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AIDS: An Epidemiologic Overview

D. Peter Drotman, M.D., M.P.H.
Medical Epidemiologist

James W. Curran, M.D., M.P.H.
Director

AIDS Activity
Center for Infectious Diseases
Centers for Disease Control
Atlanta, Georgia 30333

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Physicians at New York University Medical Center were among the first to recognize the emergence of the acquired immunodeficiency syndrome (AIDS) as a new problem in 1981. The course that the epidemic is taking is more dramatic than the first cases may have portended. More than two and one-half years after the first cases were identified, the epidemic curve has yet to peak. This likely represents the beginning of what is to become an endemic problem in the United States.

The Centers for Disease Control (CDC) has a strict case definition of AIDS for the purposes of surveillance and epidemiologic studies. This includes as cases only those patients with reliably diagnosed opportunistic diseases. Thus, cases can be monitored for epidemiologic trends and linked with high risk populations. According to the definition of AIDS, the patients with biopsy proven Kaposi's sarcoma (KS) and/or at least one culture or biopsy proven life-threatening opportunistic infection are counted as cases. Patients with medical conditions known to be associated with immunosuppression or therapies known to be immunosuppressive are excluded. The definition was designed to be highly specific, at the cost of sacrificing some degree of sensitivity. Because the case definition allows only very well-documented and certain diagnoses, the cases CDC enumerates may only represent the tip of the "iceberg" (See Figure 1). There are probably many other disease entities that fall within the spectrum of illnesses associated with AIDS. Examples include malignancies that previously have been associated with immunosuppression, such as non-Hodgkin's lymphoma. However, other malignancies such as hepatocellular carcinoma and squamous cell carcinoma of the anal canal, neither of which, although they may be epidemic among gay men, are known to be associated with immunosuppression. Other patients may be part of the spectrum of AIDS including those with "transient" immunologic defects but with minimal or no symptoms. Others may have generalized unexplained lymphadenopathy,

nephrotic syndrome, autoimmune thrombocytopenic purpura or possibly other manifestations. These cases raise the issue that there may indeed be asymptomatic carriers of AIDS.

The epidemic curve of AIDS cases reported to CDC is shown in Figure 2. Over 95 percent of the total number of cases have been diagnosed since the first reports, about half of them in the last eight months. As of September 27, 1983, there were 2,374 cases of AIDS reported from the United States, of which at least 968 resulted in death (about 41 percent).

Table 1 shows the "marker" disease categories of AIDS. Most patients who have Pneumocystis carinii pneumonia (PCP) without KS, have multiple opportunistic infections (OI). Many patients who have KS without PCP, go on to develop other OIs. The patients diagnosed with KS only, seem to fare far better than the other groups. The reasons for this are unclear but may represent some chronological state in the clinical course of the syndrome, a difference or bias in case reporting, or some other unknown factor.

The mortality rate of AIDS is quite high, especially for cases diagnosed over one year ago (See Tables 2 and 3). The survival rate of cases that fit the surveillance case definition is very low -- about 25 percent in cases diagnosed two years ago. Because such a large fraction of the cases have been diagnosed in the most recent months, the overall case-fatality rate is an underestimate. This remarkably high mortality rate should motivate clinicians and researchers to approach new types of therapy -- like immunomodulation --aggressively.

One of the most striking aspects of this epidemic is its geographic distribution. AIDS is clearly a disease of the United States -- more than 40 states have reported cases to CDC. However, there are many cases now being recognized in at least 20 other countries on every inhabited continent (See Table 4). But, when one compares the 1,000 cases reported from New York City

alone with the relative handful of cases from large European cities, the distribution is clearly skewed towards the United States. Nearly half of AIDS cases among gay men are from New York City; 59.7 percent of all AIDS cases are from New York City, Los Angeles, and San Francisco (See Table 5). Nearly 75 percent of intravenous drug abusers diagnosed with AIDS are from the New York City metropolitan area including Newark, New Jersey. More than 75 percent of all Haitians diagnosed with AIDS are from Miami or the New York City-Newark metropolitan areas. This very striking geographical distribution of disease could not be a random phenomenon.

The second striking observation is the predominance of cases among men -- particularly gay men. Ninety-three percent of all cases reported are among men and 75 percent of these are either homosexual or bisexual in orientation (See Table 6). KS is much more common among gay men than intravenous drug abusers, or Haitians or persons with hemophilia (See Table 7). This, of course, begs explanation -- as yet, there is none. However, a two step model of AIDS causation can be imagined: an infectious agent causes the underlying immunodeficiency and some other factor determines what manifestation occurs. For instance, in this model Toxoplasma gondii, a protozoan very common in Haiti, is the proximate cause of central nervous system toxoplasmosis which is common among Haitian AIDS patients, but is less common among other AIDS patients. One could speculate that use of nitrite inhalants or repeated cytomegalovirus infection (CMV) which may be more common among gay men than the other groups should be considered in this context. Definitive studies should be undertaken.

Initially, CDC concentrated its epidemiologic studies toward an easily apprehended solution to the problem: a simple causal explanation, like a factor easily removed from the environment. Amyl and butyl nitrites or "poppers" were one of the first factors investigated because they are commonly

used by gay men and not by other groups. Although CDC studies have shown that they are used more frequently by gay men afflicted with AIDS than by controls, the results remain inconclusive -- "poppers" are correlated with many factors including frequency of sexual activities, numbers of different sexual partners, and virtually every sexually transmissable disease agent. However, AIDS itself is positively correlated with many of these factors -- numbers of sexual partners being the strongest such predictor.

The next major CDC investigations included studies of: 1) gay cases and controls outside of New York and California (in order to evaluate these locations as risk factors); 2) heterosexual cases; 3) sexual clusters of cases, and 4) lymphadenopathy trends in New York City. Other studies are underway among a large cohort of gay men in San Francisco, Haitians in the United States, infants with unexplained cellular immunodeficiency, hemophiliacs, and transfusion associated cases. In this chapter, we will discuss the national case control study and the sexual cluster investigation.

National Case Control Study of Homosexually Active Men

Epidemiologic aspects of AIDS among gay men are described in results from the national case-control study (Jaffe, et al., 1983). In this collaborative study, 50 living cases were matched for age, race, sexual orientation, metropolitan area of residence, and interviewer. (All interviewers were CDC physicians.) Interviews were extensive, typically lasting more than an hour. The questions covered sociodemographic characteristics, medical, occupational, family, and travel histories, exposure to toxic substances, use of medical and recreational drugs including inhalant sexual stimulants, and sexual history. Cases and controls donated blood and urine for laboratory testing.

Information was analysed by using stepwise linear logistical regression. The most important variables in this analysis were measures of homosexual activity such as numbers of sexual partners over a lifetime or per

year or the number of male sex partners in the year preceding the onset of symptoms. The AIDS cases in this study had a median number of lifetime sexual partners that was double that of the matched controls. These controls were not chosen to be representative of the gay populations in Manhattan, San Francisco, Los Angeles, and Atlanta where the study was conducted. Rather, the controls were chosen mainly from among gay men who had been treated for sexually transmitted diseases (STDs) -- gay men who were likely to have been sexually active. One group of controls was chosen from venereal disease or "free" clinics catering to gay men. They, therefore, were comprised of people who had sought care for STDs. Another group of controls came from the private practice of physicians who specialized in caring for gay men, especially in the treatment of STDs. This selection of controls who themselves are very sexually active makes the dramatic differences between cases and controls even more significant. Selected variables from this study are listed in Table 8. Histories of syphilis, non-B hepatitis, and enteric parasites are important because they represent additional factors confirming the indicators of sexual activity. Since the infections are sexually transmitted among gay men, their preponderance among cases versus controls is noteworthy. Interestingly, history of syphilis has been the strongest marker of all the STDs in virtually every study of AIDS CDC has undertaken. Syphilis is far less common than gonorrhea, herpes, or some other STDs and though the full explanation for its apparently important association with AIDS is unclear, it is consistent with a hypothesis that AIDS too may be sexually transmitted. In terms of drug usage, the most important variable was the number of different "street" drugs used over a lifetime. Cases had used six different drugs in their lifetimes, while controls had used only four. Usage of amyl or butyl nitrites (poppers) was not significantly higher among cases compared to controls. The data also show that cases were more likely to have engaged in insertive "fisting" or

"rimming" or analingus within the last year than controls. However, a significant number of cases deny ever engaging in fisting or rimming. Whether these activities have any etiologic pertinence to AIDS is unknown.

Serologic testing was performed on many specimens donated by the cases and controls (Rogers, et al., 1983). One of the tests used was the microhemagglutination Treponema pallidum (MHA-TP) test which measures for the presence of treponemal antibody directly, and thus is a specific test for syphilis, both present and past infections. The results were significantly more likely to be positive among the cases than among the three control groups (See Table 9). This further confirmation of past syphilitic infection supports the previous observation that sexual activity with a large number of partners is an important discriminator between case and controls.

Serologic testing for hepatitis A revealed that 86% of cases, compared to lower percentages of age-matched controls (54-63%), had hepatitis A antibody. This confirms the noted greater history of non-B hepatitis among cases and would seem to correlate with risk factors such as frequency of rimming, or other sexual practices, which may be associated with AIDS. There was no increased prevalence of hepatitis B surface antigen carriage, and there was no significant difference between cases (94%) and controls (88%) in the prevalence of hepatitis B markers. This degree of prevalence is approximately what one would expect to find among sexually active gay men in their thirties living in New York City, Los Angeles, and San Francisco.

Investigation of a Sexual Cluster of AIDS Patients

The hypothesis generated by the first case control study was that AIDS is a sexually transmittable disease. To followup on this hypothesis, Drs. David Auerbach and William Darrow, from Los Angeles and CDC, upon request of the Los Angeles County Department of Health Services, interviewed thirteen of the first nineteen AIDS cases reported from Los Angeles and Orange Counties

(Auerbach et al., in press). In instances where the patient had died, their lovers or sexual partners were interviewed to obtain information about the deceased. They discovered that nine of the thirteen cases had direct sexual contact with another person who had or later developed AIDS. Four of them had sexual contact with the same man with KS -- the man was not from California. In an interview, that KS patient reported having had direct contact with another four AIDS cases in New York City, even though he was not from New York City. By his estimate, he had had approximately 750 sexual partners during the previous three years (1979-81). He was able to name 73 of these -- mostly sexual contacts during the last year. He was first diagnosed -- in retrospect, by lymph node biopsy -- in 1980. Five of his nine AIDS contacts had had direct sexual contact with him prior to the time he developed skin lesions. Seven had direct sexual contact before he noticed his KS lesions. The time between sexual contact with this pivotal KS case and the development of AIDS in the contact cases ranges from 4 to 36 months. Further calculations involving what eventually proved to be a large sexual cluster, revealed that a year to year-and-a-half span might be regarded as a minimal induction period for AIDS. Longer periods are less likely to have been recognized or are yet to appear.

When the sex contacts in the expanded AIDS cluster were interviewed, a pattern familiar to sexually transmitted disease investigators emerged. More and more connections were made both in Los Angeles and New York. Ultimately, 40 AIDS patients were linked to one another by direct sexual contact accounting for over 15% of the first 240 cases reported among homosexual men in the United States. The investigators believe that this pattern is not due to chance occurrence and that AIDS is indeed transmitted sexually.

Conclusions

Although epidemiologic investigations have provided valuable insight into the patterns of distribution of AIDS, identifying risk factors, routes of transmission, and certain parameters of AIDS (such as its incubation period), the search for the etiologic agent in the laboratory continues. That may well be the scene of the next step forward in the pursuit of our ultimate goal--prevention of AIDS. However, even without knowing the cause of AIDS, preventive measures are at hand (MMWR, 1983). The U. S. Public Health Service recommendations are listed in Table 10. Until more progress is made, clinicians should report cases they diagnose to their State or local health department. This facilitates evaluation of prevention recommendations and lays the foundation for further study.

References

1. Jaffe HW, Choi K, Thomas PA, et al. National case-control study of Kaposi's sarcoma and Pneumocystis carinii pneumonia in homosexual men: Part 1, epidemiologic results. Ann Int Med 1983;99:145-51.

2. Rogers MF, Morens DM, Steward JA, et al. National case-control study of Kaposi's sarcoma and Pneumocystis carinii pneumonia in homosexual men: Part 2, laboratory results. Ann Int Med 1983;99:151-8.

3. Auerbach DM, Darrow WW, Jaffe HW, Curran JW. A cluster of cases of the acquired immune deficiency syndrome: patients linked by sexual contact. Am J Med (in press).

4. CDC. Prevention of acquired immune deficiency syndrome (AIDS): report of inter-agency recommendations. Morbid Mortal Weekly Rep 1983;32:101-3.

Table 1

Diseases Considered at Least Moderately
Indicative of Underlying Cellular Immunodeficiency

Protozoan Infections
- *Pneumocystis carinii* pneumonia
- *Toxoplasma gondii* encephalitis or disseminated infection (excluding congenital infection
- Chronic (> 1 month) *Cryptosporidium* enteritis

Fungal Infections
- *Candida* esophagitis
- Cryptococcal meningitis or disseminated infection

Cancers
- Kaposi's sarcoma (in a person under age 60)
- Primary brain lymphoma (limited to the brain)

Bacterial Infection
- Disseminated (not just pulmonary or lymphatic) *Mycobacterium avium-intracellulare*

Non-Congenital Viral Infections
- Chronic (> 1 month) mucocutaneous herpes simplex
- Histologically evident cytomegalovirus infection of an organ other than liver or lymph node
- Progressive multifocal leukoencephalopathy

TABLE 2.

AIDS: Reported Cases and Case-Fatality Ratios By Disease CAtegory, United States June 1, 1981 to September 27, 1983

Disease Category	Cases	Deaths	Case-Fatality Ratio
KS without PCP	614	131	21%
Both KS and PCP	172	98	57%
PCP without KS	1227	563	46%
Other opportunistic diseases	361	176	49%
Total	2374	968	41%

HHS/PHS/CDC

TABLE 3.

Reported Cases of AIDS and Case-Fatality Rates by Half-Year of Diagnosis, United States 1979 to September 27, 1983

	Number of Cases	Number of Deaths	Case-Fatality Rate
1979 Jan–June	1	1	100%
July–Dec	7	6	86%
1980 Jan–June	18	14	78%
July–Dec	26	25	96%
1981 Jan–June	75	64	85%
July–Dec	157	118	75%
1982 Jan–June	320	196	61%
July–Dec	571	243	43%
1983 Jan–June	927	251	27%
July–Sept 27	266	47	18%
Totals*	2374	968	41%

*Table totals include 6 cases diagnosed prior to 1979 including 3 deaths.

HHS/PHS/CDC

TABLE 4

Reported Cases of AIDS From Outside the United States June 1, 1981 to September 2, 1983

Region	Number of Cases
Western Europe	44
Haiti	36
Canada	27
Africa	5
South America	2
Mexico	2
Caribbean	2
Middle East	2
Asia	1
Australia	1
Unknown	1
Total	123

HHS/PHS/CDC

TABLE 5

Reported Cases of AIDS, United States
By Standard Metropolitan Statistical Area (SMSA) of Residence
June 1, 1981 to September 27, 1983

SMSA of Residence	Cases	Percentage of Total Cases	Cases per Million Population*
New York City	970	40.9%	106.4
San Francisco	286	12.0%	88.0
Miami	107	4.5%	65.8
Newark	63	2.7%	32.0
Los Angeles	161	6.8%	21.5
Elsewhere, U.S.A.	787	33.1%	3.9
Total	2374	100.0%	10.5

*Based on 1980 Census Data

HHS/PHS/CDC

TABLE 6

AIDS: Reported Cases in Men, United States By Disease Category and Sexual Orientation June 1, 1981 to September 27, 1983

Disease Category	Sexual Orientation			
	Homosexual/ Bisexual	Hetero-sexual	Unknown	Total
KS without PCP	566	34	3	603
Both KS and PCP	166	5	0	171
PCP without KS	784	292	53	1129
Other opportunistic diseases	189	104	21	314
Total	1705	435	77	2217

HHS/PHS/CDC

TABLE 7

Acquired Immune Deficiency Syndrome (AIDS)
By Disease Category and Hierarchical Patient Characteristics*
June 1, 1981 to September 27, 1983

	Homosexual/ Bisexual Men	IV Drug Users	Haitians	Hemo philiacs	None Apparent/ Unknown
KS without PCP	566	13	13	0	22
Both KS and PCP	166	4	1	0	1
PCP without KS	784	287	47	15	94
Other opportunistic diseases	189	90	54	1	27
TOTAL	1705	394	115	16	144

*Cases with multiple characteristics are tabulated only in the group listed first

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Table 8

National Case-Control Study of AIDS
in Homosexual Men
Frequency of Selected Variables Associated with KS and PCP

Variable	Cases (N=50)	Controls	
		Clinic (N=78)	Private (N=42)
Number of male sex partners per year (median)	61	27	25
Proportion of sex partners from bathhouses (median)	50%	23%	4%
Age at initiating regular sex with men (median)	19 yrs.	20 yrs.	22 yrs.
History of syphilis	68%	36%	36%
History of non-B hepatitis	48%	30%	33%
Treatment for enteric parasites	44%	19%	50%
Number of different "street" drugs ever used (median)	6	4	4
Lifetime use of nitrite inhalants (median)	336 days	168 days	264 days
"Fisting" at least once in the past year	52%	33%	38%
"Rimming" at least once in the last year	78%	64%	62%

Table 9

National Case-control Study of AIDS in Homosexual Men

Results of Serologic Testing for Syphilis
in Cases and Controls

	Prevalence of Positive Results			
		Controls		
Serologic Tests	Cases (N=50)	Friends (N=19)	VD Clinic (N=61)	Private Practice (N=37)
RPR $\geq$ 1+	26%	11%	25%	16%
MHA-TP $\geq$ 1+	70%	32%	41%	30%

Table 10

Although the cause of AIDS remains unknown, the Public Health Service recommends the following actions:

1. 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.
2. As a temporary measure, members of groups at increased risk for AIDS should refrain from donating plasma and/or blood. This recommendation includes all individuals belonging to such groups, even though many individuals are at little risk of AIDS. Centers collecting plasma and/or blood should inform potential donors of this recommendation. The Food and Drug Administration (FDA) is preparing new recommendations for manufacturers of plasma derivatives and for establishments collecting plasma or blood. This is an interim measure to protect recipients of blood products and blood until specific laboratory tests are available.
3. Studies should be conducted to evaluate screening procedures for their effectiveness in identifying and excluding plasma and blood with a high probability of transmitting AIDS. These procedures should include specific laboratory tests as well as careful histories and physical examinations.
4. Physicians should adhere strictly to medical indications for transfusions, and autologous blood transfusions are encouraged.
5. Work should continue toward development of safer blood products for use by hemophilia patients.

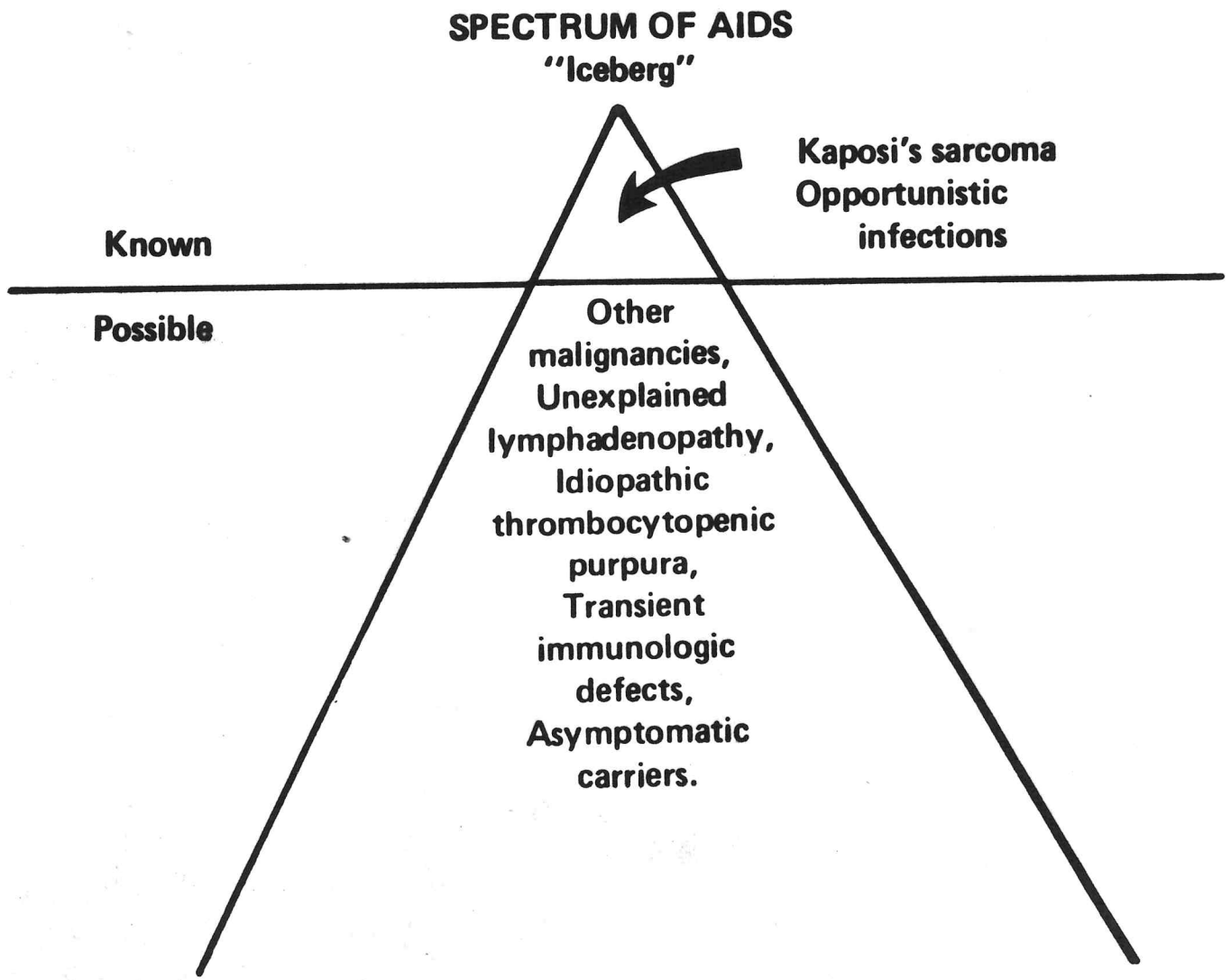
SPECTRUM OF AIDS
"Iceberg"
Kaposi's sarcoma
Opportunistic
infections
Known
Possible
Other
malignancies,
Unexplained
lymphadenopathy,
Idiopathic
thrombocytopenic
purpura,
Transient
immunologic
defects,
Asymptomatic
carriers.

FIGURE 1

FIGURE 2

REPORTED CASES OF AIDS, UNITED STATES, JANUARY 1978 – JUNE 1983, BY QUARTER YEAR OF DIAGNOSIS