Sexual lifestyle and clinical findings related to HTLV-III/LAV status in homosexual men

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SUMMARY A study of 304 sexually active homosexual men, most of whom had multiple casual partners, showed that receptive anogenital intercourse, independent of anal bleeding, was the only risk factor for HTLV-III/LAV transmission. There was no evidence that HTLV-III/LAV infection, measured by seropositivity, was transmitted by oroanal or orogenital routes, or that insertive penile intercourse constituted a risk. The strongest predictor of seropositivity proved to be homosexual activity for more than five years, which may lead to enhanced susceptibility to infection. Sexual exposure to European men seemed to be even more hazardous than sexual exposure to men from the United States of America, and emphasised the epidemiological importance of the promiscuous homosexual abroad. Skin complaints were the most common presenting symptoms in men with antibody to HTLV-III/LAV. Extrainguinal lymphadenopathy was the commonest sign, which was present in just under half of those who were seropositive. More than one quarter of seropositive patients had had sexual intercourse with a woman in the five years before being tested.

Introduction

Several studies have sought to relate the lifestyle and sexual practices of homosexual men to the development of the acquired immune deficiency syndrome (AIDS). The first studies concentrated on the sexual habits of men with Kaposi's sarcoma.^{1,2} Later studies examined the habits of men with human T cell lymphotropic virus type III or lymphadenopathy associated virus (HTLV-III/LAV) infection as indicated by the presence of antibody.^{3,4} All these reports have come from the United States of America, mostly from New York. They have drawn patients and controls from diverse sources, and have reported on relatively small numbers. They have all found that AIDS and seropositivity are associated with having increased numbers of sexual partners and the practice of receptive anogenital intercourse. A report from Denmark investigated serum samples and lifestyle data of 250 homosexual men in 1981; 22 (8.8%) were seropositive, and this was associated with an increased

incidence of receptive anal intercourse.⁵ The study published here was a prospective one of a cohort of patients attending one outpatient clinic.

Patients and methods

We studied a group of homosexual men who attended a department of genitourinary medicine in West London during the six months from November 1984 to May 1985. Patients were assessed if they were willing to be tested for antibody to HTLV-III/LAV and to complete the study questionnaire. All the patients who entered the study underwent a physical examination and routine tests for sexually transmitted diseases (STDs); these findings were recorded before their anti-HTLV-III/LAV status was known.

QUESTIONNAIRE

The same short study questionnaire was completed by all participants. They were asked to indicate the most appropriate of predetermined responses. Completion and comprehension were checked by one of us (ST). The questionnaire asked participants for estimates of the lifetime number of sexual partners and for the number of partners in the preceding 12 months. The question regarding sexual relationships with foreign

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nationals was phrased to include those occurring in this country as well as those occurring abroad. The questionnaire also asked how long homosexual practices had been followed. The incidence of various sexual practices was recorded on a five point scale (never, occasionally, sometimes, usually, or always). Time since the last act of heterosexual intercourse was recorded by interval in years, months, or days (or as "never"). The clinical records were checked for a history of any of seven sexually transmitted diseases.

ANTIBODY TO HTLV-III/LAV

Antibody to HTLV-III/LAV was measured by a competitive radioimmunoassay (COMPRIA).⁶ Specimens giving positive results were tested by "capture" radioimmunoassay (RIA)⁷ and a commercial enzyme linked immunoassay (Elavia, Pasteur Diagnostics) to confirm that they contained antibody to HTLV-III/LAV.

STATISTICAL METHODS

The data from clinical examination, the questionnaire, and results of tests for syphilis, hepatitis B, and antibody to HTLV-III/LAV were analysed by the SPSS software on the University of London Computer Centre's Amdahl computer; tests used were Student's *t* test and the χ^2 test. Tests of trend were as described by Snedecor.⁸ Multivariate analysis was carried out by stepwise logistic regression using a programme provided by BMDP software.

Results

Of 304 patients who entered the study, 98 (32%) had serum antibody to HTLV-III/LAV by COMPRIA. All 98 positive patients' results were confirmed by capture RIA or Elavia. The mean age of the seropositive patients was 33 (range 19-50) years and of the seronegative patients was 33.7 (range 18-61) years. Two hundred and seventy nine (92%) were currently engaging in sexual practices with casual partners.

CLINICAL FINDINGS AND PREVIOUS STDs

Table I shows clinical details related to antibody

TABLE I HTLV-III/LAV seropositivity and clinical findings

Clinical findings	No (%) HTLV-III/LAV:		
	Positive (n=98)	Negative (n=206)	<i>p</i> (χ^2 ; df=1)
Lymphadenopathy	45 (46)	25 (12)	<0.0001
Skin disease	27 (28)	30 (15)	0.007
Contact history	17 (17)	15 (7)	0.008
Non-STD symptoms	38 (39)	59 (29)	0.05
Complaints of poor health	18 (18)	23 (11)	0.09

status. Skin diseases were significantly more common in patients with antibody to HTLV-III/LAV ($p=0.007$). These included (in order of incidence) seborrhoeic dermatitis, psoriasis, acne, folliculitis, fungal infections, and eczema. Generalised lymphadenopathy (defined as palpable nodes in more than one extrainguinal site) occurred in 46% (45/98) of seropositive patients and in 12% (25/206) of seronegative patients ($p<0.0001$). Symptoms not attributable to sexually transmitted diseases (such as sore throat, cough, diarrhoea, and anal pain or discharge) and complaints related to general health (such as flu like illness and feeling run down or depressed) were more common, though not appreciably so, in seropositive patients. AIDS was diagnosed in one seropositive and two seronegative patients, both of whom subsequently became seropositive. On retesting the original serum samples, the first of these two was found to be weakly positive and the second was confirmed as being negative. The patient has, however remained in good health since his initial illness, and the diagnosis of AIDS remains in doubt; it was made on the basis of severe oral candidiasis and pneumonia that responded to high dose cotrimoxazole, but *Pneumocystis carinii* was not recovered.

Table II shows HTLV-III/LAV antibody status related to previous STDs and the results of routine

TABLE II HTLV-III/LAV seropositivity and previous sexually transmitted diseases

	No (%) HTLV-III/LAV:		
	Positive (n=98)	Negative (n=206)	<i>p</i> (χ^2 ; df=1)
Syphilis	59 (60)	65 (32)	<0.0001
TPHA positive	54 (55)	63 (31)	<0.0001
HBsAg positive	74 (76)	100 (49)	<0.0001
Hepatitis	60 (61)	81 (39)	0.0003
Anogenital herpes	26 (27)	29 (14)	0.008
Gonorrhoea	82 (84)	141 (69)	0.006
Anogenital warts	38 (39)	56 (27)	0.04
NSU/Chlamydial infection	70 (71)	141 (68)	0.6
Glandular fever	17 (17)	31 (15)	0.6

TPHA = *Treponema pallidum* haemagglutination assay.

HBsAg = Hepatitis B surface antigen.

NSU = Non-specific urethritis.

serological testing for syphilis (by the *Treponema pallidum* haemagglutination assay (TPHA) and the Venereal Disease Research Laboratory (VDRL) test) and for hepatitis B (by tests for hepatitis B surface antigen (HBsAg) and antibody to HBs). Antibody to HTLV-III/LAV correlated very strongly ($p<0.0001$)

with past infection with *T pallidum* and hepatitis B virus and strongly with previous gonorrhoea ($p=0.006$) and genital herpes ($p=0.008$). By contrast, genital warts correlated weakly ($P=0.04$) and previous non-specific or chlamydial infection and glandular fever showed no significant relation to antibody to HTLV-III/LAV.

SEXUAL BEHAVIOUR

The results of the inquiry into sexual behaviour are divided into three parts. Table III refers to the numbers of sexual partners and duration of homosexual activity, table IV refers to the stability of relationships and the nationality and sex of partners, and table V refers to sexual practices with casual partners.

TABLE III HTLV-III/LAV seropositivity, duration of homosexual activity, and numbers of sexual partners

	<i>n</i>	Anti-HTLV-III/LAV No (%) positive	
Homosexually active (years):			
1-5 years	60	7 (12)	}
6-10 years	85	34 (40)	
>10 years	159	57 (36)	
Lifetime sexual partners:			
1-10	7		}
11-20	18	1 (6)	
21-50	45	10 (22)	
>50	234	87 (37)	
Partners in previous year:			
1-5	93	22 (24)	}
6-10	68	22 (32)	
11-20	71	21 (30)	
>20	72	33 (46)	

* = Positive trend ($p<0.01$).

Multiplicity of sexual partners was strongly related to anti-HTLV-III/LAV seropositivity. Significantly greater risk was found in men who had had more than 20 lifetime partners ($p=0.003$ with Yates's correction) and also in men who had had more than 20 partners in the preceding year ($p=0.005$). Of the men who had antibody to HTLV-III/LAV, 93% (91/98) had been homosexually active for more than five years, compared with 74% (153/206) of those who were seronegative ($p=0.0001$). There was a significant positive trend between these three variables and seropositivity. Indeed, seropositivity was more than three times greater in men who had been homosexually active for 6-10 years (40%) than in those who had been homosexually active for 1-5 years (12%) (figure). None of the seven patients with fewer than 10 sexual partners in his lifetime, and only one of the 18 with fewer than 20 partners, was seropositive.

FIGURE Anti-HTLV-III/LAV seropositivity and duration of sexual lifestyle in 304 homosexual men.

Of the seropositive men, (55%) (54/98) had a regular sexual partner (for at least six months) and these men were just as likely to be seropositive as were men without regular partners (table IV). Previous sexual intercourse with a woman was not reported significantly more often by seronegative patients nor was heterosexual intercourse within the previous five years (reported by 27% (26/98) of those who were seropositive and 36% (75/206) of those who were seronegative). This difference did reach significance in men who had had heterosexual intercourse within the previous two years ($p=0.03$). Sexual relationships with non-Britons were associated with seropositivity most significantly in respect of Europeans ($p=0.0008$) and less so with Americans ($p=0.03$). Having Canadian, Caribbean, or central African sexual partners was not associated with a significantly increased risk, but the numbers were small.

TABLE IV HTLV-III/LAV seropositivity and regular, foreign, and female sexual partners

	No (%) HTLV-III/LAV:		<i>p</i> (χ^2 ; <i>df</i> =1)
	Positive (<i>n</i> =98)	Negative (<i>n</i> =206)	
A regular partner (for > 6 months)	54 (55)	95 (46)	0.14
Foreign partners:			
European	72 (74)	110 (53)	0.0008
American	45 (46)	68 (33)	0.03
Female partners:			
Lifetime	60 (61)	148 (72)	0.06
In previous 5 years	26 (27)	75 (36)	0.09
In previous 2 years	11 (11)	45 (22)	0.03

Of sexual practices (table V), receptive anogenital intercourse had much the strongest correlation with anti-HTLV-III/LAV seropositivity ($p<0.0001$); retention of semen in the rectum ($p=0.004$) and bleeding after anogenital intercourse ($p=0.005$) showed

TABLE V Association between HTLV-III/LAV seropositivity and frequency of sexual practices with casual partners

Practice	No (%) of patients practising	p (χ^2 ; $df=3$)*
Receptive anogenital	260 (86)	<0.0001
Insertive brachioproctal	69 (23)	0.002
Semen retained in rectum	213 (70)	0.004
Use of drugs	204 (67)	0.004
Receptive anilingual	238 (78)	0.004
Receptive brachioproctal	43 (14)	0.09
Swallowing of semen	191 (63)	0.2
Insertive anilingual	171 (56)	0.4
Insertive anogenital	262 (86)	0.7

*Anti-HTLV-III/LAV result $\times$ frequency of practice (never, occasionally, sometimes, or usually or always)

weaker but still significant correlations with anti-HTLV-III/LAV seropositivity. Only four seropositive patients did not report currently engaging in casual receptive anogenital intercourse, but all four had taken this role with their regular sexual partners, two of whom were known to be seropositive. The third patient's regular sexual partner, who defaulted after treatment for primary syphilis, had not been tested; and the fourth patient's regular partner was unwilling to be tested. Other sexual practices that seemed to offer significantly increased risks of HTLV-III/LAV infection were the use of drugs before sexual acts ($p=0.004$), insertive brachioproctal intercourse (fisting) ($p=0.002$), and receptive anilingus (rimming) ($p=0.004$). By contrast, insertive anogenital intercourse, insertive anilingus, receptive fisting, and the swallowing of semen did not show any significant relationship with anti-HTLV-III/LAV seropositivity.

The use of drugs, principally nitrites, before sexual acts was not significantly associated with anal bleeding after receptive anogenital intercourse ($p=0.12$) but was strongly related to having multiple (more than 10) sexual partners in the preceding year ($p<0.0001$). For this reason drug use was not considered to be independently related to anti-HTLV-III/LAV seropositivity.

Logistic Regression

The analyses that consider the various sexual practices and potential risk factors one at a time do not, of course, take account of the interrelationships between them. To deal with this aspect of the data, stepwise logistic regression was carried out, the results of which are summarised in table VI. Ten variables expressing aspects of sexual behaviour most strongly related to anti-HTLV-III/LAV seropositivity on univariate analysis were examined by this method. The strongest predictor, with a relative risk of 4.7 for anti-HTLV-III/LAV seropositivity, was a history of having male sexual partners for more than five years. Next strongest, with a relative risk of 4.3, was receptive anogenital intercourse. The three remaining risk factors that satisfied the entry criterion of $p<0.05$ for the stepwise regression were having European (non-British) sexual partners (relative risk 2.1), using drugs for sexual practices (relative risk 1.9), and practising insertive brachioproctal intercourse (relative risk 1.8). These relative risks, being obtained from the stepwise logistic regression, express the additional predictive power of the risk factors. The risk factors eliminated were more than 50 lifetime sexual partners, more than 20 partners in the previous year, receptive anilingus, retaining semen, and anal bleeding after receptive anogenital intercourse.

HEPATITIS B INFECTION AND SYPHILIS

The correlations of lifestyle data, other STDs, and homosexual practices with hepatitis B virus (HBV) seropositivity (to HBsAg or anti HBs) were mostly similar to those with anti-HTLV-III/LAV seropositivity, but there were some interesting differences (table VII). Hepatitis B infection was not associated with skin disease, but there was a significant relation with both insertive and receptive anilingus ($p<0.05$), which did not exist for anti-HTLV-III/LAV seropositivity. Swallowing of semen seemed to present no risk for either infection. Lymphadenopathy correlated with hepatitis B infection ($p=0.003$) but not as significantly as with anti-HTLV-III/LAV seropositivity. A history of syphilis (indicated by a positive TPHA result) showed similar correlations,

TABLE VI Summary of stepwise logistic regression

Predictor	χ^2	p	Relative risk	95% Confidence interval for relative risk
Male partners for > 5 years	16.24	<0.001	4.7	2.0-11.2
Receptive anogenital intercourse	8.69	0.003	4.3	1.4-12.8
European partners	6.64	0.01	2.1	1.2-3.6
Use of drugs	4.16	0.04	1.9	1.0-3.5
Insertive brachioproctal intercourse	3.85	0.049	1.8	1.0-3.3

TABLE VII Associations of homosexual practices, multiple partners, and disease with: anti-HTLV-III/LAV seropositivity, hepatitis B virus (HBV) infection, and syphilis (TPHA)

Lifestyle and clinical data	HTLV-III/LAV p	HBV p	TPHA p
Receptive anogenital*	<0.0001	0.0004	0.01
Receptive anilingual*	0.004	0.002	0.01
Semen swallowed*	0.2	0.8	0.3
Insertive anilingual*	0.4	0.04	0.1
Insertive anogenital*	0.7	0.05	0.7
>20 Partners in previous year†	0.005	0.2	0.5
Lymphadenopathy†	<0.0001	0.003	0.8
Current skin disease†	0.007	0.6	0.8
Previous NSU/chlamydial infection†	0.6	0.009	1.0

* χ^2 , df=3.† χ^2 , df=1.TPHA = *Treponema pallidum* haemagglutination assay.

NSU = Non-specific urethritis.

significantly ($p=0.01$) in respect of receptive anilingus and receptive anogenital intercourse. These were the only sexual practice risk factors common to all three infections. Except for hepatitis B, insertive acts did not carry significant risks. Recent promiscuity (more than 20 partners in the previous year) was not associated with evidence of either hepatitis B infection or syphilis.

Discussion

This study confirms that receptive anogenital intercourse and multiple partners are the major risk factors for sexual acquisition of HTLV-III/LAV infection. The strongest predictor of anti-HTLV-III/LAV seropositivity, however, was homosexual activity for more than five years. The numbers of sexual partners either in the lifetime or in the previous year were eliminated as predictors by the stepwise logistic regression, presumably because they correlate with time and do not contribute more predictive power. There were disproportionately fewer seropositive patients, however, among those with up to five years of homosexual activity, (figure) a finding that cannot be explained by less promiscuity because this group and the group with more than five years' homosexual activity reported similar numbers of recent sexual partners. This raises the possibility that transmission of HTLV-III/LAV may depend on a factor related to more than simply a chance transmitting sexual act. A large number of such acts over a period of years, with one or more partners, might increase the patient's susceptibility to infection. Immunosuppression by allogeneic semen in the rectum,⁹ or perhaps infection by another common immunosuppressive agent, such as cytomegalovirus, might act in this way.

Insertive anogenital intercourse and insertive anilingus were not shown to present any risk, and the

swallowing of semen did not emerge as a risk in univariate analysis of the data. This absence of risk for the insertive male homosexual has relevance for female to male transmission by any form of heterosexual intercourse. It suggests that such transmission is unlikely. Though sexual relationships with American homosexuals might have been thought to be the more hazardous, relationships with European homosexuals were an even greater risk. It is clear that the promiscuous male homosexual who travels abroad has played a major part in the spread of HTLV-III/LAV infection.

A higher proportion of seropositive men (55%) than seronegative men (46%) reported having a regular sexual partner. This was an unexpected finding, which has important epidemiological implications in terms of the effect of repeated exposure to HTLV-III/LAV. Also of concern, in view of the consequences of heterosexual transmission, was the reporting of intercourse with women by a third of the cohort (including 27% of those who were seropositive) within the previous five years.

Though the strong correlation of anti-HTLV-III/LAV seropositivity with extrainguinal lymphadenopathy ($p<0.0001$) was anticipated, its association with common skin diseases in otherwise asymptomatic men is a new finding. Skin problems, including some atypical skin diseases, have been noted in homosexual men suffering from AIDS or persistent generalised lymphadenopathy (PGL).¹⁰ Our findings indicate that skin disease may be a presenting as well as a late feature of HTLV-III/LAV infection.

Most of the common STDs had occurred more often in anti-HTLV-III/LAV seropositive men, probably because they had had significantly more partners. The absence of association with non-specific urethritis and chlamydial infection is not readily explained. A history of "glandular fever" did not appear more

commonly among the seropositive group, which suggests that this is not a common marker of acute HTLV-III/LAV infection.

Though the findings concerning hepatitis B infection were compatible with an oroanal route of transmission, there is no evidence that this was the case in respect of HTLV-III/LAV infection. Taken with the lack of risk attached to swallowing semen, our findings support the view that HTLV-III/LAV does not infect by the oral route.

The typical anti-HTLV-III LAV seropositive Briton was a man in his thirties who had been homosexually active for more than five years and had had more than 20 partners, among whom would have been a European. Receptive anogenital intercourse would be an essential part of his sexual activity, which was also likely to include insertive fisting and the use of nitrites. A rash due to a common skin disease was the most likely early symptom, though this was present in less than one third of cases, and extrainguinal lymphadenopathy was the most likely physical finding. Receptive anogenital intercourse was the practice that carried by far the greatest and maybe the only substantial risk of HTLV-III/LAV infection, anal bleeding induced by intercourse having been eliminated as a risk factor by stepwise logistic regression. Indeed, it can be concluded that seropositive men should not under any circumstances practise insertive anogenital intercourse, as the inoculation of HTLV-III/LAV into the rectum may transmit the agent of an incurable disease to a seronegative person.¹¹ In this respect, people at risk who do not establish that they are anti-HTLV-III/LAV negative, have it confirmed by regular testing,

and practise mutual monogamy, should behave as though they were seropositive.

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