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T-lymphocyte subpopulations in homosexual men. *N. Engl. J. Med.* 307:729-31, 1982.
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Lymphocyte subsets were measured in 81 male homosexuals with no history of immune dysfunction. Compared with 20 male heterosexual controls, the homosexual group had significantly fewer OKT4+ cells, more OKT8+ cells, and lower OKT4/OKT8 ratios. These abnormalities were associated with constitutional symptoms and sexual promiscuity. [The *SCI*® indicates that this paper has been cited in over 300 publications.]

OKT4 and OKT8 Lymphocytes in Homosexual Men

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April 29, 1988

In 1981 I began a fellowship in infectious diseases with Michael Lange at St. Luke's-Roosevelt Hospital Center in New York. During that year we saw infrequent but increasing cases of idiopathic immunodeficiency and opportunistic infections in previously healthy gay men. In retrospect, these were some of the earliest cases of AIDS in New York. At that time, however, the nature and scope of this problem was unknown.

Based on our clinical experience, it appeared that life-threatening illness was preceded by a period of constitutional symptoms in the absence of opportunistic infection. We hypothesized that the immunodeficiency syndrome might be preceded by a period of asymptomatic deterioration of immune function and that subclinical cases might be identified.

Such cases might yield insight into the disease processes that were obscured by the overwhelming complications of the terminal illness.

Eighty-one healthy gay male volunteers, with no history of immune deficiency or opportunistic infection, were studied. Based on the limited number of AIDS cases reported at that time, we anticipated that few or possibly none of these volunteers would be found to have immunologic abnormalities. We were quite surprised to find that 80 percent of these men had decreased relative and absolute numbers of CD4+ lymphocytes, increased T8+ lymphocytes, and decreased T4/T8 ratios compared with heterosexual male controls. This abnormality was associated with persons having large numbers of sexual contacts and constitutional symptoms. There was no association with the use of inhaled nitrites (suggested to be a factor in the immunodeficiency syndrome at that time) nor with active cytomegalovirus (CMV) infection based on antibody titer.

This manuscript was the first published report that large numbers of apparently healthy gay men had the cardinal immunologic defect of AIDS and was an early indication of the scope of the AIDS epidemic. I believe that our work was cited frequently because of its timely publication and because we provided preliminary information about the natural history of AIDS, the nature of the AIDS-related complex, the behavioral risk factors for AIDS, and the contribution of secondary factors such as CMV and nitrites to AIDS. These topics were greatly expanded in numerous subsequent studies by other investigators.^{1,2} Ours was one of the first and presently continues as one of the longest running prospective studies of the AIDS prodrome.

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2. Stevens C E, Taylor P E, Zang E A, Morrison J M, Harley E J, Rodriguez de Cordoba S, Bacino C, Ting R C Y, Bodner A J, Sarngadharan M G, Gallo R C & Rubenstein P. Human T-cell lymphotropic virus type III infection in a cohort of homosexual men in New York City. *J. Amer. Med. Assn.* 255:2167-72, 1986. (Cited 30 times.)

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