals were recruited from bars and a small number (11 men) were patients of an internist at a university-based medical center.

The participants filled out an anonymous self-administered questionnaire that dealt with demographic information, alcohol and drug use, sexual practices, and recent medical history. Each then underwent a directed physical examination and was asked to donate blood, although serologic tests for HIV infection were not available at that time. Serum was obtained from 301 (94%) of the participants, and these comprise the study group.

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**TABLE 1**  
DEMOGRAPHIC CHARACTERISTICS OF HIV INFECTION:  
THE CLEVELAND MEN'S STUDY (n=301)

Race	Total	% HIV-positive	Odds ratio	P
White	280 (93.6%)	17.8	1.00 <sup>†</sup>	.357
Nonwhite	19 (6.4%)	26.3	1.64	
	299			

  

Age (years)	Total	% HIV-positive	Odds ratio	P*
<21	10	20.0	2.30	.037
21-30	129	21.7	2.28	
31-40	111	19.8	2.09	
≥41	51	11.4	1.00 <sup>†</sup>	

\*Test for linear trend  
†Referent

All samples were subsequently tested for HIV antibodies by enzyme-linked immunosorbent assay (Litton Bionetics HTLV-III Bio-Enzabead test, Sunnyvale, Calif; or Genetic Systems LAV-EIA test, Seattle, Wash). All reactive sera were retested; only repeatedly reactive samples were considered positive.

For all statistical analyses, serostatus was the sole independent variable. Independent variables were first tested with the chi-square analysis of contingency table or, when appropriate, the chi-square test for trends.<sup>11</sup> Two-by-two tables were evaluated using the Yates (continuity) correction, and odds ratios with 95% confidence limits by the method of Woolf.<sup>11</sup> Factors significantly associated with seropositivity were noted for inclusion in the multivariate analyses. Analysis with a stepwise multiple logistic regression model was performed to identify independent predictors using the LR module of the BMDP statistical package.<sup>12</sup> Statistical significance was set at  $P < .05$ .

**RESULTS**

The mean age of the participants in the study group was 32.7, with the youngest participant 17 and the oldest 71 (Table 1). The majority were white (93.6%), with only 4.0% black, 2.0% Hispanic, and a sole participant who was Native American.

Fifty-six of the 301 participants tested positive for HIV antibodies (18.6%). Race was not significantly associated with serostatus, although 26% of nonwhites as opposed to 18% of whites were seropositive (Table 1). A significant difference in risk may have been missed due to the low number of nonwhite participants.

Also evident in Table 1 is a significant trend for serostatus by age. None of the participants over age 50 was HIV-seropositive, and the mean age of seropositive

**TABLE 2**  
ALCOHOL AND ILLICIT DRUG USE AND HIV INFECTION:  
THE CLEVELAND MEN'S STUDY (n=301)

	Total	% HIV-positive	Odds ratio	P
<b>Alcohol (drinks per week)</b>				
None	44	15.9	1.00 <sup>†</sup>	.089*
1-6	94	14.9	0.93	
7-24	130	19.2	1.26	
> 24	32	31.2	2.40	
<b>Beer (drinks per week)</b>				
None	127	13.4	1.00 <sup>†</sup>	.009*
1-6	109	20.2	1.64	
7-24	55	21.8	1.81	
> 24	10	50.0	6.47	
<b>Wine (drinks per week)</b>				
None	155	18.1	1.00 <sup>†</sup>	.920
Some	146	19.2	1.08	
<b>Liquor (drinks per week)</b>				
None	112	18.1	1.00 <sup>†</sup>	.738
Some	188	19.6	0.90	
<b>Amphetamine use since 1982</b>				
None	224	16.1	1.00 <sup>†</sup>	.002*
1-10	38	15.8	0.98	
11-100	25	24.0	1.65	
> 100	11	63.6	9.14	
<b>Intravenous drug use since 1982</b>				
None	288	17.4	1.00 <sup>†</sup>	0.022
Some	10	50.0	4.76	
<b>Marijuana use since 1982</b>				
None	129	17.2	1.00 <sup>†</sup>	.693
Some	169	19.2	1.18	
<b>Cocaine use since 1982</b>				
None	225	17.5	1.00 <sup>†</sup>	.380
Some	73	21.6	1.34	
<b>Quaalude use since 1982</b>				
None	267	17.7	1.00 <sup>†</sup>	.265
Some	31	25.0	1.63	

\*Test for linear trend  
†Referent

persons was 30.2 years, compared with 33.3 years for seronegative persons.

The weekly consumption of three types of alcohol (beer, wine, and "hard liquor") was examined for a relationship with seropositivity. Of these, only beer consumption was significantly associated with serostatus, with seropositivity increasing from 13.4% in those who did not drink beer to 50.0% in the heaviest beer drinkers (Table 2).

The association between serostatus and the use of a number of different types of recreational drugs also was analyzed (Table 2). When all drug use was considered, the use of recreational drugs was not significantly associated with seropositivity; however, when analyzed individually, use of amphetamines ( $P=.002$ ) or injected drugs ( $P=.022$ ) was associated with seropositivity.

The yearly number of different male sexual contacts during the preceding 4 years was grouped into four strata for clarity of analysis (Table 3). A significant trend by serostatus was found, and the percent of seropositives among sexually active homosexuals was highest for those with more than 20 different contacts per year.

The relationship between location of sexual encounters and HIV seropositivity was also examined. The number of times in which participants engaged in sex in bathhouses, back rooms, parks, rest areas, or high-prevalence cities (New York, Los Angeles, San Francisco) was analyzed for an association with serostatus. Table 3 lists the summary data for the frequency according to setting. Significant associations between serostatus and sexual encounters in any of these environments were seen only for the annual frequency of sex in a bathhouse and the yearly number of sexual contacts in New York City. The frequency of sex in a bathhouse was associated in a linear-trend fashion, with a seropositivity of 38.5% for respondents who averaged more than 20 contacts per year ( $P=.02$  to  $.04$  for each of the years 1980 to 1983). No associations were evident for group sex or sex at other locations. In addition, only frequency of sexual contact in New York City also was associated with seropositivity. Sexual contact in other high-risk cities was not associated with a greater risk of seropositivity, but too few subjects travelled to these regions to draw meaningful conclusions about risk associated with sexual contact there.

Of the 12 sexual practices examined, significant associations with serostatus were found for four (Table 4). These were receptive anal-genital contact, insertive anal-genital contact, receptive fisting, and insertive oral-anal contact. Four other practices were of borderline significance; passive and active manual-genital contact, receptive anal-oral contact, and insertive fisting. These associations were positive, ie, they were detrimental for all practices except active and passive manual-genital contact, which appeared to have a trend towards protection. The practice most strongly associated with seropositivity was receptive anal-genital contact ( $P<.0001$ ). It should be noted that the questionnaire asked only the number of times a specific practice was performed, not with how many different partners each practice was performed.

The only sexual practice that remained significantly associated with serostatus in the multiple logistic regression analysis (Table 5) was receptive anal-genital contact. When compared with persons who had not

TABLE 3  
SEXUAL ACTIVITY IN PRECEDING 4 YEARS (1980-83):  
THE CLEVELAND MEN'S STUDY (n=301)

	Total	% HIV-positive	Odds ratio	P
<b>Number of sexual contacts per year</b>				
None	1	—	1.00 <sup>†</sup>	.37
1-5	95	14.7	1.00 <sup>†</sup>	
6-20	82	14.7	1.00	
> 20	118	25.4	1.99	
Mean ± SD				
		HIV-positive: 49 ± 73	t=2.29; P=.026	
		HIV-negative: 24 ± 37		
<b>Engaged in group sex since 1982</b>				
None	157	14.0	1.00 <sup>†</sup>	.114*
1-5	105	24.8	2.02	
6-20	31	16.1	1.18	
20	6	33.3	3.07	
<b>Sex in a bathhouse (yearly frequency)</b>				
None	105	12.4	1.00 <sup>†</sup>	.003*
1-5	98	16.3	1.38	
6-20	45	22.2	2.02	
20	26	38.5	4.42	
<b>Sex in a back room (yearly frequency)</b>				
None	136	13.9	1.00 <sup>†</sup>	.124*
1-5	69	21.7	1.71	
6-20	40	20.0	1.54	
20	24	25.0	2.05	
<b>Sex in a rest area or park (yearly frequency)</b>				
None	178	18.0	1.00 <sup>†</sup>	.953*
1-5	54	16.7	0.91	
6-20	26	15.4	0.83	
20	13	23.1	1.37	
<b>Contacts per year in New York City</b>				
None	186	16.1	1.00 <sup>†</sup>	.022*
1-5	72	25.0	1.73	
6-20	10	40.0	3.47	
20	0	0	—	
<b>Contacts per year in San Francisco</b>				
None	216	17.6	1.00 <sup>†</sup>	.516*
1-5	42	23.8	1.46	
6-20	0	0	—	
20	1	0	—	
<b>Contacts per year in Los Angeles</b>				
None	227	17.6	1.00 <sup>†</sup>	.241*
1-5	32	31.3	2.13	
6-20	1	0	—	
20	1	0	—	
<b>Sex with someone who died later</b>				
No	129	17.8	1.00 <sup>†</sup>	.300
Yes	11	36.4	2.63	
Don't know	159	17.6	0.99	

\*Test for linear trend  
†Referent

**TABLE 4**  
SEXUAL PRACTICES AND SEROPOSITIVITY: CLEVELAND MEN'S STUDY (n=301)

	Total	% HIV-positive	Odds ratio	P		Total	% HIV-positive	Odds ratio	P
<b>Receptive anal-genital</b>					<b>Insertive digital-anal</b>				
None	87	9.2	1.00 <sup>†</sup>	.0001*	None	58	15.5	1.00 <sup>†</sup>	.457*
1-9	97	13.4	1.53		1-9	129	17.0	1.12	
10-49	79	38.6	3.81		10-49	87	22.9	1.63	
50-99	19	36.8	5.76		50-99	11	0	0	
≥ 100	13	38.5	6.17		≥ 100	11	27.3	2.04	
<b>Insertive anal-genital</b>					<b>Receptive oral-anal</b>				
None	63	9.5	1.00 <sup>†</sup>	.033*	None	84	17.9	1.00 <sup>†</sup>	.086*
1-9	115	19.1	2.25		1-9	138	15.2	0.83	
10-49	97	22.7	2.79		10-49	64	23.4	1.41	
50-99	13	15.4	1.73		50-99	4	23.0	1.53	
≥ 100	8	37.5	5.70		≥ 100	6	50.0	4.60	
<b>Receptive fisting</b>					<b>Insertive oral-anal</b>				
None	283	17.3	1.00 <sup>†</sup>	.004*	None	110	15.4	1.00 <sup>†</sup>	.008*
1-9	8	25.0	1.59		1-9	109	15.6	1.01	
10-49	3	67.0	9.55		10-49	63	22.2	1.56	
50-99	1	100.0	-		50-99	5	40.0	3.65	
≥ 100	0	-	-		≥ 100	10	50.0	5.47	
<b>Insertive fisting</b>					<b>Active manual-genital</b>				
None	256	16.8	1.00 <sup>†</sup>	.083*	None	66	25.7	1.00 <sup>†</sup>	.065*
1-9	31	25.8	1.72		1-9	98	18.4	0.64	
10-49	7	42.8	3.72		10-49	91	16.5	0.57	
50-99	0	0	0		50-99	19	5.3	0.16	
≥100	1	0	0		≥ 100	20	15.0	0.51	
<b>Receptive oral-genital</b>					<b>Passive manual-genital</b>				
None	28	17.9	1.00 <sup>†</sup>	.129*	None	64	26.5	1.00 <sup>†</sup>	.088*
1-9	111	15.3	0.83		1-9	107	17.7	0.60	
10-49	115	20.0	1.15		10-49	86	15.1	0.49	
50-99	17	17.6	0.99		50-99	16	12.5	0.39	
≥ 100	26	30.8	2.04		≥ 100	21	14.3	0.46	
<b>Insertive oral-genital</b>					<b>Condom used</b>				
None	36	16.7	1.00 <sup>†</sup>	.091*	Always	1	0	1.00 <sup>†</sup>	.104*
1-9	94	13.8	0.80		> Half the time	4	50.0	1.00 <sup>†</sup>	
10-49	120	20.0	1.25		< Half the time	13	30.8	0.67	
50-99	23	34.8	2.67		Never	269	16.7	0.28	
≥ 100	22	22.7	1.47						
<b>Receptive digital-anal</b>					<b>Partner wears condom</b>				
None	60	16.7	1.00 <sup>†</sup>	.302*	Always	2	0	1.00 <sup>†</sup>	.633*
1-9	129	16.3	0.97		> Half the time	3	33.7	1.00 <sup>†</sup>	
10-49	83	21.7	1.38		< Half the time	9	33.3	2.00	
50-99	19	26.3	1.79		Never	263	17.9	0.87	
≥ 100	6	16.7	1.00						

\*Test for trend  
†Referent

engaged in this activity in the prior 12 months, the odds ratios for persons with one to nine such encounters was 2.4. For persons with more than 100 encounters, the odds ratio increased to 12.0.

**DISCUSSION**

HIV seroprevalence in this study was 18.6%. This is lower than reported in most other studies of HIV infection in homosexual males, where seroprevalence ranged from 20% to 70% for the same time period. It should be noted that at the time of participation in this study,

serologic tests for HIV infection were not yet available. Therefore, the respondents did not participate in the study in order to receive HIV-antibody testing. This should have helped to reduce any self-selection bias that might have otherwise occurred. The results of other cross-sectional studies examining risk factors for HIV infection are summarized in *Table 6*. It is important to recognize that cross-sectional analyses present a single look at an epidemic and conclusions drawn from these analyses must be interpreted with caution.

Age has been previously shown to be an independent predictor of serostatus in only one study, the



Multicenter AIDS Cohort (MAC) Study, which is an ongoing assessment of nearly 5,000 homosexual males in Los Angeles, Pittsburgh, Chicago, and Baltimore.<sup>1</sup> In the MAC study, a higher prevalence of HIV infection was seen in 25- to 44-year-old men (and especially in the 25- to 34-year-olds) than in younger or older persons. In our study, 21- to 40-year olds were more likely to be seropositive, although this association was significant only in univariate analysis.

Race was also an independent predictor of serostatus in the MAC study, with nonwhites having the highest rate of seropositivity (26.3%). A similar trend was apparent in our study, although the difference was not significant, perhaps due to the low numbers of non-white participants.

Alcohol consumption has not been shown to be a significant independent predictor of HIV infection. However, when overall consumption was examined here, a borderline association was seen primarily because of the high rates of seropositivity noted in heavy drinkers. Furthermore, consumption of beer alone was a significant predictor of seropositivity, with heavy drinkers at greater risk for seropositivity (50%), although this association did not remain independent in the regression. The relationship between alcohol consumption and serostatus may be due to behavioral factors such as more traumatic or riskier sexual practices or both, although a physiologic mechanism such as diminished host defenses<sup>13</sup> or enhanced susceptibility to viral infection<sup>14</sup> may also be important. The fact that a number of the study participants were recruited from bars may introduce some selective bias regarding this relationship. Unfortunately, due to the anonymous nature in which this study was performed, the exact number of participants recruited this way is unknown, and any stratified analysis based on site of recruitment cannot be performed.

Different types of drug use have been variably associated with HIV infection in homosexual men. Injected or intravenous drug use carries a well-known risk of infection from needle-sharing. In some previous studies, intravenous drug users either were eliminated or were too few in number to appear associated with seropositivity. In our study, this relationship was significant, producing a seropositivity of 50% in intravenous drug users as compared with 17% in non-users. The association of other drug use with HIV infection has been inconsistent, with marijuana, cocaine, amphetamines, and nitrites being found as risk factors in some studies<sup>1,7,9</sup> but not most. Similarly, we found a significant association between am-

**TABLE 5**  
STEPWISE LOGISTIC REGRESSION FOR HIV SEROPOSITIVITY:  
THE CLEVELAND MEN'S STUDY (n=267)\*

Multivariate predictor	Number of men	Odds ratio	95% Confidence interval
<b>Intravenous drug use</b>			
None	257	1.00	
Some	10	4.87	(1.15, 20.70)
<b>Receptive anal-genital intercourse†</b>			
None	78	1.00	
1 - 9	90	2.38	(0.78, 7.24)
10 - 49	72	6.03	(2.06, 17.60)
50 - 99	17	5.35	(1.29, 22.20)
≥ 100	10	12.00	(2.44, 59.00)

\*Number of men in regression model

†Number in last twelve months

Note: Variables included age; beer consumption; amphetamine use; intravenous drug use; average yearly number of sexual partners; average yearly visits to a bathhouse; receptive anal-genital intercourse; receptive fisting; insertive oral-anal intercourse; insertive anal-genital intercourse

phetamine use and seropositivity, but this did not remain an independent predictor after multivariate analysis. As others have hypothesized, the variable association of drugs (other than intravenous drugs) and serostatus is most likely due to other related behaviors.

A number of studies have shown significant independent associations between the number of homosexual partners and serostatus.<sup>2-4,10</sup> However, three groups have provided evidence that it is not the number of partners that is most important, but rather the number with whom one had receptive anal intercourse.<sup>1,7,9</sup> In our study, a significant association was seen for the yearly number of sexual contacts with a clear trend towards higher seropositivity with increased numbers of partners in all years.

Having sexual contact in bathhouses was previously shown to be an independent predictor of HIV infection in only one study,<sup>9</sup> although it may not have been examined in others. This was also observed in this study, with seropositivity increasing to almost 40% among those with 20 or more sexual contacts in a bathhouse. Sexual contact in bathhouses was only weakly correlated with several higher-risk sexual practices and was not independently associated with HIV infection. The number of sexual contacts in bathhouses suggests that bathhouses may be places of high seroprevalence and risk of infection, where even a limited number of contacts places a person at increased risk. That sexual contact in back rooms, parks, or rest areas was not shown to be associated with seropositivity may indicate that the partners en-

TABLE 6  
INDEPENDENT RISK FACTORS FOR HIV INFECTION

	Study											
	Coedert et al <sup>3</sup> New York, 1982	Jeffries et al <sup>4</sup> Vancouver, 1982-1984	Melbye et al <sup>6</sup> Denmark, 1981	Mayer et al <sup>5</sup> Boston, 1983-1984	Winkelstein et al <sup>10</sup> San Francisco, 1984	Stevens et al <sup>8</sup> New York, 1984	Van Griensven et al <sup>9</sup> Netherlands, 1984-1985	Moss et al <sup>7</sup> San Francisco, 1983-1984	Frazer et al <sup>2</sup> Melbourne, 1983	Chmiel et al <sup>1</sup> Los Angeles, Chicago, Baltimore, Pittsburgh, 1984-1985	Cleveland Men's Study Cleveland, 1984	
Sample size	66	250	250	79	1006	378	741	272	100	4943	301	
Percent seropositive	53	34	9	56	48	44	31	56	22	38	19	
Risk factor												
Higher number of partners	+	+			+				+			
Contact in high-prevalence area			+						+	+		
Contact in bathhouses							+					
Contact in clubs		+										
Contact in public places								-				
Contact with known AIDS case						+				+		
Receptive anal intercourse	+	+	+	+	+	+	+	+	+	+	+	
Insertive anal intercourse	-											
Receptive oral-genital sex				+								
Receptive anal-oral sex											+	
Receptive fisting	+	+					+			†		
Insertive fisting		+										
Rectal trauma*										+		
Douching or enemas					+	+		+		†		
Manual-genital sex								-			-	
Nitrite use							+	+				
Intravenous drug use					+	+						
Marijuana use							+					
Cocaine use											+	
Methylenedioxyamphetamine use											+	
History of gonorrhea		+		+							+	
History of hepatitis B		+		+							+	
History of syphilis								+			+	
History of giardiasis				+				+				
History of amoebiasis				+								
History of anal herpes											+	
History of rectal bleeding						+						
Black race											+	
Age 25-44											+	
Education < graduate school											+	

\*Defined as receptive fisting, rectal douching or enemas, or rectal bleeding

†See rectal trauma

Key: +, positive association; -, negative association

countered in these places either were less likely to be infected or that the sexual activities there were less risky, or both.

A few studies have shown association between HIV infection and sexual activity in areas of high prevalence.<sup>1,2,6</sup> A similar association was noted here, but not consistently. Furthermore, this relationship was due entirely to individuals who had sex in New York City with virtually no contribution from those few who had sex in Los Angeles and San Francisco. The significance of having sexual contacts in New York did not remain predictive in the regression.

The sexual practice which has been most highly and consistently associated with HIV infection is receptive anal intercourse. Receptive anal intercourse also was shown to be a significant risk factor in this study and remained the only significant risk factor in a prospective analysis of the MAC Study.<sup>15</sup> Other studies have shown that rectal trauma, douching or using enemas before sex, and certain anal conditions such as rectal bleeding, anal warts, and anal herpes<sup>1,7,8,10,16</sup> are also associated with seropositivity. These findings suggest that transmission of HIV is facilitated through traumatized rectal mucosa via semen. In our study as well, receptive anal intercourse was the most significant risk factor, both in univariate and regression analyses. Unfortunately, direct information regarding the number of partners with whom participants had receptive anal intercourse was not available from the questionnaire; furthermore, the frequency of sexual practices was obtained for only the preceding 12 months.

Other sexual practices, with the exception of receptive rectal fisting, have not commonly been independent risk factors for HIV infection. Although significant associations have been noted on univariate analysis in some studies,<sup>1,4,9</sup> these usually do not remain so after regression analysis. This is probably due to the high degree of interrelatedness of the various sexual practices. Bivariate analyses revealed a multiple significant correlation between different sexual practices. Most apparent was the correlation between "active" and "passive" participation in the same practice (eg, active and passive manual-genital contact were strong-

ly correlated,  $r=0.839$ ,  $P<.001$ ; active and passive oral-anal contact were strongly correlated,  $r=0.70$ ,  $P<.001$ ). In our study as well, three practices which initially seemed significant fell out in the regression. Insertive oral-anal intercourse, receptive fisting, and insertive anal intercourse each were significantly correlated with receptive anal intercourse ( $r=0.33$ ,  $0.46$ ,  $0.32$ ;  $P<.001$  for each), and receptive fisting also was engaged in by too few participants. One previous study<sup>9</sup> noted that manual-genital contact, both active and passive, was protective. In our univariate analysis protection associated with these practices approached but did not reach significance.

Different illnesses have been variably associated with HIV infection in previous studies. Gonorrhea and hepatitis have been most frequent, although not in the majority of studies. We too noted that a history of gonorrhea was a nearly significant predictor on univariate analysis ( $P=.0233$ ). Too few participants in our study had syphilis or enteric infections for these to show significant associations.

One potential methodological problem with our study was the use of the ELISA alone to identify seropositivity. Confirmatory Western blot tests were not performed, as it was felt that the specificity of these tests (99.6% and 99.9%, respectively)<sup>17,18</sup> and their presumed positive predictive values in this risk population were sufficiently high to justify analysis based on these results alone.

In summary, a large body of data has been gathered regarding risk factors for HIV infection in homosexual men. The real importance of this information is how it can be used to prevent infection by affecting the behavior of individuals at risk. The successful application of findings such as these to public health education has recently been demonstrated in San Francisco.<sup>19</sup> Hopefully, the later arrival of HIV infection in low prevalence regions such as ours will allow institution of earlier and more effective behavioral changes.

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