The Vancouver Lymphadenopathy-AIDS Study: 1. Persistent generalized lymphadenopathy

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The Vancouver Lymphadenopathy-AIDS (acquired immune deficiency syndrome) Study is an ongoing prospective study of over 700 homosexual men attending six primary care practices in central Vancouver. A case-control study of risk factors for persistent generalized lymphadenopathy in homosexual men was conducted in five of the practices. The participants completed a questionnaire and underwent a complete physical examination at the time of enrolment and at a subsequent visit not less than 3 months later, and laboratory tests were performed after both visits. Persistent generalized lymphadenopathy was defined as the presence of lymph nodes greater than 1 cm in diameter at two or more extrainguinal sites for more than 3 months. Of the 519 patients who had completed both visits by February 1984, 126 (24%) were found to have the disease, and two controls without lymphadenopathy were frequency-matched on the basis of age and practice to each subject. More than 100 male sexual partners during one's lifetime, frequent receptive anal intercourse, a history of gonorrhea, use of illicit drugs and sexual contact in Los Angeles were identified as independent risk factors for persistent generalized lymphadenopathy. The similarity of these risk factors to those established for AIDS supports the hypothesis of a common etiology for the two diseases, and the high prevalence rate of persistent generalized lymphadenopathy further supports the hypothesis that AIDS is an uncommon response to a relatively common agent.

Étude prospective et continue des lymphadénomégalies et du syndrome immunodéficitaire acquis (SIDA) chez plus de 700 homosexuels masculins suivis dans six clientèles de médecine générale au centre-ville de Vancouver. Elle comporte l'analyse comparative des facteurs de risque pour la survenue de lymphadénomégalie généralisée persistante chez les sujets provenant de cinq des clientèles. Après leur avoir demandé de répondre à un questionnaire, on leur fait un examen complet et des épreuves de laboratoire qui seront répétés au bout d'au moins 3 mois. On définit la lymphadénomégalie généralisée persistante comme l'existence de ganglions dont le diamètre dépasse 1 cm dans au moins deux régions extra-inguinales pendant plus de 3 mois. On la trouve chez 126 (24%) des 519 sujets qui ont passé la visite de contrôle avant février 1984. Pour chacun d'entre eux on choisit dans la même clientèle deux témoins sans adénomégalie appariés quant à l'âge. Sont apparus comme facteurs indépendants de risque pour la survenue d'une lymphadénomégalie généralisée persistante un nombre de partenaires masculins dépassant 100 pour la vie entière, le coït anal passif fréquent, des antécédents de gonorrhée, l'usage de drogues et les contacts sexuels à Los Angeles. La similitude de ces facteurs à ceux déjà connus pour le SIDA ajoute du poids à l'hypothèse que les deux maladies partagent une même étiologie. La prévalence élevée de lymphadénomégalie généralisée persistante renforce l'idée que le SIDA constitue une conséquence relativement rare de la présence d'un agent pathogène assez répandu.

An epidemic of acquired immune deficiency syndrome (AIDS), manifested by opportunistic infections, Kaposi's sarcoma and lymphoma, has been reported in homosexual and bisexual men.[1] In the United States a national case-control study of Kaposi's sarcoma and *Pneumocystis carinii* pneumonia in this group identified several risk factors, including a large number of male sexual partners per year, frequent exposure to feces, syphilis, non-B hepatitis and the use of illicit substances.[2] Other studies have confirmed some of these associations.[3,4]

Concurrent with the AIDS epidemic, an increased incidence of persistent generalized lymphadenopathy has been seen in previously healthy homosexual men.[5] The characteristics of the population affected appear to be similar to those observed in people with AIDS.[6] In a study of homosexual patients with generalized lymphadenopathy referred to a university teaching hospital, opportunistic infections, Kaposi's sarcoma or lymphoma developed in 17% of the subjects within an average of 14 months.[7] In another group of referred patients with persistent generalized lymphadenopathy AIDS developed in 19% after 15 to 30 months of follow-up.[8] Some patients with lymphadenopathy have been shown to have behavioural risk factors associated with AIDS as well as laboratory evidence of immune dysfunction similar to that seen in patients with AIDS.[6-11]

Published data on persistent generalized lymphadenopathy have been derived exclusively from referred or clinic-based populations. We are currently conducting a general-practice-based prospective study in over 700 homosexual men to determine the prevalence and incidence of persistent generalized lymphadenopa-

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thy in this group, risk factors for the development of the syndrome, the prevalence of human T-lymphotropic retrovirus (HTLV-III) seropositivity and the incidence of seroconversion, and the interrelation of HTLV-III seropositivity, immune function and clinical status. We report on a case–control study to identify epidemiologic risk factors for the development of persistent generalized lymphadenopathy.

Methods

Six general practices in central Vancouver were involved in the study. Recruiting began in November 1982, when no cases of AIDS (as defined by the Centers for Disease Control [CDC], Atlanta[5]) were recorded in Vancouver. Two of the practices provide care almost exclusively to homosexual men, and the others have substantial numbers of homosexual male patients. During the recruitment period (November 1982 to February 1984) any regular patient known to be predominantly or exclusively homosexual who attended the office for any reason was asked by his practitioner to participate in the study. The refusal rate was approximately 5%. Since two of the practices recruited virtually all of their homosexual patients, selection bias in these practices was minimized. Furthermore, because only patients already enrolled in the practices were eligible for inclusion, self-referral of other homosexuals who were aware of the study or who had lymphadenopathy was also minimized.

Once they had given informed consent, the participants completed a self-administered questionnaire and underwent a complete physical examination, including measurement of lymph node size. Questions were phrased in the vernacular. The areas of interest were sexual partners, sexual practices, history of infectious disease, use of illicit drugs and sexual contact in other cities. The participants completed a second questionnaire and underwent a second physical examination not less than 3 months after enrolment. Laboratory tests were performed after both visits. All the questionnaires were coded, and strict confidentiality was maintained.

Persistent generalized lymphadenopathy was defined as the presence of lymph nodes greater than 1 cm in diameter at two or more extrainguinal sites for more than 3 months. Only subjects who had such lymphadenopathy at both visits were included; this ensured persistence of the lymphadenopathy for at least 3 months. Subjects were eligible only if the lymphadenopathy could not be explained by the practitioner as due to a current illness or as drug-induced.

Only patients who were free of lymphadenopathy at both visits were selected as controls. Two controls were frequency-matched to each subject on the basis of age (within 4 years) and practice. Of necessity, we were forced to select as controls 26 patients (10%) who were free of lymphadenopathy at the first visit but who had yet to undergo their second visit at the time of analysis.

To assess the extent of interobserver variability we conducted a separate experiment in which 16 participants were independently assessed by each practitioner as to the presence or absence of generalized lymphadenopathy as defined. Kappa values[12] were determined for each pair of practitioners, and each practitioner was assigned as a summary score the mean of the five κ values from his agreement with each of his five counterparts. The lowest value was 0.30, which was considered unacceptable; moreover, the practitioner associated with this value had the lowest lymphadenopathy detection rate. We decided to exclude this practice from the case–control study, which resulted in the exclusion of 5 subjects and 10 controls. It is unlikely that this affected the risk estimates. The remaining κ values, which ranged from 0.58 to 0.73, were considered acceptable.

Univariate analysis was based on Mantel–Haenszel methods.[13] All p values are two-sided, and the 95% confidence intervals are the test-based limits proposed by Miettinen.[14] Missing and unknown values were omitted from analysis. For multivariate analysis we used the factor analysis (principal component method) and stepwise logistic regression programs of the BMDP Statistical Software Package.[15] Because of collinearity, the illicit-drug variables were grouped to form a single variable (use of illicit drugs). This was suggested by factor analysis (factor scores greater than 0.2) and allowed comparison with other studies in which a similar variable was analysed.[2]

Results

By February 1984, 726 men in the five remaining practices had been recruited into the study. Of these, 519 had undergone both visits at the time of analysis. There were 126 cases of persistent generalized lymphadenopathy among the 519, a prevalence rate of 24%; in the two practices that enrolled virtually all their homosexual patients the rates were 29% and 22%. Accordingly, 252 controls were selected. The follow-up rates for participants who had or did not have generalized lymphadenopathy at the first visit were over 90%; thus, the risk estimates were not biased by differential surveillance. There were no significant differences between the subjects and controls with regard to income, racial or ethnic background, or place of birth.

Sexual partners

The relative risk for persistent generalized lymphadenopathy in men with more than 100 male sexual partners in their lifetime or more than 20 partners in the previous year was significantly elevated, at 2.5 and 1.7 respectively ($p < 0.001$) (Table I). As these variables are likely to be confounded, we adjusted each with the other using the Mantel–Haenszel method.[13] A significantly elevated relative risk of 2.3 ($p < 0.001$) in men with more than 100 partners in their lifetime was found even after adjustment for number of partners in the previous year. However, there was no elevated risk in men with more than 20 partners in the previous year when the lifetime number of partners was taken into account. We found no significant association between persistent generalized lymphadenopathy and age at which regular sex with men was initiated, with or without adjustment for lifetime number of partners.

Sexual practices

Receptive anal intercourse ($p < 0.001$), insertive fisting (manual stimulation of the rectum) ($p < 0.01$) and receptive fisting ($p < 0.001$) were found to be significantly associated with persistent generalized lymphadenopathy (Table II). Because of the established association of the disease with lifetime number of partners and because a large number of partners is likely to be confounded with various sexual and lifestyle variables, we carried out all further univariate analysis both with and without adjustment for lifetime number of partners. After such adjustment, receptive anal intercourse and receptive fisting remained significantly associated with persistent generalized lymphadenopathy ($p < 0.001$). Swallowing semen did not appear to confer any increased risk. There was a significant association with sexual contact in bathhouses ($p = 0.04$), but not when lifetime number of partners was taken into account. We found no association with proportion of contacts occurring in bars, discotheques or public washrooms.

History of infectious disease

A history of gonorrhea ($p < 0.001$), hepatitis ($p < 0.05$) or scabies ($p < 0.05$) was significantly associated with persistent generalized lymphadenopathy (Table III). However, only a history of gonorrhea remained significantly associated ($p < 0.05$) after adjustment for lifetime number of partners. Rectal gonorrhea was more highly associated than was urethral or pharyngeal gonorrhea. No association with syphilis was detected. In addition to the diseases listed in Table III, we considered specific enteric pathogens (*Salmonella*, *Shigella*, *Campylobacter*, *Giardia* and *Entamoeba*) as well as nonspecific urethritis, venereal warts, pubic lice, mononucleosis, herpes simplex and gay bowel syndrome; we found no associations with persistent generalized lymphadenopathy.

Use of illicit drugs

The use of various illicit drugs was found to be strongly associated with persistent generalized lym-

Table I—Relative risk for persistent generalized lymphadenopathy associated with sexual partners and age at initiation of regular sex with men in 126 men with the disease and 252 controls

Variable	No. (and %) of subjects (n = 126)	No. (and %) of controls (n = 252)	Relative risk (and 95% confidence interval [CI])	Adjusted relative risk (and 95% CI)
More than 100 male sexual partners in lifetime	99 (79)	150 (60)	2.5 (1.5–4.0)*	2.3 (1.2–4.1)*†
More than 20 male sexual partners in previous year	72 (57)	111 (44)	1.7 (1.1–2.6)*	1.1 (0.7–1.9)‡
Initiation of regular sex with men at 19 years or younger	73 (60)	128 (51)	1.3 (0.9–2.1)	1.3 (0.8–2.0)‡

*$p < 0.001$.
†Adjusted for number of male sexual partners in previous year.
‡Adjusted for number of male sexual partners in lifetime.

Table II—Relative risk for persistent generalized lymphadenopathy associated with sexual practices

Practice*	No. (and %) of subjects	No. (and %) of controls	Relative risk (and 95% CI)	Adjusted relative risk (and 95% CI)†
Oral–genital contact‡				
Insertive	81 (64)	166 (66)	1.0 (0.6–1.5)	0.9 (0.6–1.5)
Receptive	90 (71)	199 (79)	0.7 (0.4–1.2)	0.7 (0.4–1.1)
Anal intercourse‡				
Insertive	75 (60)	127 (50)	1.5 (0.9–2.3)	1.3 (0.8–2.1)
Receptive	80 (64)	104 (41)	2.5 (1.6–3.9)¶	2.4 (1.5–3.7)¶
Oral–anal contact§				
Insertive	46 (37)	93 (37)	1.0 (0.6–1.6)	0.9 (0.6–1.5)
Receptive	61 (48)	118 (47)	1.1 (0.7–1.7)	1.0 (0.7–1.6)
Fisting‖				
Insertive	55 (44)	69 (27)	2.1 (1.3–3.3)**	1.6 (0.9–2.7)
Receptive	35 (28)	22 (9)	4.1 (2.3–7.1)¶	3.5 (1.9–6.4)¶
Swallowing semen‖	36 (29)	58 (23)	1.3 (0.8–2.2)	1.4 (0.8–2.3)
Sexual contact in bathhouses‡	76 (60)	124 (49)	1.6 (1.0–2.4)††	1.2 (0.7–1.9)

*Proportion of sexual encounters that included this practice: ‡> 25%: §> 5% and ‖any.
†Adjusted for number of male sexual partners in lifetime.
¶$p < 0.001$.
**$p < 0.01$.
††$p < 0.05$.

phadenopathy (Table IV). Use of methylene-dioxy amphetamine (MDA) ($p < 0.01$), lysergic acid diethylamide (LSD) ($p < 0.01$), cocaine ($p < 0.05$) or marijuana ($p < 0.05$) was associated even after adjustment for lifetime number of partners. We found no association with use of amphetamines ("speed") or nitrite inhalants ("poppers"). Further analysis of the use of nitrite inhalants showed no evidence of any dose response or any difference with type of nitrite used (butyl or amyl). Since heroin or other intravenously taken drugs were used by only a small number of the participants, it was difficult to detect significant associations. No associations were found with use of alcohol or tobacco.

Sexual contact in other cities

Sexual contact with more than 10 partners in the preceding 5 years in Los Angeles ($p < 0.001$), San Francisco ($p < 0.01$) or Seattle ($p < 0.01$) was

Table III—Relative risk for persistent generalized lymphadenopathy associated with history of infectious disease

Disease	No. (and %) of subjects	No. (and %) of controls	Relative risk (and 95% CI)	Adjusted relative risk (and 95% CI)*
Gonorrhea	103 (82)	164 (65)	2.4 (1.4–4.0)†	2.0 (1.1–3.4)‡
Hepatitis	88 (70)	143 (57)	1.8 (1.1–2.8)‡	1.4 (0.8–2.3)
Scabies	40 (32)	56 (22)	1.6 (1.0–2.6)‡	1.4 (0.9–2.3)
Syphilis	37 (29)	70 (28)	1.1 (0.7–1.7)	0.9 (0.6–1.5)

*Adjusted for number of male sexual partners in lifetime.
†$p < 0.001$.
‡$p < 0.05$.

Table IV—Relative risk for persistent generalized lymphadenopathy associated with use of illicit drugs

Drug	No. (and %) of subjects	No. (and %) of controls	Relative risk (and 95% CI)	Adjusted relative risk (and 95% CI)*
Methylene-dioxy amphetamine (MDA)†	83 (66)	113 (45)	2.4 (1.5–3.7)§	2.0 (1.3–3.3)‖
Lysergic acid diethylamide (LSD)†	80 (64)	109 (43)	2.3 (1.5–3.6)§	2.1 (1.3–3.3)‖
Cocaine†	65 (52)	92 (37)	1.9 (1.2–2.9)‖	1.8 (1.1–2.8)¶
Marijuana‡	80 (64)	126 (50)	1.8 (1.2–2.8)‖	1.7 (1.1–2.6)¶
Amphetamines†	42 (33)	63 (25)	1.5 (0.9–2.4)	1.3 (0.8–2.1)
Nitrite inhalants‡	68 (54)	127 (50)	1.2 (0.7–1.8)	1.0 (0.7–1.7)
Heroin†	8 (6)	10 (4)	1.6 (0.6–4.2)	1.5 (0.6–4.0)

*Adjusted for number of male sexual partners in lifetime.
†Ever used.
‡Used more than once a month.
§$p < 0.001$.
‖$p < 0.01$.
¶$p < 0.05$.

Table V—Relative risk for persistent generalized lymphadenopathy associated with sexual contact in other cities

City*	No. (and %) of subjects	No. (and %) of controls	Relative risk (and 95% CI)	Adjusted relative risk (and 95% CI)†
Los Angeles	17 (14)	8 (3)	4.8 (2.1–10.6)‡	3.7 (1.5–8.9)§
San Francisco	33 (26)	34 (14)	2.3 (1.4–3.9)§	1.9 (1.1–3.3)‖
Seattle	41 (33)	51 (20)	1.9 (1.2–3.1)§	1.5 (0.9–2.5)
New York	9 (7)	15 (6)	1.2 (0.5–2.9)	1.0 (0,4–2.4)

*More than 10 sexual partners in city in previous 5 years.
†Adjusted for number of male sexual partners in lifetime.
‡$p < 0.001$.
§$p < 0.01$.
‖$p < 0.05$.

significantly associated with persistent generalized lymphadenopathy (Table V). After adjustment for lifetime number of partners, the association with Los Angeles ($p < 0.01$) and San Francisco ($p < 0.05$) was less strongly significant, while that with Seattle was not statistically significant. We did not detect any risk associated with sexual contact in New York. Sexual contact in other cities did not occur often enough for analysis.

Multivariate analysis

More than 100 sexual partners in one's lifetime, receptive anal intercourse, a history of gonorrhea, use of illicit drugs and sexual contact in Los Angeles remained significantly associated with persistent generalized lymphadenopathy in the final model (Table VI). Interactions were tested at each step, but none was statistically significant.

Discussion

Recent studies of persistent generalized lymphadenopathy have been based primarily in clinics or tertiary care centres. By using a stable, primary-care-based population, we attempted to define as general a group of homosexual men as possible so as to more accurately assess the prevalence, incidence, risk factors and natural history of the disease.

The problems in obtaining a true random sample of homosexual men have been recognized.[2] For example, an unknown proportion of homosexual men do not openly acknowledge their sexual orientation and are therefore not accessible to sampling. It is difficult to gauge how well a group such as ours, whose members have chosen to attend predominantly homosexual medical practices, represents the general male homosexual population. At the very least, we avoided some of the bias associated with the use of tertiary care or clinic-based populations.

Our data suggest that a large number of male sexual partners is associated with persistent generalized lymphadenopathy. The suggestion that lifetime number of partners may be of greater importance than number of partners in the previous year must be interpreted with caution. A large number of male sexual partners is an established risk factor for AIDS,[2,4,8] and sexual activity has been observed to be elevated in patients with persistent generalized lymphadenopathy.[10]

Table VI—Results of logistic regression analysis

Risk factor	Coefficient	Relative risk	p
More than 100 male sexual partners in lifetime	0.591	1.8	0.034
Receptive anal intercourse	0.527	1.7	0.032
History of gonorrhea	0.588	1.8	0.048
Use of illicit drugs*	0.856	2.4	0.002
Sexual contact in Los Angeles	0.472	1.6	0.050

*MDA, LSD, cocaine, amphetamines or heroin.

We also detected an elevated risk in men who frequently practised receptive anal intercourse; the risk appeared to be independent of the effect of number of partners. Receptive anal intercourse has been suggested to be a risk factor for AIDS,[4,16,17] although this was not confirmed in the CDC study.[2,18] The practice of fisting has also been found to be associated with AIDS,[4] and the results of our univariate analysis suggested a similar association with persistent generalized lymphadenopathy. However, it was not found to be significantly associated in the multivariate analysis, but the number of participants who reported this practice was small.

We found an elevated risk for those with a history of gonorrhea. This has not been identified as an independent risk factor for AIDS.[2-4] On the other hand, although syphilis and non-B hepatitis have been found to be associated with AIDS,[2] we did not find any association that was independent of the other factors.

Men who used illicit drugs were at elevated risk for persistent generalized lymphadenopathy, and this risk persisted despite adjustment for the other factors. An association between AIDS and illicit drug use has previously been reported.[2] We found no association between persistent generalized lymphadenopathy and the use of nitrite inhalants. These drugs were found to be associated with AIDS by Marmor and colleagues,[3] but subsequent analysis of the data involving more sexual practice variables suggested that the observed association may have been confounded by sexual behaviours.[4] In the CDC study no association between AIDS and the use of nitrite inhalants was found,[2] whereas these substances were implicated in the development of AIDS in patients with persistent generalized lymphadenopathy.[8]

We found persistent generalized lymphadenopathy to be associated with recent sexual contact in Los Angeles and San Francisco, although only the former association remained significant in the multivariate analysis. Sexual contact in AIDS-endemic areas has been found to be associated with the development of AIDS.[19] It is noteworthy that we did not find sexual contact in New York to be significant, although an association may have been missed because of small numbers.

Two additional points should be made with regard to analysis of our data. First, although we attempted individual matching on the basis of age, medical practice and date of entry into the study, this was not possible in many cases because of the relatively small pool of available controls. We chose to be conservative and analysed the data on the basis of frequency matching. Second, our population might represent a relatively homogeneous subset of the general male homosexual population with regard to the various risk factors. Thus, any case–control study carried out within the population may suffer from a degree of overmatching with respect to these variables. The net effect of these two observations, if any, is that our estimates may be biased toward unity, and we may have underestimated the true risk for persistent generalized lymphadenopathy associated with the various factors studied.

Our findings suggest that several established risk

factors for AIDS are also risk factors for persistent generalized lymphadenopathy and support the hypothesis of a common etiology for the two diseases. With the recent discovery of lymphadenopathy-associated retrovirus (LAV)/HTLV-III as the putative AIDS agent,[20] there is additional evidence to suggest this agent as a cause of persistent generalized lymphadenopathy. Montagnier and associates in France isolated LAV from a homosexual man with lymphadenopathy[20] and the same type of retrovirus both from cultured lymphocytes from several patients with AIDS[21] and from two siblings with hemophilia B, one of whom had AIDS.[22] Gallo and coworkers[23] isolated HTLV-III not only from patients with AIDS but also from 18 of 21 patients with pre-AIDS, defined as unexplained chronic lymphadenopathy or reduced number of helper T lymphocytes. It has been suggested that HTLV-III and LAV may be identical.[24]

Under the hypothesis of a common viral etiology for persistent generalized lymphadenopathy and AIDS, one might relate a large number of male sexual partners to exposure to the agent, frequent receptive anal intercourse to primary route of inoculation, and frequent sexual contact in endemic areas to increased exposure. To account for the observed independent effect of illicit drug use, several hypotheses can be proposed. First, such drugs may have a common direct immunologic mechanism that potentiates the action of the etiologic agent. There is little evidence, however, to support such a complicated hypothesis. Second, repeated use of these drugs may cause a nonspecific stress response, which is known to alter immune reactivity and may potentiate the action of the agent. Third, the use of illicit drugs may be confounded with some lifestyle factor not reflected in the other variables. Similarly, the association between persistent generalized lymphadenopathy and gonorrhea may be due to an association of the latter with some lifestyle factor rather than a specific biologic action of gonococcal infection. This may be true of syphilis and nitrite inhalants as well and may account for their inconsistent associations with AIDS.

In summary, the striking similarities between risk factors for AIDS and for persistent generalized lymphadenopathy support the hypothesis of a shared etiology. It has been suggested by Abrams and colleagues[10] that the latter may be an alternative phenotypic response to the AIDS agent, although it is entirely unclear which host factors determine the type of response exhibited. If we accept this hypothesis, our data suggest that up to the study period approximately one quarter of our population had contracted the agent and had shown the lymphadenopathic response.

That the prevalence of the AIDS agent within the community may be of this magnitude is consistent with other observations. Several investigators have found evidence of immune dysfunction in substantial proportions of apparently healthy, asymptomatic homosexual men.[11,16,25-28] Direct evidence of infection has been provided by Sarngadharan and associates,[29] who detected antibodies to HTLV-III in 7 of 17 asymptomatic homosexual men, and by Brun-Vezinet and coworkers,[30] who found antibodies to LAV in 8 of 44 such men. Antibody to HTLV-III was also detected in 22 of 250 Danish homosexual men in 1981[31] and in 35 of 66 homosexual men in New York City in 1982.[32] The prevalence rates of HTLV-III seropositivity in male homosexuals visiting a sexually transmitted disease clinic in San Francisco in 1978, 1980 and 1984 were 1%, 25% and 65% respectively.[33] Whereas AIDS may once have been regarded as a common response to an uncommon agent, these data suggest that it is, in fact, an uncommon response to a common agent. The crucial question thus becomes that of identifying not merely risk factors for infection with the agent but risk factors for the development of AIDS in those who have been infected.

The natural history of persistent generalized lymphadenopathy remains unclear, although in referred populations AIDS developed in 17% to 19% of patients with persistent generalized lymphadenopathy who were followed for 1 to 2 years.[7,8] These estimates are likely to be high because of the selected nature of the populations under study. In our prospective study we will attempt to elucidate the natural history of persistent generalized lymphadenopathy, its relation to AIDS and the possible effect of reduction in behavioural risk factors. More important, we are currently analysing stored blood samples from our population for antibodies to HTLV-III; the results will be reported in the subsequent parts of this series.

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