Cluster of Cases of the Acquired Immune Deficiency Syndrome

Patients Linked by Sexual Contact

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The possibility that homosexual men with the acquired immune deficiency syndrome (AIDS) had been sexual partners of each other was studied. Of the first 19 homosexual male AIDS patients reported from southern California, names of sexual partners were obtained for 13. Nine of the 13 patients had sexual contact with one or more AIDS patients within five years of the onset of symptoms. Four of the patients from southern California had contact with a non-Californian AIDS patient, who was also the sexual partner of four AIDS patients from New York City. Ultimately, 40 patients in 10 cities were linked by sexual contact. On the basis of six pairs of patients, a mean latency period of 10.5 months (range seven to 14 months) is estimated between sexual contact and symptom onset. The finding of a cluster of AIDS patients linked by sexual contact is consistent with the hypothesis that AIDS is caused by an infectious agent.

Acquired immune deficiency syndrome (AIDS) was first suggested in June 1981 by a report from Los Angeles of Pneumocystis carinii pneumonia in five previously healthy homosexual men [1]. Subsequently, Kaposi's sarcoma [2] and a variety of opportunistic infections other than P. carinii pneumonia, such as chronic, progressive herpes simplex virus infection, central nervous system toxoplasmosis, cryptococcal meningitis, and disseminated cytomegalovirus infection [3–5], were also found to be manifestations of AIDS. The abnormality in cellular immune function has been indicated by cutaneous anergy, lymphopenia, and T cell deficiency [3].

AIDS appeared suddenly and almost simultaneously in several metropolitan areas of the United States. Homosexual men living in New York City, San Francisco, and Los Angeles accounted for the greatest number of reported cases [6]. A case-control study conducted by the Centers for Disease Control in October and November 1981 concluded that a large number of sexual partners was the most important risk factor among these homosexual men [7]. AIDS has also been found in intravenous drug users [8], Haitians living in the United States [9], and patients with hemophilia [10]. Recently, AIDS or illnesses suggestive of AIDS have been reported in a recipient of a platelet transfusion from an AIDS patient [11], in children born to mothers who are Haitian [12] or have used drugs intravenously [13], and in women who had sexual relations with men belonging to AIDS risk groups [14]. Epidemiologic information suggests that an infectious agent may cause AIDS.

If AIDS is caused by an infectious agent, evidence of person-to-person spread might be expected. None of the five homosexual men first reported from Los Angeles with P. carinii pneumonia gave

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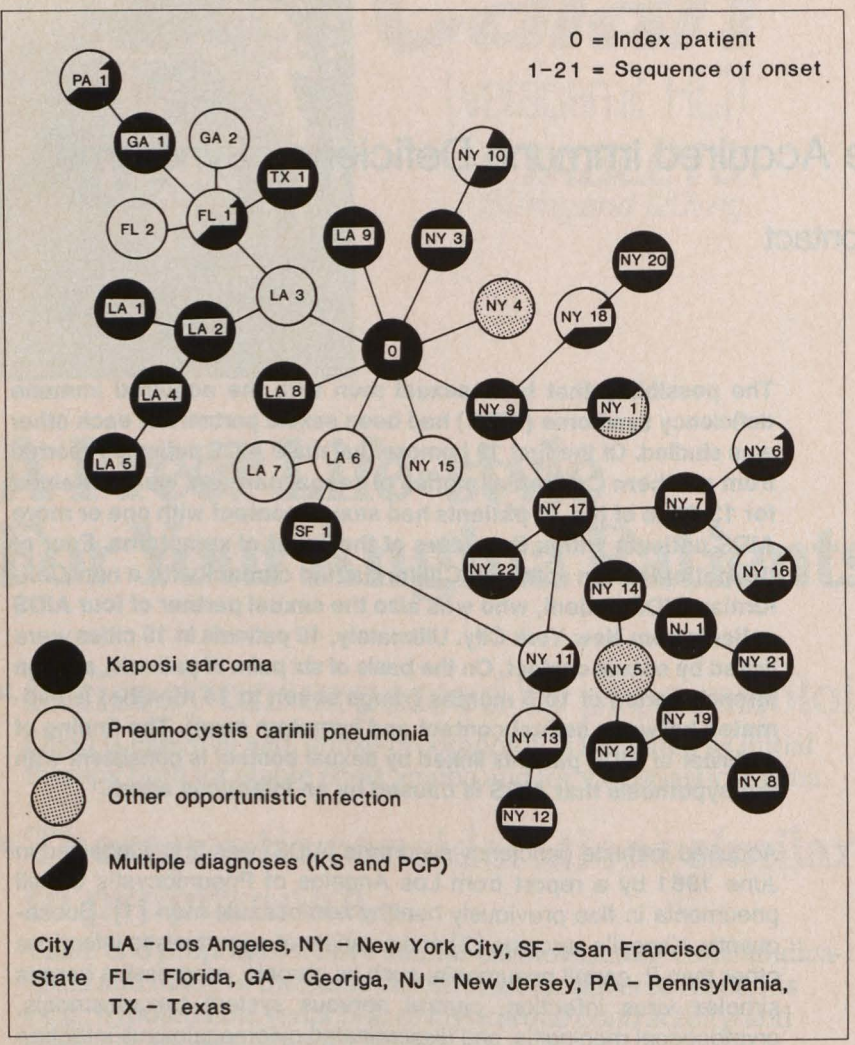

Figure 1. *Sexual contacts among homosexual men with AIDS. Each* ***circle*** *represents an AIDS patient.* ***Lines*** *connecting the circles represent sexual exposures. Indicated city or state is place of residence of a patient at the time of diagnosis. "0" indicates Patient 0 (described in text).*

histories of sexual contact with other patients [1]. In a subsequent series of 41 cases of Kaposi's sarcoma reported from New York City, four homosexually active men were reported to have had "transient, intimate sexual contact with other men in this Kaposi's sarcoma group" [15]. In March 1982, several persons in southern California informally reported to public health officials that some men in whom AIDS was later diagnosed had attended the same social gatherings and may have had sexual contacts with one another. Consequently, an investigation was initiated to assess the social and sexual relationships among homosexual men in whom AIDS had been diagnosed.

PATIENTS AND METHODS

All 19 cases of biopsy-confirmed Kaposi's sarcoma or P. carinii pneumonia in previously healthy homosexual men residing in Los Angeles or contiguous Orange County and reported to the Centers for Disease Control as of April 12, 1982, were included in the initial investigation. Patients with AIDS from outside southern California were included in this study only if previously obtained information suggested their association with another AIDS patient.

Written, informed consent was obtained from each patient or his sexual contact before interviews were conducted. Patients were interviewed in person by one or more of us and asked to name their sexual partners during the five-year period before they became ill. For those who had died, we interviewed their close companions and asked them to name the sexual partners of the deceased patient. Patients who had been interviewed during earlier studies conducted by the Centers for Disease Control were not re-interviewed for information obtained previously, but were asked to name their sexual partners.

Homosexual men with AIDS who could be linked by sexual contact were considered to belong to a cluster of AIDS patients if the sexual exposure occurred within five years of the onset of illness. Sexual contact reported by one patient (or his surviving companion) had to be confirmed (or not denied) by the other patient (or his companion).

Patients included in the cluster ("linked" patients) were compared with homosexual male AIDS patients not known

to be sexual partners of other AIDS patients ("nonlinked" patients). Among the linked and nonlinked patients were groups of patients who had been interviewed in depth regarding their behavioral patterns. Two sources of data were analyzed: surveillance information on all cases reported to the Centers for Disease Control as of April 12, 1982, and interview records of all patients interviewed by Centers for Disease Control representatives as of October 12, 1982.

Tests of significance (chi-square with 1 degree of freedom) and estimates of relative risk (odd ratios for 2 × 2 tables) derived by the method of Mantel and Haenszel [16] and by Mantel's extension [17] were used to assess differences between the linked and nonlinked patients. Ninety-five percent confidence intervals were calculated with estimates of relative risk and levels of statistical significance.

RESULTS

Of the 19 patients with Kaposi's sarcoma or P. carinii pneumonia reported from southern California, eight were alive and 11 had died at the time this investigation was initiated. Interviews were conducted with the eight living patients and with the close companions of seven of the dead patients. Names of sexual contacts were obtained during 13 of the interviews. Nine of the 13 patients were found to have had sexual exposure with other AIDS patients within five years of the onset of symptoms. Four of these nine had had sexual exposures with more than one other patient. The observation that nine of 15 patients who were interviewed named at least one other reported patient as his sexual partner was not expected and seemed highly unusual (see Appendix).

AIDS developed in four men in southern California after they had sexual contact with a non-Californian, Patient 0 (**Figure 1**). In Patient 0, lymphadenopathy developed in December 1979, and Kaposi's sarcoma was diagnosed in May 1980. He estimated that he had had approximately 250 different male sexual partners each year from 1979 through 1981 and was able to name 72 of his 750 partners for this three-year period. Eight of these 72 named partners were AIDS patients: four from southern California and four from New York City.

Because Patient 0 appeared to link AIDS patients from southern California and New York City, we extended our investigation beyond the Los Angeles-Orange County metropolitan area. Ultimately, we were able to link 40 AIDS patients by sexual contact to at least one other reported patient. Of the 40 linked patients, 22 resided in New York City, nine resided in Los Angeles or contiguous Orange County, and another nine were living in eight other cities in North America when their illnesses were diagnosed. Twenty-four of these men had Kaposi's sarcoma, six had P. carinii pneumonia, eight had both Kaposi's sarcoma and P. carinii pneumonia, one had disseminated cytomegalovirus infection, and one had central nervous system toxoplasmosis. Thirty-six of these men were white (not Hispanic), three were Hispanic (two originally from Puerto Rico and one originally from Mexico), and one was black. Their median age was 36 years.

TABLE I Comparison of Demographic and Clinical Features for Homosexual Men with AIDS Linked and Nonlinked by Sexual Contact

Patient Characteristic	Percent of Patients		Odds Ratio	Confidence Limits	p Value
	Linked (n = 40)	Nonlinked (n = 208)			
Kaposi's sarcoma only	57.5	33.7	2.7	1.4–5.2	0.004
White	87.5	72.6	2.6	1.0–6.9	0.047
Intravenous drug use	3.6	12.9	4.0	0.6–27.0	0.154
Exclusively homosexual	95.0	89.4	2.2	0.5–9.6	0.275
Resident of Manhattan	52.5	48.6	1.2	0.6–2.3	0.648
Deceased when reported	35.0	34.6	1.0	0.5–2.1	0.963
Age 35 years or older	60.0	60.1	1.0	0.5–2.0	0.991

These 40 patients were compared with the 208 other homosexual male patients with AIDS who were reported to the Centers for Disease Control as of April 12, 1982, but not named as sexual partners of patients included in the cluster (**Table I**). The 40 linked patients (16.1 percent of the total reported) were significantly more likely to be white and to have only Kaposi's sarcoma than the 208 other patients. However, the two groups were not significantly different with respect to all other variables available from surveillance reports.

The 29 patients who were linked and interviewed (72.5 percent of 40 patients) and the 49 nonlinked patients who were interviewed (23.6 percent of 208 patients) were compared with respect to selected behavioral characteristics (**Table II**). The 29 linked patients were significantly more likely than the 49 nonlinked patients to have met sexual partners in bathhouses, have been frequent users of inhaled amyl or butyl nitrite, and have participated in the sexual practice of "fisting" (manual-rectal intercourse). Patients in both groups tended to have large numbers of sexual partners. Use of recreational drugs other than nitrite inhalants and participation in sexual activities other than "fisting" were not significantly different for the two groups.

To estimate a possible latency period for AIDS among members of the cluster, we looked at the 20 patients who apparently had had sexual exposures with only one other reported patient. Nine of these 20 reported having had sexual relations with their partners for a period lasting no longer than 30 days. Of the nine, three showed symptoms before or at about the same time as their partners, and six noted symptoms after

TABLE II **Selected Interview Variables for Homosexual Men with AIDS Linked and Nonlinked by Sexual Contact**

Interview Variable	Percent of Patients: Linked (n = 29)	Percent of Patients: Nonlinked (n = 49)	Odds Ratio	Confidence Limits	p Value
Met a sexual contact in bathhouse in year before onset	96.6	73.5	10.1	1.7–59.8	0.010
Used nitrite inhalants more than 1,000 times in lifetime	86.2	53.1	5.5	1.8–17.2	0.003
Inserted hand or fist into partner's rectum during year before onset	82.8	44.9	5.9	2.0–17.1	0.001
Received partner's hand or fist into rectum during year before onset	51.7	18.4	4.8	1.8–12.9	0.002
Had 50 or more male sexual partners in year before onset	75.9	57.1	2.4	0.9–6.5	0.096
Had 1,000 or more sexual partners during lifetime	65.5	44.9	2.3	0.9–6.0	0.078
White	89.7	75.5	2.8	0.7–10.6	0.126
Kaposi's sarcoma only	82.8	69.4	2.1	0.7–6.6	0.191

TABLE III **Possible Latency Periods for Homosexual Men with AIDS**

Possible Source Patient	Linked Patient	Date of Exposure	Symptom Onset	Latency (months)
LA 4	LA 5	12/80	7/81	7
FL 1	GA 2	10/80	6/81	8
Patient 0	LA 9	11/80	8/81	9
NY 18	NY 20	7/80	7/81	12
Patient 0	LA 8	2/80	3/81	13
Patient 0	NY 15	4/80	6/81	14
				$\bar{X}$ = 10.5

their partners became ill (**Table III**). In these six patients, symptoms were first noticed a mean of 10.5 months (range of seven to 14) after having had sexual contact with one of four partners who also was a reported patient.

The four partners may have been sources of AIDS. Three of the possible sources of AIDS were asymptomatic at the time of sexual exposure. The fourth possible source was Patient 0. Lymphadenopathy had already developed in Patient 0 when he had sexual contact with two men in whom AIDS subsequently developed, and he had skin lesions of Kaposi's sarcoma at the time of sexual contact with a third.

COMMENTS

Although the cause of AIDS is unknown, it may be caused by an infectious agent that is transmissible from person to person in a manner analogous to hepatitis B virus infection: through sexual contact; through parenteral exposure by intravenous drug abusers who share needles; through blood products, particularly in patients with hemophilia who received clotting factor concentrates; and, perhaps, through mothers who are Haitian or intravenous drug users to their infants. The existence of a cluster of AIDS cases linked by homosexual contact is consistent with an infectious-agent hypothesis.

The cluster may represent a group of homosexual men who were brought together by a common interest in sexual relations with many different partners or in specific sexual practices, such as manual-rectal intercourse. Frequent social contacts among some patients enabled them to identify other patients by name. Although these men were sexual partners of each other, nonsexual activities, such as drug use, may have contributed to the development of AIDS.

If the infectious-agent hypothesis is true, Patient 0 may be an example of a "carrier" of such an agent. He had had sexual contact with eight other AIDS patients and was the possible source of AIDS for at least three of them. Two of these three men had been his partners before he had overt signs of Kaposi's sarcoma. The existence of an asymptomatic carrier state of AIDS has been suggested by a report of AIDS-like illness in an infant who had received a platelet transfusion from a man who had no symptoms when he donated blood, but had AIDS eight months later [11]. Furthermore, abnormalities in T lymphocytes have been described among asymptomatic homosexual men in New York City [18] and among persons with hemophilia [19,20]. Whether these immune abnormalities are a reflection of "asymptomatic AIDS" or are unrelated to AIDS is not yet known.

The estimated mean latency period of 10 to 11 months for the six AIDS patients described in this study is similar to the estimated mean latency period for the development of Kaposi's sarcoma among renal transplant recipients. Kaposi's sarcoma developed in 15 renal allograft transplant recipients an average of 15 months following renal transplantation (range three to 46 months) in one study [21], and 20 Kaposi's sarcoma patients showed signs of Kaposi's sarcoma an average

of 16 months after transplantation (range four to 53 months) in another [22].

The observation of a cluster formed on the basis of reported sexual exposures reinforces case-control study findings [7] regarding the importance of sexual activities in the development of AIDS among homosexual men. Sexual partners of AIDS patients appear to be at increased risk for AIDS. This conclusion is reflected in interim Public Health Service recommendations for the prevention of AIDS: "Sexual contact should be avoided with persons known or suspected to have AIDS. Members of high-risk groups should be aware that multiple sexual partners increase the probability of developing AIDS" [23].

ACKNOWLEDGMENT

We gratefully acknowledge the cooperation and support of many professional colleagues, including Shirley L. Fannin, M.D.; Thomas Prendergast, M.D.; Michael S. Gottlieb, M.D.; Joel D. Weisman, D.O.; Eugene Rogolsky, M.D.; John P. Orkwis; Alvin E. Friedman-Kien, M.D.; Linda Laubenstein, M.D.; Regina Dwyer, R.N.; Harry W. Haverkos, M.D.; Mary E. Guinan, Ph.D., M.D.; Martha F. Rogers, M.D.; Thomas J. Spira, M.D.; Pauline A. Thomas, M.D.; James M. Monroe; and Rebecca Reiss. Most importantly, we thank the many patients and their friends who openly described to us many aspects of their personal lives and interpersonal experiences.

APPENDIX

The problem of determining the likelihood that nine of 15 homosexual men with AIDS would name at least one other homosexual man with AIDS as his sexual partner can be approached in a variety of ways. A simple approach is presented here. Start with any sexual partner of any one of the patients interviewed in southern California. Observe each partner to determine if he has been reported as a patient or not. Count the number of patients who were interviewed and the number who named at least one other patient as his sexual partner. Nine of 15 patients said that they had had sexual contact with at least one other patient. For this observation to be insignificant at the 95 percent level of confidence, we note that, following the formula for binomial expansion,

$$\sum_{x=9}^{15} \binom{15}{x} p^x (1-p)^{15-x} > 0.05.$$

The iteratively estimated value of p is 0.3597. A greater value of p would make the observation in southern California less significant. Since p is approximately equal to 0.3597, then it follows that the probability of no contact (1 − p) would be 0.6403. Since we were concerned with the large number of sexual partners of patients, the probability of no contact can be evaluated with the Poisson distribution. In the Poisson distribution, the probability of no contact is evaluated by $e^{-\theta n} = 0.6403$, which implies that $\theta = \log e(0.6403)/n$. Among the 15 patients interviewed, we find that the average number of sexual partners over a period of five years is 610. Now, when n is equal to 610, the contact parameter, θ, is equal to 0.000731. If there are exactly 19 patients with AIDS in southern California, then the homosexual population in southern California, estimated by $19/\theta$, would be approximately 26,000. On the other hand, if we estimate the homosexual male population in southern California to be at least 250,000, then we would expect to find the number of AIDS cases in southern California, estimated at 250,000 (θ), to be 183. Finally, if there are only 19 patients and at least 250,000 homosexual men, then the average number of sexual partners for a five-year period would have to be about 6,000, almost 10 times as many as the average reported by the 15 patients who were interviewed. From this exercise, we conclude that the observation of nine of 15 patients in southern California naming at least one other patient as a sexual partner would be highly unusual.

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