Studies in Homosexual Patients With and Without Lymphadenopathy

Relationships to the Acquired Immune Deficiency Syndrome

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• We studied the immunologic function of 19 sexually active homosexual men, ten of whom had persistent lymphadenopathy. Analysis of mononuclear cell populations distinguished homosexuals from heterosexual controls since, as a group, homosexuals had increased percentages of natural killer cells (Leu 7+), decreased helper-inducer T lymphocytes (OKT-4+), increased suppressor/cytotoxic (OKT-8+) T lymphocytes, low OKT-4:OKT-8 ratios, and depressed mitogenic responses. Homosexuals without lymphadenopathy were distinguishable from controls by increased percentages of Ia+ cells, decreased OKT-4+ cells, and decreased OKT-4:OKT-8 ratios. Four had positive findings simultaneously for hepatitis B surface antigen (HBsAg) and surface antibody, and five had positive findings for HBsAg alone. Homosexuals with lymphadenopathy were distinguishable from controls by increased percentages of Leu 7+ cells, increased total lymphocyte numbers per cubic millimeter, decreased percentages of both OKT-4+ and OKT-8+ cells, abnormal OKT-4:OKT-8 ratios, and depressed mitogenic responses. Only histories of larger numbers of sexually acquired diseases, higher numbers of OKT-8+ cells per cubic millimeter, and lower mitogenic responses in homosexuals with lymphadenopathy distinguished this group from homosexuals without lymphadenopathy. Furthermore, none of the nine patients tested in this group was HBsAg positive. We conclude that homosexuals without lymphadenopathy are distinguishable from those with lymphadenopathy by both immunologic and serologic abnormalities.

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A syndrome of chronic, generalized lymphadenopathy has recently been noted in homosexual men and patients receiving transfusions of blood or blood products.[1-4] The exact relationship of this syndrome to the development of the acquired immune deficiency syndrome (AIDS) in these same patient groups is unclear. At least two observations suggest that the two may be related. First, persistent lymphadenopathy has preceded the development of AIDS in homosexuals.[5,6] Second, similar, apparently specific histopathologic findings have been noted in lymph nodes from homosexuals with isolated lymphadenopathy and AIDS.[7]

We report the results of an extensive immunologic investigation of 19 sexually active homosexual males, ten of whom had persistent lymphadenopathy. Patients with lymphadenopathy had greater numbers of sexually acquired diseases, and a lymphocytosis with an increase of total T-suppressor/cytotoxic cells that distinguished the group from both controls and homosexuals without lymphadenopathy. Lymphocyte mitogenic responses also distinguished both homosexual groups from each other and were profoundly abnormal in patients with lymphadenopathy.

SUBJECTS AND METHODS

Study Population

The 19 homosexual males studied were examined at the Ochsner Medical Institution or Tulane Medical Center, New Orleans. All of the patients were initially self-referred and requested medical care and long-term follow-up. All lived in the New Orleans area and most were seen as outpatients.

Extensive histories were taken from each patient to obtain data on the numbers and types of previous sexually acquired diseases, drug abuse, use of bathhouses, and frequency of sexual exposure. Patients were questioned specifically about recent weight loss, malaise, anorexia, or recurrent infections. Available medical records were also reviewed. An extensive physical examination was performed with special attention to detect lymphadenopathy.

Nineteen healthy heterosexual men age-matched to the homosexual study group served as controls for the immunologic tests performed.

Immunologic Evaluation

Delayed hypersensitivity skin tests were performed as previously described[8] and induration recorded at 24 and 48 hours. Skin test antigens included at least five of the following antigens: purified protein derivative (5 tuberculin units), *Candida albicans* (1:100), streptokinase-streptodornase (4 units streptokinase/40 units streptodornase), mumps (2 colony-forming units), tri-

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Table 1.—Clinical Data on Homosexuals in Study*

Patient No./ Age, yr	Reason for Consultation	Other Complaints	Previous Sexually Transmitted Diseases	History of IV Drug Abuse	History of Nitrite Use	Other Diagnoses
			Patients Without Lymphadenopathy			
1/50	Herpes zoster	Headache, undocumented fever	Hepatitis B	No	Yes	Herpes zoster, HBsAg positive
2/41	Sexual partner had AIDS	None	Hepatitis B	No	Yes	None, HBsAg positive
3/65	Acute proctitis	None	Hepatitis B	No	No	Condyloma acuminatum
4/39	AIDS evaluation	None	None	Unclear	No	Epidermal cysts, recurrent
5/35	Cutaneous herpes	None	Hepatitis B, condyloma acuminatum	No	Yes	Cutaneous herpes
6/25	Follow-up for hepatitis	None	Hepatitis B, syphilis, gonococcal urethritis	No	Yes	None
7/37	AIDS evaluation	Fatigue, undocumented weight loss	Hepatitis B	No	Unclear	Chronic persistent hepatitis, HBsAg positive
8/27	Headaches	Recurrent upper respiratory tract infections, fatigue	Hepatitis B	No	No	Chronic persistent hepatitis, HBsAg positive
9/24	Follow-up of previous hepatitis	Fatigue	Hepatitis B	Yes	No	HBsAg positive
			Patients With Lymphadenopathy			
10/25	Diarrhea	None	Syphilis, urethritis, hepatitis B	No	No	Chlamydial proctitis
11†/20	Bloody diarrhea	Fever, weight loss	Syphilis	No	No	Acute proctitis, cause unknown
12†/39	Sore throat	None	Gonococcal urethritis, proctitis, syphilis, amoebic dysentery, hepatitis B	No	Yes	Gonorrheal pharangitis
13†/33	Skin lesions	Malaise	Gonococcal urethritis, hepatitis B	No	Yes	Secondary syphilis
14†/32	Lymphadenopathy	None	Syphilis, gonococcal proctitis, hepatitis B	No	Yes	None
15/37	Sore throat	None	Syphilis, dysentery	No	No	Candida esophagitis
16/32	Lymphadenopathy	None	Syphilis, hepatitis	Unclear	Yes	None
17†/31	Lymphadenopathy, penile discharge	None	Hepatitis B	Unclear	Unclear	Nonspecific urethritis
18/43	Lymphadenopathy	Recurrent urinary and respiratory tract infections	Syphilis, condyloma acuminatum, amebiasis, hepatitis B	No	No	None
19/35	Wart on penis	Weight loss, malaise	Syphilis, condyloma acuminatum, hepatitis B	No	Yes	Condyloma latum

*AIDS indicates acquired immune deficiency syndrome; HBsAg, hepatitis-B surface antigen; IV, intravenous.
†Lymph node biopsy specimen showed reactive hyperplasia.

chophytin (1:60), tetanus toxoid (1:100), and histoplasmin (1:100). Tests were judged positive if 10 mm or more of induration was present at either time period. Patients failing to react to any skin test antigen were judged "anergic" and their skin test results considered negative.

Serologic Studies.—Serum samples were analyzed for the presence of hepatitis B surface antigen (HBsAg) and IgG antibody to hepatitis B surface antigen (HBsAb) by radioimmunoassay using commercial reagents.[9,10] The presence of complement-fixing antibody in the serum for cytomegalovirus (CMV) and herpes simplex was determined by indirect fluorescence (FIAX Test Kit).[11] Antibodies to *Toxoplasma* were also determined by that technique,[12] as were antibodies to *Treponema pallidum*.

Evaluation of Mononuclear Cell Populations.—Peripheral blood mononuclear cell populations were isolated from whole blood by density-gradient separation over Hypaque-Ficoll. Mononuclear cell populations were detected using monoclonal antibodies, E-rosette reactive cells (OKT-11), T-helper/T-inducer cells (OKT-4), and T-suppressor/cytotoxic cells (OKT-8).[13] Cells bearing Ia-matrix antigen (monoclonal antibody HLA-DR) and the natural killer-cell antigen (Leu 7) were also detected using monoclonal antibodies.[14,15] These studies were performed by direct immunofluorescence with counting on a fluorescence-activated cell sorter (FACS III). Each analysis consisted of 25,000 cells utilizing the 488-nm laser line with the following gain settings of scatter: 4×5 and fluorescence: 2×1 at 500 mV. The percent of positive cells was calculated after correction for background staining with daily results confirmed by fluorescence microscopy. B-lymphocyte percentages were similarly determined using polyclonal F(ab')2 goat antihuman immunoglobulin.[16] Total numbers of lymphocytes were calculated by multiplying the leukocyte count by the percentage of lymphocytes in the differential cell count. Absolute numbers of lymphocyte subpopulations were calculated by multiplication of their percentages by the total lymphocyte count with results expressed as cells per cubic millimeter. Staining of monocytes in mononuclear cell preparations was performed using α-naphthyl-butyrate esterase stain.[17] Serum immunoglobulin determinations (IgG, IgM, and IgA) were performed by nephelometry using commercial reagents.

Lymphocyte proliferation induced by the T-cell mitogen phyto-

Table 2.—Laboratory Data on Homosexuals in Study*

HBsAg	HBsAb	RPR	FTA-ABS	*Toxoplasma* Titer†	Herpes Titer‡	CMV Titer§	Positive Delayed Skin Test‖	Serum IgG¶	Serum IgM	Serum IgA	WBC/cu mm ×10³	PMN/cu mm ×10³#
Patients Without Lymphadenopathy												
5/9	7/9	0/7	1/4	0/7	7/7	7/7	6/8	1,942±638 (873-5,010)	208±50 (46-391)	254±29 (187-377)	6.80±0.88 (3.5-11.9)	3.84±0.55 (2.1-7.2)
Patients With Lymphadenopathy												
0/9	7/9	7/8	6/8	2/7	3/5	4/6	4/6	1,920±402 (912-3,950)	214±32 (107-388)	348±85 (140-650)	6.46±0.89 (2.7-12.3)	2.83±0.37 (1.1-5.3)

*HBsAg indicates hepatitis B surface antigen; HBsAB, hepatitis B surface antibody; RPR, rapid plasma reagin; and CMV, cytomegalovirus.
†Titer of greater than 1:16 is considered positive.
‡Titer of greater than 1:8 is considered positive.
§Titer of greater than 1:8 is considered positive.
‖Positive to one or more of five skin test antigens as described in the text.
¶Reported as mean±SEM and range of values in mg/dL.
#PMN indicates polymorphonuclear leukocytes.

Table 3.—Mononuclear Cell Populations in Homosexuals and Control Subjects

	% B Cells	% Monocytes	% Leu 7	% Ia+	% OKT-11	% OKT-3	Lymphocytes ×10³/cu mm
Control subjects	12.2±1.0	18.8±1.5	9.2±1.0	26.5±1.5	71.3±1.34	59.3±1.8	2.2±0.13
Homosexuals	9.9±1.5	18.7±1.8	14.0±1.8*	30.9±2.8	70.0±4.5	58.0±2.9	2.78±0.40
Group 1	8.1±1.8	20.2±3.1	13.2±3.1	34.1±3.8*	67.5±3.8	56.8±4.5	2.48±0.43
Group 2	9.3±1.4	16.9±2.1	15.0±2.6*	27.9±4.0	73.0±2.7	58.6±4.2	3.06*±0.68

**PE*.05 when compared with control values. Data are reported as mean±SEM.

Table 4.—T-Lymphocyte Subpopulations in Homosexuals and Control Subjects

	% OKT-4	Total OKT-4/cu mm	% OKT-8	Total OKT-8/cu mm	OKT-4:OKT-8 Ratio
Control subjects	35.1±1.5	849±61	22.5±1.7	554±56	1.76±0.14
Homosexuals	26.0±2.4*	809±120	29.0±2.3*	929±173*	1.06±0.15*
Group 1	25.9±3.8*	745±179	26.0±2.0	668±82	1.05±0.18*
Group 2	26.3±3.2*	866±168	31.8±3.9*	1,164±309*†	1.08±0.24*

**PF*.05 when compared with control value. Data are reported as mean±SEM.
†*PF*.10 when compared with group 1 value.

hemagglutinin (PHA) was evaluated across a dose range of 1 to 50 mg/L of PHA. Standard microculture techniques were employed with 1×10^5 mononuclear cells per well in round-bottomed plates, and RPMI 1640 media containing 10% heat inactivated pooled human serum and antibiotics. Cells were cultured for four days, the time of maximum response in our system.[18] Cultures were harvested using an automated cell harvester 16 hours after the addition of 1 μCi; per well of tritiated thymidine. Radiolabeled nucleotide was assayed in a liquid scintillation counter and recorded as counts per minute, where counts per minute were equal to cell cultures stimulated with PHA less counts per minute from similar but unstimulated cultures.

Statistical Analysis

Statistical analyses were performed using Student's *t* test adjusted for multiple comparisons[19] and (for PHA dose-response curves) analysis of variance and covariance with repeated measures.[20]

RESULTS

Clinical Characteristics of the Study Population

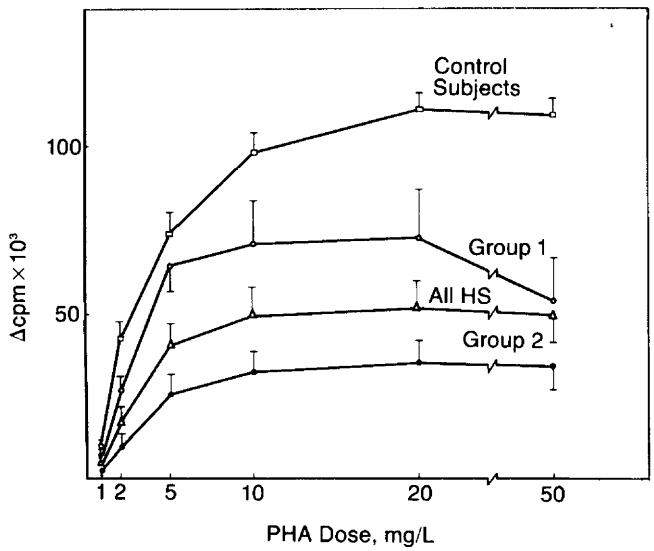
Homosexuals in the study ranged from 20 to 65 years of age (Table 1). All were sexually active and many visited bathhouses. However, data as to the number and frequency of sexual contacts were thought to be too equivocal to allow comparisons among patients and are not reported. Nine patients acknowledged use of nitrites but only one admitted intravenous drug abuse. Most patients had histories of multiple sexually transmitted diseases.

A variety of complaints resulted in request for initial medical evaluation; no single complaint was predominant. Eight patients had histories of fever, weight loss, malaise, fatigue, or recurrent viral infections. Two patients (patients 1 and 5) had active herpes infections at the time of study.

Patients could be grouped into two groups on the basis of the absence (group 1) or presence (group 2) of generalized lymphadenopathy. The ten patients in group 2 were diagnosed as having the "benign reactive lymphadenopathic syndrome"[1] by the presence of chronic, unexplained lymphadenopathy of at least two months' duration with at least three nodes greater than 1.5 cm at two or more extrainguinal sites. All of these individuals were subsequently observed for at least one additional month after the study, during which time their lymphadenopathy persisted. During the course of the study, additional diagnoses were made and are listed in Table 1.

Two group 2 patients (patients 13 and 19) had secondary luetic lesions treated previous to our immunologic evaluation. Thus, syphilis provided a possible explanation for their lymphadenopathy. However, lymphadenopathy predated the skin lesions of patient 13 by six months, and he described a primary lesion that occurred after the onset of lymphadenopathy. Syphilis, therefore, seems an unlikely explanation for the lymphadenopathy. The lymphadenopathy of patient 13 persisted despite adequate therapy for syphilis, as did the lymphadenopathy in patient 19.

One patient in group 1 (patient 6) and two patients in group 2 (patients 10 and 15) were leukopenic (total leukocyte count, ≤4,300/cu mm). Three patients (two in group 1,



Dose-response curves to mitogen phytohemagglutinin (PHA) in control subjects, combined homosexual groups (all HS), nine homosexuals without lymphadenopathy (group 1), and ten homosexuals with lymphadenopathy (group 2). Results are expressed as means ± SEMs.

patients 1 and 6, and one in group 2, patient 15) were lymphopenic (lymphocyte count, ≤1,500/cu mm). No patient was neutropenic (neutrophil count, ≤1,100/cu mm).

Immunologic Evaluation

Serologic Studies.—Fifteen of 18 patients tested had serologic markers for hepatitis B. Five patients, all in group 1, had detectable HBsAg, but 14 patients among the two groups had HBsAb (Table 2). Four patients in group 1 had simultaneous positive results for HBsAg an HBsAb. Of the patients tested, 11 of 13 had detectable antibody to CMV, and ten of 12 had antibody to herpes simplex virus. Antibodies to *Toxoplasma* were uncommon. Positive serologic findings for syphilis were present in six of eight patients tested in group 2, but in only one of nine patients in group 1.

Mean values of serum IgG and IgM in both groups were significantly greater ($P \leq .05$) than those of the 19 controls (Table 2). The mean IgA value for group 2 was greater than that of group 1 but not significantly so. Control values were 1,133 ± 59 mg/dL for IgG, 138 ± 16 mg/mL for IgM, and 255 ± 25 mg/mL for IgA. Serum immunoglobulin values were not notably different among the two groups of homosexuals.

Mononuclear Cell Populations.—Percentages and total numbers per cubic millimeter of mononuclear cell populations were determined. Although both values are discussed, percentages, but not absolute numbers, are shown in Table 3.

Percentages of monocytes, B lymphocytes, and T cells, were not different among controls and homosexuals or the two homosexual groups. The total lymphocyte count in homosexuals with lymphadenopathy (group 2) was significantly greater ($P \leq .05$) than that of the control group; it was also greater, although not significantly so ($P \geq .05$), than the total lymphocyte count of patients without lymphadenopathy (group 1). Cells with the surface antigen associated with natural killer-cell activity (Leu 7) were significantly greater ($P \leq .05$) in percentage and absolute number in group 2 patients as compared with control values. The percentage of these cells in group 2 patients was larger than in group 1, but not significantly so ($P \geq .05$). In contrast, percentages of Ia+ cells were greater in group 1 patients than in controls, while values in group 2 were similar to those seen in controls. Total numbers of both Ia+ and Leu 7+ cells were significantly greater ($P \leq .05$) in groups 1 and 2, respectively, than in the control group, but not different among the two homosexual groups.

T-Lymphocyte Subpopulations.—Percentages, but not total numbers, of OKT-4+ were significantly reduced ($P \leq .05$) in both homosexual groups as compared with controls, but were not different among the two groups (Table 4). Percentages and total numbers of OKT-8+ were significantly increased ($P \leq .05$) only in group 2 homosexuals. Ratios of OKT-4:OKT-8 lymphocytes were lower than control values in both homosexual groups but not different among the groups.

Skin Test and Lymphocyte Mitogenic Responses.—Eight homosexuals in each group completed delayed hypersensitivity skin testing. Results were similar in both groups; six were positive to one or more antigens, and two were negative.

Lymphocyte proliferative responses to the mitogen PHA were depressed across the entire range of PHA doses in the homosexual group (Figure). Although PHA responses were lower in group 1 patients than those of controls, the group 1 dose-response curves were not notably different from the control curve. Dose-response curves of group 2 patients were significantly different ($P \leq .05$) from those of group 1 homosexuals, the homosexual group as a whole, and control values.

Analysis of Immunologic Variables in Asymptomatic Patient Subgroups.—Results of immunologic studies in seven patients who had no systemic complaints (ie, no malaise, fatigue, weight loss, or fever), no active or recent clinical illness, and who were neither leukopenic nor lymphopenic, were analyzed. This analysis included data from patients 2, 3, and 4 in group 1 and patients 12, 14, 16, and 17 from group 2. Results of analysis of mononuclear cell populations in these subgroups of groups 1 and 2 were similar to those in the intact groups. For instance, percentages of OKT-4+ (21.3 ± 2.6 *v* 23.4 ± 2.6) and OKT-8+ (23.4 ± 1.7 *v* 30.8 ± 5.7) T cells were not significantly different ($P \geq .05$) between the group 1 and group 2 subgroups, respectively. Total numbers of OKT-8+ cells were greater in the group 2 subgroup (1,414 ± 65 *v* 863 ± 148), although these values were not significant at the $P \leq .05$ level. Ratios of T-lymphocyte subsets (OKT-4:OKT-8) from group 1 (0.90 ± 0.7) and group 2 (0.93 ± 0.3) were not significantly different ($P \geq .05$). Dose-response curves to PHA were more severely depressed in the patients with lymphadenopathy at all PHA doses than in those without, but the two dose-response curves were not significantly different at the $P \leq .05$ level. However, differences in responses were large. For instance, at the peak mitogenic dose of 20 mg/L, responses in the subset of patients from group 1 averaged 74,478 ± 21,686, while those from group 2 were 28,098 ± 11,858.

COMMENT

A number of reports have appeared recently describing the clinical features of AIDS in homosexual men. It appears that the syndrome represents a spectrum of disease consisting of at least the following three entities: (1) immunologic abnormalities in otherwise asymptomatic individuals[21]; (2) a syndrome of chronic lymphadenopathy often associated with constitutional symptoms of non–life-threatening opportunistic infections[1]; and (3) a state associated with profound cell-mediated immunodeficiency with Kaposi's sarcoma,[5,6,22,23] fatal opportunistic infections,[24-27] or a combi-

nation of the two.[5] Only the third entity is currently classified as AIDS for the purpose of case definition.[28] It is tempting to speculate that these various categories of disease represent manifestations of a single immunologic insult, perhaps from the same agent, or are "stages" of an evolving disease process. It is also possible that these stages are unrelated to each other and may be caused by different, unrelated events. These relationships remain obscure, at least in part due to a paucity of detailed clinical and immunologic data that might be useful in separating them one from another.

In our study, patients with lymphadenopathy clearly had histories of larger numbers of previous sexually transmitted diseases. We have found it difficult to control for the effects of these diseases on either chronic lymphadenopathy or immunologic variables in studies of active homosexuals since, as shown in our study, most sexually active homosexual patients have clinical or serologic evidence of infection at any given time. Similar numbers of patients with lymphadenopathy had recent active medical problems when compared with patients without lymphadenopathy; abnormalities in immunologic variables were consistent among the two patient groups when asymptomatic subgroups of each were studied. These results support our contention that the two groups can be distinguished by some immunologic tests. To the contrary, relative percentages of total T cells, T-helper–T-inducer cells, and ratios of helper-inducer to suppressor-cytotoxic T lymphocytes failed to distinguish patients with lymphadenopathy from those without. These results appear to be similar to those of a previous study, although statistical evaluations focused on comparisons of the two study groups to heterosexual controls.[23]

Homosexuals with lymphadenopathy in our study were distinguished by several immunologic findings. Total numbers of circulating lymphocytes were higher in this group than in patients without lymphadenopathy, and greater numbers of these lymphocytes were of the suppressor/cytotoxic and natural killer-cell phenotypes. Functional studies of natural killer cells have been reported in only a few patients with AIDS,[26] and in none with the chronic lymphadenopathy syndrome. Speculation concerning the meaning of increased numbers of natural killer cells in homosexuals can better be made when results of such functional studies are available. In a previous study of immunologic abnormalities in eight homosexual men with lymphadenopathy, total lymphocyte numbers and total T-lymphocyte numbers were greater, but not substantially so, in homosexuals with lymphadenopathy than without.[23] To date, marked lymphopenia, which seems to predominantly involve the OKT-4+ T-cell population over the OKT-8+ and B-lymphocyte populations, appears to regularly develop in AIDS patients with opportunistic infections.[24-27] It has recently been suggested that a preferential augmentation of the T-suppressor cell population as compared with a diminution of the T-helper/inducer population may identify homosexuals with a lower risk for the development of Kaposi's sarcoma or opportunistic infections.[29] If this suggestion proves true, the lack of lymphopenia and the lymphocytosis of OKT-8+ cells in homosexuals with lymphadenopathy in this study suggest that lymphadenopathy in itself may not be associated with a bad prognosis.

Group 2 homosexuals were also distinguished from those in group 1 by their degree of T-lymphocyte dysfunction, a finding noted but not evaluated statistically in a previous study.[23] This abnormality was not explicable in our patients by differences in the number of cultured T-helper/inducer lymphocytes, the primary lymphocyte population responding to PHA.[30] Previous investigations have suggested that defective lymphocyte mitogenic function in patients with AIDS are multifactorial, and include intrinsic lymphocyte defects and absorbable T-lymphocyte–specific blocking factors.[31] Since pooled normal human serum was used in all of our cultures, it is unlikely that blocking factors caused the abnormalities noted. More likely is the probability that T-suppressor/cytotoxic cells present in culture were responsible for these more severe aberrations of lymphocyte function. Surprisingly, percentages of "activated" mononuclear cells as detected by the presence of Ia surface antigen were not greater in group 2; to the contrary, they were greater in group 1 patients. This finding is probably related to the fact that in cell preparations for group 1 patients there were greater percentages of monocytes that, like lymphocytes, also may display Ia antigen.[32] Regardless, these data show that since homosexuals with lymphadenopathy have clinical and immunologic features that distinguish them from those without lymphadenopathy, studies of AIDS must carefully separate the two groups. Otherwise, the results of such studies may be unknowingly influenced by abnormalities that predominate in one group or the other.

The possibility that the reactive lymphadenopathy syndrome represents a secondary feature of chronic viral infection and is unrelated to AIDS has been the subject of ongoing discussion. This is of special interest as many of the immunologic abnormalities reported in AIDS also occur with viral infection.[33,34] The majority of our patients had serologic evidence of infection with more than one virus, an observation that supports this contention. In that regard, the results of serologic studies for hepatitis B deserve further comment. The high rate of positivity of these studies was not in itself surprising, but the restriction of detectable HBsAg antigenemia to patients without lymphadenopathy was. Furthermore, serum samples from four of five of these patients were evaluated on multiple occasions and found to be persistently positive for both HBsAb and HBsAg. This uncommon finding was recently noted in a group of nine patients with hepatitis, six of whom had renal disease,[35] a feature not noted in our patients. The mean of OKT-4:OKT-8 ratios and other lymphocyte variables in our patients with both hepatitis antigen and antibody were not different from those of the other group 1 patients, so we do not have evidence that they were more immunosuppressed than other patients. This possibility, however, requires further evaluation, as does the possibility that simultaneous HBsAg and HBsAb positivity is more common than previously thought.[36]

The possibility that the presence of chronic active hepatitis, known to be associated with lymphocyte abnormalities, played a part in our findings can be dismissed. Only two of our patients had mild elevations of liver enzyme levels; both had chronic persistent hepatitis shown on biopsy specimens. In that regard, a recent study suggested that abnormal OKT-4:OKT-8 ratios in chronic active hepatitis may be more closely related to homosexuality than to hepatitis.[37]

Acquired immune deficiency syndrome with opportunistic infections or the reactive lymphadenopathy syndrome has been described as developing in hemophiliacs.[2,4,38,39] These individuals appear to have few of the risk factors for AIDS suggested to exist in homosexual populations[40] other than chronic viral infections transmitted by blood products. A recent report showed that hemophiliacs with lymphadenopathy like homosexuals with lymphadenopathy, have more severely depressed lymphocyte mitogenic responses than those without lymphadenopathy.[4] Higher percentages of Leu 7+ cells in patients with lymphadenopathy than in

those without it were also noted in that study. Further studies are required to see if these two groups share other clinical and immunologic abnormalities and what these findings will tell about the cause and prognosis of the benign reactive lymphadenopathy syndrome. We plan long-term follow-up of all the individuals in this study, as sequential immunologic studies will be required to determine the importance of the immunologic differences noted between the two homosexual groups studied.

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