

DECREASED HELPER T LYMPHOCYTES IN HOMOSEXUAL MEN

II. SEXUAL PRACTICES

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In June 1982, the sexual practices of 245 homosexual male outpatients of
private physicians were evaluated in relationship to decreased numbers of helper
T lymphocytes, an abnormality that is characteristic of the acquired immunode-
ficiency syndrome (AIDS). Three risk groups were defined a priori—85 high-risk
men from central Manhattan ("New York"), 96 intermediate-risk men from Wash-
ington, DC, with AIDS-area homosexual contacts ("Washington-exposed"), and
64 low-risk Washington, DC, men without such contacts ("Washington-unex-
posed"). An increasing number of homosexual partners was correlated with
decreasing helper T-cell counts ($R = -0.29$, $p = 0.009$) and decreasing
helper:suppressor T-cell ratios ($R = -0.32$, $p = 0.005$) in the entire study group
combined and in New York subjects separately. Suppressor T-cell counts were
unrelated to the number of partners in all three groups. Increasingly frequent
receptive anal intercourse correlated with decreasing helper T-cell counts most
clearly in the New York City group ($R = -0.23$, $p = 0.04$), somewhat less so in
the Washington-exposed group ($R = -0.18$, $p = 0.07$), and not at all in the
Washington-unexposed group ($R = -0.09$, $p = 0.48$). This association persisted
in the New York and Washington-exposed groups after adjusting for seven other
sexual practices, the number of homosexual partners, and five other potentially
confounding variables. A transmissible agent associated with receptive anal
intercourse best explains these data. The cause of these low helper T-cell counts
may also be the cause of AIDS.

homosexuality; immunity, cellular; immunologic deficiency syndromes; regres-
sion analysis; retrovirus infections; semen

The acquired immunodeficiency syn-
drome (AIDS) is an illness that appears to
be caused, at least in part, by an agent
which may be transmitted by homosexual
or heterosexual contact (1, 2) and rarely by
transfusion of blood or blood products (3,

4). With intensive laboratory efforts, it now
appears that this agent has been identified
as a human retrovirus termed HTLV-III
(5-9). In the absence of this discovery, ep-
idemiologic studies of persons at high risk
of AIDS relied on indirect indices of risk,

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Abbreviation: AIDS, acquired immunodeficiency
syndrome.

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TABLE 1
Average frequency of sexual activities in three groups of homosexual men, June 1982

Factor	Frequency in the past year by study group*			p values	
	New York	Washington-exposed	Washington-unexposed	Heterogeneity	Trend
No. of sexual partners	78 ± 15†	42 ± 6	26 ± 6	0.001	0.0004
No. of sexual acts					
Anal intercourse					
Insertive	26.3 ± 4.0	34.6 ± 5.1	21.3 ± 4.5	0.13	0.62
Receptive	26.8 ± 4.0‡	33.3 ± 4.8	21.9 ± 4.1	0.21	0.59
Fellatio					
Insertive	29.3 ± 4.0	37.2 ± 5.2§	21.4 ± 4.4	0.07	0.37
Receptive	28.8 ± 4.9	29.8 ± 4.7	24.2 ± 5.0	0.73	0.57
Anilinctus					
Insertive	13.9 ± 3.3†	14.8 ± 3.3	8.0 ± 2.7	0.34	0.27
Receptive	17.2 ± 2.9	17.0 ± 3.8	10.4 ± 2.9	0.34	0.21
Fisting					
Insertive	4.6 ± 1.9	3.3 ± 2.1	1.1 ± 0.6	0.48	0.23
Receptive	1.8 ± 0.9	0.9 ± 0.4	0.1 ± 0.07	0.23	0.09

* Mean ± standard error for the preceding year.

† Negative correlation with helper T-cell count, $p < 0.01$.

‡ Negative correlation with helper T-cell count, $p < 0.05$.

§ Positive correlation with helper T-cell count, $p = 0.001$.

TABLE 2
Mean helper T-cell counts with frequency of receptive anal intercourse in three groups of homosexual men, June 1982

Study group	No. of receptive anal intercourse acts*	No. of subjects†	Mean (±standard error) helper T-cell count‡	p values	
				Heterogeneity	Trend
New York	Low (0-4)	25	716 ± 68	0.02	0.03
	Intermediate (5-19)	31	502 ± 54		
	High (≥20)	27	531 ± 39		
Washington-exposed	Low (0-4)	28	635 ± 49	0.15	0.06
	Intermediate (5-19)	30	550 ± 37		
	High (≥20)	36	522 ± 40		
Washington-unexposed	Low (0-4)	19	695 ± 56	0.21	0.21
	Intermediate (5-19)	24	728 ± 68		
	High (≥20)	16	565 ± 64		

* In the preceding year.

† Number of subjects does not equal 245 because nine subjects did not answer the question.

‡ Cells/mm³.

with 0 (714 ± 82 cells/mm³) and 1-4 (716 ± 95 cells/mm³) receptive anal intercourse acts. In addition, at a very high frequency of anal receptive acts per year (≥50), there was no further decline in T-cell counts. Of the 58 New York men who engaged in intermediate- or high-frequency receptive anal intercourse, 22 (38 per cent) had helper T-cell counts <400 cells/mm³.

In the Washington-exposed group, a gradual trend ($p = 0.06$) was evident between mean helper T-cell counts and receptive anal intercourse (table 2). In these men, there was a difference of nearly 200 cells/mm³ between no receptive anal intercourse acts (712 ± 86 cells/mm³) and ≥20 such acts (522 ± 40 cells/mm³). In the Washington-unexposed group, there was a

nonsignificant decrease in mean helper T-cell counts (565 ± 64 cells/mm³) with frequent (≥ 20) receptive anal intercourse. As in the New York men, mean helper T-cell counts were not progressively lower in either group of Washington men with very frequent (≥ 50) receptive anal intercourse. Of the 52 Washington subjects who engaged in high-frequency (≥ 20) receptive anal intercourse, 17 (33 per cent) had helper T-cell counts < 400 cells/mm³.

Interrelationships of sexual practices

Two linear regression models for helper T-cell counts were used to control the interrelationships of sexual practices and lifestyle variables (table 3). The first model included frequencies of eight sexual practices and the number of homosexual partners. The second model included these nine variables and five additional potentially confounding variables (frequency of nitrite inhalant use, age, race, presenting illness, and suppressor T-cell count).

In the first model (table 3), with all men combined, helper T-cell counts were lower

with more sexual partners (partial $F = 3.05$, $p = 0.08$) and frequent receptive anal intercourse (partial $F = 5.25$, $p = 0.02$). In contrast, frequent insertive fellatio (partial $F = 3.06$, $p = 0.08$) was associated with higher helper T-cell counts. In the New York and Washington-exposed groups, helper T-cell counts were inversely related to the frequency of receptive anal intercourse (New York partial $F = 4.92$, $p = 0.03$; Washington-exposed partial $F = 3.24$, $p = 0.08$), while this effect was absent in the Washington-unexposed group (partial $F = 0.75$, $p = 0.39$). Helper T-cell counts were higher with insertive fellatio (partial $F = 4.14$, $p = 0.05$) only in the Washington-exposed group. In the Washington-unexposed group, helper T-cell counts tended to be lower with receptive anilingus (partial $F = 2.96$, $p = 0.09$) and higher with insertive anal intercourse (partial $F = 2.35$, $p = 0.13$). There were no correlations with the other sexual practices in any of the three study groups (partial $F \leq 1.50$, $p \geq 0.22$).

Five additional variables were controlled in the second model (table 3). In the New

on, June 1982

p values	
Heterogeneity	Trend
0.001	0.0004
0.13	0.62
0.21	0.59
0.07	0.37
0.73	0.57
0.34	0.27
0.34	0.21
0.48	0.23
0.23	0.09

groups of homosexual men,

p values	
Heterogeneity	Trend
0.02	0.03
0.15	0.06
0.21	0.21

question.

on-exposed group, a 0.06) was evident between cell counts and receptive (table 2). In these reference of nearly 200 receptive anal intercourse (≥ 20 cells/mm³) and ≥ 20 cells/mm³). In the exposed group, there was a

TABLE 3

Contribution of three variables to two linear regression models of helper T-cell counts in three groups of homosexual men, June 1982

Study group	Variables with consistent β^* in all groups	First model†			Second model†		
		β^*	Partial F	p value	β^*	Partial F	p value
All combined‡	No. of sexual partners	-	3.05	0.08	-	6.91	0.009
	Receptive anal intercourse	-	5.25	0.02	-	3.53	0.06
	Insertive fellatio	+	3.06	0.08	+	2.13	0.15
New York	No. of sexual partners	-	1.88	0.18	-	3.82	0.06
	Receptive anal intercourse	-	4.92	0.03	-	3.17	0.08
	Insertive fellatio	+	1.09	0.30	+	1.00	0.32
Washington-exposed	No. of sexual partners	-	0.00	1.00	-	0.30	0.59
	Receptive anal intercourse	-	3.24	0.08	-	3.28	0.07
	Insertive fellatio	+	4.14	0.05	+	2.98	0.09
Washington-unexposed	No. of sexual partners	-	0.17	0.68	+	0.03	0.87
	Receptive anal intercourse	-	0.75	0.39	-	0.02	0.89
	Insertive fellatio	+	0.04	0.84	-	0.06	0.80

* Direction of association with the helper T-cell count.

† First and second models adjusted for eight different sexual practices and number of homosexual partners. The second model also adjusted for frequency of nitrite inhalant use, age, race, presenting illness, and suppressor T-cell count. Except for inconsistent associations noted in the text for the Washington-unexposed group, the six sexual practices not presented in table 3 had partial $F \leq 1.40$, $p \geq 0.22$.

‡ With all subjects combined, the models were additionally adjusted by the three study groups.

York group, helper T-cell counts were lower with more sexual partners (partial $F = 3.82$, $p = 0.06$) and with more receptive anal intercourse (partial $F = 3.17$, $p = 0.08$). In the Washington-exposed group, this effect was seen only for receptive anal intercourse (partial $F = 3.28$, $p = 0.07$). Of the seven sexual practices other than receptive anal intercourse, none was related to decreasing helper T-cell counts in the second model (partial $F \leq 1.43$, $p \geq 0.24$). Three sexual practices were related to increasing helper T-cell counts in the second model: insertive fellatio (partial $F = 2.98$, $p = 0.09$) in the Washington-exposed group, and receptive fellatio (partial $F = 3.38$, $p = 0.07$) and receptive fisting (partial $F = 3.59$, $p = 0.07$) in the Washington-unexposed group. Helper T-cell counts were unrelated to the five additional variables in the second model, except for a positive association with the suppressor T-cell count in all three groups of men (partial $F = 6.06$ – 9.40 , $p = 0.02$ – 0.004) and a negative association with the frequency of nitrite inhalant use in the Washington-unexposed group (partial $F = 4.05$, $p = 0.05$).

DISCUSSION

AIDS appears to be a sexually transmitted disease, but attempts to define the mode of transmission have yielded conflicting results (13–16). We have recently shown that homosexual men who reside in an area where AIDS is uncommon can “acquire” a low helper T-cell count, the distinctive immunologic abnormality of AIDS (17), through homosexual contacts in areas where AIDS is endemic (10, 11). The current study shows that frequent receptive anal intercourse in an AIDS-endemic area is related to decreasing helper T-cell counts. Receptive anal intercourse was not a risk factor when performed in areas at low-risk for AIDS, strongly suggesting that the low helper T-cell counts of men with endemic-area homosexual partners are related to their risk of AIDS.

In our study, the correlation between de-

creasing helper T-cell counts and receptive anal intercourse was strong in the New York group, weaker in the Washington-exposed group, and absent in the Washington-unexposed group. In the New York group, a threshold effect was evident, with mean helper T-cell counts sharply decreased with five or more receptive anal intercourse acts but not further decreased with 20 or more such acts. This suggests a single, rather than a cumulative, exposure. In the Washington-exposed group, the threshold effect was probably blurred by the practice of receptive anal intercourse with both endemic-area and nonendemic-area partners. In the Washington-unexposed group, the mean helper T-cell count decreased slightly with high-frequency (≥ 20) receptive anal intercourse, an observation that is consistent with a threshold effect for a putative agent in a low-prevalence area. As in New York, the lack of further decrease in helper T-cell counts with very frequent (≥ 50) receptive anal intercourse by Washington men supports a single-exposure hypothesis.

This is strong evidence that receptive anal intercourse is related to low helper T-cell counts and is not simply a surrogate for some unconsidered factor. To show clearly that one particular sexual practice is related to the condition of interest, however, the frequency of other sexual practices and the number of different sexual partners must be considered. Controlling for other factors that may influence the helper T-cell count, such as age and race, improves the specificity of the conclusion. Cytomegalovirus may be transmitted among homosexual men by receptive anal intercourse (20), but the confounding of this variable by other sexual practices and by the number of different partners has not been thoroughly evaluated (21). Our linear regression models have shown an association of receptive anal intercourse with low helper T-cell counts that persists after adjustment for 13 other variables, including seven specific

T-cell counts and receptive se was strong in the New eaker in the Washington- and absent in the Washing- group. In the New York old effect was evident, with T-cell counts sharply de- ive or more receptive anal s but not further decreased e such acts. This suggests a an a cumulative, exposure. ngton-exposed group, the t was probably blurred by receptive anal intercourse mic-area and nonendemic- In the Washington-unex- e mean helper T-cell count tly with high-frequency anal intercourse, an obser- onsistent with a threshold ative agent in a low-preva- in New York, the lack of e in helper T-cell counts ent (≥ 50) receptive anal Washington men supports a hypothesis. g evidence that receptive is related to low helper T- is not simply a surrogate sidered factor. To show particular sexual practice condition of interest, how- cy of other sexual practices of different sexual partners red. Controlling for other y influence the helper T- as age and race, improves the conclusion. Cytomeg- transmitted among homo- receptive anal intercourse ounding of this variable practices and by the num- partners has not been thor- (21). Our linear regression wn an association of recep- rse with low helper T-cell sts after adjustment for 13 including seven specific

sexual practices, that might influence the helper T-cell count.

Four associations with *higher* helper T-cell counts were noted: insertive fellatio in the Washington-exposed group, and insertive anal intercourse, receptive fellatio, and receptive fisting in the Washington-unexposed group. There is no likely biologic explanation for these four different "protective" practices. In fact, the helper T-cell counts in these men are not abnormally elevated (11, 17) but are more normal than in the men with low counts. The findings suggest that men with normal helper T-cell counts probably preferred a variety of practices other than receptive anal intercourse and thereby avoided the etiologic agent that causes helper T-cell deficiency.

Other investigators have reported that receptive anal intercourse is associated with an increased suppressor T-cell count (22) and that this T-cell pattern is not characteristic of AIDS (17). Our current larger and more detailed study indicates that suppressor T-cell counts (unlike AIDS itself (12, 13), helper:suppressor ratios, and helper T-cell counts) are not correlated with the total number of homosexual partners. Since no adverse effects of a high suppressor T-cell count have been suggested, we have not pursued further the determinants of this condition in homosexual men.

A direct immunosuppressive effect of sperm has been postulated as a contributing cause of AIDS (23). The geographic differences in our study make it unlikely that sperm per se causes decreased helper T-cell counts, since the New York and Washington men receiving equal doses of semen (i.e., equal numbers of anal intercourse acts) did not have similar helper T-cell counts. Likewise, nitrite inhalant use (which is frequently used during receptive anal intercourse) was related to decreasing helper T-cell counts only in the Washington-unexposed men, suggesting that recreational nitrites do not detectably reduce

helper T-cell counts in men with homosexual contacts in AIDS-endemic areas.

The pattern of dose-response relationships between the New York and Washington-exposed and -unexposed groups is consistent with a single-exposure hypothesis. The data suggest that the likelihood of this exposure is highest in the New York group, intermediate in the Washington-exposed group, and rare in the Washington-unexposed group. The most likely mechanism for the low helper T-cell counts in this study is that a viral or other agent is transmitted through anal intercourse. The mode of transmission is uncertain, although the data support the concept that the putative agent is excreted in seminal fluid, gains access to the blood stream via rectal mucosal abrasions, and results in an infection that is cytotoxic to T lymphocytes of the helper phenotype. Alternatively, it is also possible that infectious feces with or without blood could be passed by common contacts. This hypothesis is supported by Marmor's finding (16) that ejaculation by the partner was not an independent risk factor for AIDS beyond the sheer number of receptive anal contacts. The possibility of infectious feces is also suggested by our finding (before adjusting for other variables) that anilinctus is correlated with low helper T-cell counts in New York men and by similar observations in the case-control study of AIDS conducted by the Centers for Disease Control, Atlanta, Georgia (13, 14). Thus, it seems that avoidance of multiple partners and use of condoms may be necessary for effective prophylaxis against AIDS. The recent identification of the agent that is the primary cause of AIDS (5, 6) and the development of assays for this agent (7, 8) have already clarified the mode of transmission (9) and will help clarify the measures required to limit its spread.

REFERENCES

1. Centers for Disease Control. A cluster of Kaposi's sarcoma and *Pneumocystis carinii* pneumonia among homosexual male residents of Los Angeles and Orange counties, California. MMWR 1982;31:305-7.

2. Harris C, Small CB, Klein RS, et al. Immunodeficiency in female sexual partners of men with the acquired immunodeficiency syndrome. *N Engl J Med* 1983;308:1181-4.
3. Curran JW, Lawrence DN, Jaffe H, et al. Acquired immunodeficiency syndrome (AIDS) associated with transfusions. *N Engl J Med* 1984;310:69-75.
4. Ammann AJ, Cowan MJ, Wara DW, et al. Acquired immunodeficiency in an infant: possible transmission by means of blood products. *Lancet* 1983;1:956-8.
5. Popovic M, Sarngadharan MG, Read E, et al. Detection, isolation, and continuous production of cytopathic retroviruses (HTLV-III) from patients with AIDS and pre-AIDS. *Science* 1984;224:497-500.
6. Gallo RC, Salahuddin SZ, Popovic M, et al. Frequent detection and isolation of cytopathic retroviruses (HTLV-III) from patients with AIDS and at risk for AIDS. *Science* 1984;224:500-3.
7. Schupbach J, Popovic M, Gilden RV, et al. Serological analysis of a subgroup of human T-lymphotropic retroviruses (HTLV-III) associated with AIDS. *Science* 1984;224:503-5.
8. Sarngadharan MG, Popovic M, Bruch L, et al. Antibodies reactive with human T-lymphotropic retroviruses (HTLV-III) in the serum of patients with AIDS. *Science* 1984;224:506-8.
9. Goedert JJ, Sarngadharan MG, Biggar RJ, et al. Determinants of retrovirus (HTLV-III) antibody and immunodeficiency conditions in homosexual men. *Lancet* 1984;2:711-16.
10. Biggar RJ, Melbye M, Ebbesen P, et al. Low T-lymphocyte ratios in homosexual men: epidemiologic evidence for a transmissible agent. *JAMA* 1984;251:1441-6.
11. Goedert JJ, Biggar RJ, Winn DM, et al. Decreased helper T lymphocytes in homosexual men. I. Sexual contact in high-incidence areas for the acquired immunodeficiency syndrome. *Am J Epidemiol* 1985;121:629-36.
12. Marmor M, Friedman-Kien AE, Laubenstein L, et al. Risk factors for Kaposi's sarcoma in homosexual men. *Lancet* 1982;1:1083-7.
13. Jaffe HW, Choi K, Thomas PA, et al. National case-control study of Kaposi's sarcoma and *Pneumocystis carinii* pneumonia in homosexual men. Part 1. Epidemiologic results. *Ann Intern Med* 1983;99:145-51.
14. Rogers MF, Morens DM, Stewart JA, et al. National case-control study of Kaposi's sarcoma and *Pneumocystis carinii* pneumonia in homosexual men. Part 2. Laboratory results. *Ann Intern Med* 1983;99:151-8.
15. Darrow WW, Jaffe HW, Curran JW. Passive anal intercourse as a risk factor for AIDS in homosexual men. *Lancet* 1983;2:160.
16. Marmor M. Epidemic Kaposi's sarcoma and sexual practices among male homosexuals. In: Friedman-Kien AE, Laubenstein L, eds. *Progress in AIDS: Proceedings of the Symposium on Epidemic Kaposi's Sarcoma and Opportunistic Infections in Homosexual Men*. New York: Masson, 1984:291-6.
17. Fahey JL, Prince H, Weaver M, et al. Quantitative changes in T helper or T suppressor/cytotoxic lymphocyte subsets that distinguish acquired immune deficiency syndrome from other immune subset disorders. *Am J Med* 1984;75:95-100.
18. Snedecor GW, Cochran WG. *Statistical methods*. 6th ed. Ames, IA: Iowa State University Press, 1967.
19. Draper NR, Smith H. *Applied regression analysis*. New York: John Wiley & Sons, Inc, 1966.
20. Mintz L, Drew WL, Miner RC, et al. Cytomegalovirus infections in homosexual men: an epidemiologic study. *Ann Intern Med* 1983;99:326-9.
21. Goedert JJ, Biggar RJ. Cytomegalovirus transmission among homosexual men. *Ann Intern Med* 1984;100:156.
22. Detels R, Fahey JL, Schwartz K, et al. Relation between sexual practices and T-cell subsets in homosexually active men. *Lancet* 1983;1:609-11.
23. Shearer GM, Hurtenbach U. Is sperm immunosuppressive in male homosexuals and vasectomized men? *Immunol Today* 1982;3:153-4.