

FOCUS

A REVIEW OF AIDS RESEARCH

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Where Is AIDS Going?

AN EPIDEMIOLOGICAL UPDATE

Perhaps the most basic fact about the AIDS epidemic in this country is that it will not go away. In addition, all researchers warn that Americans can expect AIDS to get much worse before it gets better. Beyond this bottom line, serious observers — especially care givers and educators — struggle not only to absorb the daily dose of AIDS news in the media but also to perceive the nuances of current epidemiological research. The statistics reveal the present status of AIDS, but they also provide clues to where the epidemic may be going.

The Basics

James Curran, MD, head of the AIDS Activity Office for the Centers for Disease Control (CDC), reviewed the current status of the epidemic in a recent issue of the journal *SCIENCE*¹. He reported that the percentage of AIDS cases among the established risk groups had remained the same with proportional increases for each group. At the time of Curran's report (August 30), there had been 12,932 cases in the United States with more than half of these diagnosed during the preceding 12 months. More than 73% of the adult cases were among gay and bisexual men; 17% occurred among heterosexuals who used intravenous (I.V.) drugs. The CDC has now determined that 12% of the gay and bisexual men with AIDS also reported a history of I.V. drug use.

Much smaller percentages mark the spread of the disease among others at risk: heterosexual partners of individuals at risk (129 cases or 1%), transfusion recipients (195 cases of 1.5%), hemophiliacs (86 cases of 0.7%), and those individuals who, according to the CDC, "could not be classified by recognized risk factors for AIDS" (814 cases or 6.4%). Many of these individuals were born in Haiti.

AIDS continues to strike infants and children as well as adults. Seventy percent of the pediatric cases (116 of 165) were born to a parent who had AIDS or who belonged to a risk group. Other pediatric cases were linked to transfusions (25 cases or 15%) or hemophilia (9 cases or 5%). The remaining 15 individuals had no identifiable risk factor or there had been incomplete investigations.

The incidence rates of AIDS for single men in Manhattan and San Francisco, I.V. drug users in New York City and New Jersey, and hemophilia A patients were very high (>250 per 100,000). Curran notes that for these groups the 1984 incidence rates for AIDS were similar to U.S. population incidence rates of all cancers (1973-1977 average annual incidence rate of 331.5 per 100,000) and mortality rate of heart disease (1982 mortality rate of 191 per 100,000). In contrast, the incidence rate of AIDS for those not in any of the risk groups is considerably lower, about 0.1 per 100,000.

Future Directions

The prevalence of AIDS diagnoses among high risk groups in the future will be determined both by the natural history of LAV/HTLV-3 infection and the actual spread of the infection itself. The CDC now estimates that 500,000 to 1,000,000 Americans have already been infected with the virus. Researchers expect that an AIDS viral infection will affect large populations in a manner similar to other viruses; that is, a small proportion of people exposed will actually develop full-blown disease symptoms. Natural history studies being conducted in San Francisco and elsewhere are attempting to determine that proportion. Currently, the CDC suggests 5% to 20% of those exposed to the virus will develop AIDS symptoms. That percentage of the estimated one million infected individuals indicates that 200,000 Americans may develop AIDS if no cure or treatment to block the virus appears in the near future.

"The lag between virus infection and the occurrence of AIDS has prevented the community or high-risk population from recognizing the severity of the AIDS problem until a large number of individuals have been infected."

James Curran, MD, Centers for Disease Control

The other determinant for the numbers of new AIDS cases is the actual spread of the virus. Researchers know that retroviral infections in animals persist for prolonged periods, often for lifetimes. They also know that LAV/HTLV-3 can persist in humans for several years, and they assume that infected individuals can transmit the virus to others for as long as it is present.

While charting the spread of AIDS, epidemiologists also note the possible results of AIDS prevention campaigns. Thus, studies from cities like New York, San Francisco, Los Angeles, Chicago, and Denver have reported significant behavior changes among gay men as reflected in plummeting numbers of rectal gonorrhea cases. This obvious benefit for AIDS prevention is diluted somewhat by the greater prevalence of LAV/HTLV-3 infection in urban gay communities. According to Curran and others, the risk of exposure to LAV/HTLV-3 for gay and bisexual men may be greater today than it was in 1980.²

During a presentation at the International Conference on AIDS in Atlanta earlier this year, Curran explained the changing nature of risk for gay men in high incidence areas.

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THE
AIDS
HEALTH
PROJECT

A Publication of the AIDS Health Project, University of California San Francisco

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"A gay man in San Francisco with 12 partners in 1980 would have been exposed to AIDS by three of them. In 1984 sexual contact with three men may result in exposure from two of them," Curran said. He based his figures on a study showing that 64% of gay men in the city had antibodies to LAV/HTLV-3. A more recent study using a more representative sample of men in the city revealed an exposure rate of 37%. While the second number alters Curran's mathematical projections, reduction of sex partners has taken on a different meaning today than it had when AIDS first appeared.

Parallel markers for a decline in sharing needles among I.V. drug abusers are more elusive. Anecdotal reports are mixed; some observers recount incidents of concern among users about needle sharing; others note that drug abusers have not changed their needle-sharing habits.

Where AIDS is going in the years ahead will largely be determined by the effectiveness of AIDS prevention. Curran of the CDC described one of the basic problems with AIDS prevention in the United States today.

"The lag between virus infection and the occurrence of AIDS has prevented the community or high-risk population from recognizing the severity of the AIDS problem until a large number of individuals have been infected," he said.

The problem is one of perception; namely, that AIDS is a threat to someone else. Recently an atmosphere of "AIDS hysteria" has further obscured an accurate understanding of the disease and its risks. AIDS epidemiology can pierce the armor of denial and fear by alerting the public to the changing characteristics of AIDS prevalence and transmission.

Geographic Distribution

AIDS no longer happens only "over there" or "to someone else." Although the number of AIDS cases continues to surge in high-incidence cities, the epidemic is clearly spreading geographically across the country. CDC statistics show that four cities (San Francisco, New York, Los Angeles, and Miami) accounted for 73.2% of all reported cases by September of 1982. One year later this proportion had dropped to 65%. By July of 1985, the four cities represented 56.5% of the total cases. The CDC now predicts that over half of the 12,000 cases expected to be diagnosed between July 1985 and June 1986 will be from states other than New York and California.

Ethnic Distribution

The epidemiological data has shown the significant number of AIDS diagnoses among people of color from the very beginning, but much of the black population has not felt the threat of AIDS, according to Dr. Wayne Greaves, chief of infectious diseases at Howard University Hospital.³ Greaves, who is also an epidemiologist, noted that black people account for about 25 percent of the 14,000 AIDS cases, but that blacks make up only about 12.5% of the population.

Greaves linked the disproportionately large number of AIDS cases among blacks to a lesser quality of health care available and a higher proportion of blacks among intravenous drug users in high incidence areas. One study found that blacks constituted nearly 40% of the I.V. users.⁴ According to Greaves, education specially directed to the black population can dispel the myth about AIDS being a "white man's disease." A similar case for AIDS education might be made for the Hispanic population with 14% of the total AIDS cases in the nation.

AIDS prevention messages have been targeted to the major risk groups, gay and bisexual men and I.V. drug users, but few are directed to the subpopulations within those groups. Curran of the CDC called for community prevention campaigns to proceed now "before definitive evidence of their effectiveness is available." Curran added, "They should be evaluated according to their ability to prevent HTLV-3/LAV infection as well as to influence behavior."

Risk to Heterosexuals

Researchers are constantly being asked whether AIDS will extend significantly beyond the risk groups. Specifically, the question comes down to the relative risk for heterosexuals.

Anthony S. Fauci, MD, of the National Institutes for Health recently explained⁵ that extensive spread of AIDS outside the established risk groups would require both male-to-female and female-to-male transmission. Early cases of AIDS among heterosexuals were caused by male-to-female transmission. Fauci said reports indicate that female-to-male transmission is now likely occurring in this country "to a minor degree." Research from Central African nations confirms the possibility for bi-directional transmission.

Preliminary research indicates that prostitutes and their clients may provide a means for AIDS to increase its hold in the heterosexual population. Serologic evidence of AIDS virus infection in female prostitutes has been revealed in preliminary studies in some American cities.⁶ Five (5%) of 92 Seattle prostitutes were seropositive for antibodies to LAV/HTLV-3. In Miami 10 (40%) of 25 prostitutes tested positive, and eight of those positive acknowledged a history of I.V. drug abuse.

Other researchers counter that too little is known about female-to-male transmission to label prostitutes as "a reservoir of HTLV-3 infection."⁷ Dr. Stephen Schultz, Deputy Health Commissioner for Epidemiological Services of New York City, observed, "If it has occurred at all, it has been very, very infrequent."⁸

Dr. Dean Echenberg, chief epidemiologist for San Francisco, wrote in an editorial to the *Journal of the American Medical Association* that "AIDS is spreading within the heterosexual population. The only question is how fast and how widely." Echenberg called for tracing the sexual contacts of heterosexuals with AIDS to provide counseling about their risks.

The I.V. Drug Connection

Until quite recently the potential impact of AIDS transmission via intravenous drug use has been the "needle in the media closet," a reported risk factor but one seldom profiled or examined closely. With mounting concern over AIDS transmission among heterosexuals, the public has taken a closer look at the threat posed by the practice of sharing needles among I.V. drug users.

One government researcher, Harold M. Ginzburg, MD, MPH, the Associate Director of Clinical Medicine for the National Institute on Drug Abuse, estimated that the nation may have over one million I.V. drug users including half of all cocaine users and one-third of amphetamine users who prefer to administer their drugs intravenously.¹⁰ Ginzburg warned that a great many people who use I.V. drugs do not fit the popular stereotypes. The recent national awareness of cocaine abuse among people from all levels of society is but one example of the new I.V. drug user.

Ginzburg suggested last year that as public information campaigns directed toward changing sexual practices of gay men became more effective, "it is quite possible that an increasing proportion of new cases of AIDS will emanate from the drug-using community." And, in fact, in New York City the proportion of I.V. drug-related AIDS cases has increased from 18% in 1981 to 33% during the first half of this year, according to the New York State Health Department.

Although governmental agencies and societal norms may outlaw or disapprove of I.V. drug use, AIDS prevention focuses specifically on the danger of sharing needles. Several researchers and health educators have encouraged a "de-control" of syringes, making them readily available so as to discourage needle-sharing. The proponents are far from reaching a consensus on the proposal. At the very least, they assert that the public must be informed that a high percentage of drug abusers in some cities (such as New York) have been exposed to the AIDS virus, that some prostitutes are I.V. drug users, and that individuals will often be unable to determine someone's infectivity from physical appearance.

Casual Contact

According to Dr. Curran of the CDC, "It is unlikely that casual contact will play a significant role in transmission of HTLV-3/LAV infection." In mid-November Dr. James D. Mason, Acting Assistant Secretary of Health and Human Services, presented guidelines for preventing transmission of the AIDS virus in workplaces. Mason asserted that there was no need for special restrictions since "AIDS is a bloodborne, sexually transmitted disease that is not spread by casual contact."

Curran concluded his epidemiological review with the observation that he expects sexual transmission of the virus to account for most cases of AIDS in this country for several years, and that gay men and I.V. drug users will continue to be at "extraordinary risk" for contracting the disease.

With estimates of one million Americans exposed to the AIDS virus, the natural history of the infection may largely determine how much more staggering will be the numbers of new diagnoses in the near future. But the other half of the numbers equation — controlling the spread of further infection — is much more within the means of epidemiologists, health care providers, and educators. Curran concluded, "Control of AIDS and HTLV-3/LAV infection cannot await the benefits of future research. There is an urgent need for community groups and health professionals to work together and utilize the tools available to prevent AIDS"

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Diagnosis/Treatment

AIDS MARKER: Update on UCSF Discovery

Four years ago, physicians at the UC San Francisco oral medicine clinic began to see patients who presented with unusual white lesions located on the lateral borders of the tongue. A team led by oral surgeon and researcher Deborah Greenspan later described the lesions as "slightly raised, a few millimeters to 3.5x2 cm in size, poorly demarcated, and showed a corrugated or 'hairy surface.'" The lesions did not rub off as do those associated with the common "hairy tongue" related to cigarette smoking. The lesions were usually symptomless, but some patients reported soreness at lesion sites. Many of the patients had lymphadenopathy; all were gay men referred by the UCSF AIDS Clinical Research Center or by San Francisco physicians and dentists. The appearance of the unusual oral lesions coincided with the first reports of AIDS among gay men in the city.

At that time the probable cause of AIDS, LAV/HTLV-3/ARV had not been identified, and researchers strained to determine what infection or symptom might be of clinical or epidemiological use as an "AIDS marker." The new white, hairy lesion proved to be a likely candidate.

First, the researchers had to identify more fully what they were seeing in these patients. *Candida* was suspected, and cultures confirmed candidiasis in 26 of the initial 37 patients. Although standard antifungal therapies (nystatin troches,

systemic ketoconazole, or clotrimazole oral troches) resulted in negative follow-up cultures from all the 26 patients, the lesions themselves failed to disappear in any of the patients.

Further examination of tissue from five patients revealed the presence of virus similar in appearance to those of the herpes group.

Eight of the initial 37 patients developed pneumocystis pneumonia; one died; and one developed AIDS-related meningitis. Twenty-three others whose conditions were followed remained alive and well after a mean period of 9.5 months.

The appearance of the unusual oral lesions coincided with the first reports of AIDS among gay men in the city.

These initial observations posed more questions than answers, but another full year of research by Greenspan and her colleagues produced several significant findings.

More than one virus was identified by electron microscopy in biopsies obtained from the lesions. These included the human papilloma virus (HPV), the herpes simplex (HSV-2), and the Epstein-Barr virus (EBV). Dr. John Greenspan, UCSF oral biologist/pathologist and principal investigator for the laboratory studies, noted that this discovery marked the first time EBV had been found in human biopsy. That finding alone provides much-needed information for developing an effective treatment of EBV infections.

By June of 1985 the UCSF researchers had treated a total of 123 patients with hairy leukoplakia. Thirteen of them were also diagnosed with AIDS. Another 20 later developed AIDS. In addition, the researchers tested serum samples from 79 patients of the original group of 123. Of these 79, 99% tested positive for antibodies to LAV/HTLV-3/ARV.

In a report to the Centers for Disease Control, Greenspan noted that the lesions have also been identified in patients examined in Los Angeles, Baltimore, Paris, Copenhagen, and London.

The work of Greenspan and her colleagues is important to AIDS research for a number of reasons: (a) it presents new understanding of the biology of the Epstein-Barr virus and AIDS, (b) it found EBV as well as other viruses in the lesions, an outcome necessary for understanding the role of multiple viruses in cancer of the mouth and for development of treatments, (c) it alerted physicians and dentists to the presence of a new lesion that could be misdiagnosed as candidiasis, and (d), it described a condition that may be one of the earliest clinical signs leading to the development of AIDS.

This last result may be increasingly important as therapies are found for treatment of ARC and other early signs of AIDS. While physicians may be wary to treat someone who is "simply" exposed to the probable AIDS virus, they may want to advise treatments for someone who has not only been infected with the "AIDS virus" but who has also begun to manifest symptoms such as hairy leukoplakia lesions.

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BRIEFS

IN SELF-DEFENSE, by Steven B. Mizel, MD, and Peter Jaret, 240 pp. New York: Harcourt Brace Jovanovich, 1985. \$15.95.

As AIDS research delves further into the mysteries of the human immune system, the lay person — and even the non-specialist — confronts the complexities of immunology. AIDS educators, health care providers, and mental health professionals often struggle to provide an immunological context for the recent news item or a patient's diagnosis.

IN SELF-DEFENSE offers not only a concise introduction to the immune system but also an update on the latest advances in immunology. Discussions of autoimmunity, the promise of lymphokines, the allergy connection, and the basic means of defense provide the reader with the information to place AIDS research into a manageable context.

Although IN SELF-DEFENSE does not focus entirely on AIDS, authors Mizel and Jaret present a compelling and highly readable account of the revolution in medicine that promises to unlock the secrets to the vaccine, treatment, and cure of AIDS.



LYMPHADENOPATHY UPDATE

Dr. Don Abrams, AIDS researcher at SFGH, began a prospective, longitudinal natural history study of men with diffuse lymphadenopathy in 1981. He has since followed 200 men who have adenopathy in two or more extralingual sites for greater than six months' duration. Since other research has found a very high correlation between the syndrome of persistent generalized lymphadenopathy (PGL) and viral infection with HTLV-3/LAV/ARV, Abrams' study continues to provide important information about the spectrum of responses to the infection. The study has particular relevance for San Francisco since current epidemiological evidence indicates that approximately 20% of gay men in the city have findings of the diffuse lymphadenopathy.

Sixteen of the 200 men with PGL have developed CDC-defined AIDS. Of the men with AIDS, 13 were diagnosed with opportunistic infections, five with Kaposi's sarcoma, and two with lymphoma. Six have died. Abrams noted during recent medical conferences that the 8% "rate of evolution" (from PGL to AIDS) is consistent with the 10% overall rate found among 1100 patients participating in other studies elsewhere in the country.

Several features distinguished the 16 men who progressed to AIDS. The presence of oral candidiasis increased the risk of developing AIDS by a factor of 54. Eighty-three percent of the men experienced shrinking peripheral adenopathy, according to Abrams. In addition, the majority of the men experienced more severe constitutional symptoms, an elevated erythrocyte (a mature red blood cell) sedimentation rate, a peripheral cytopenia, and an antecedent history of infection with herpes zoster. Among the 16 patients, the AIDS diagnosis followed the onset of lymphadenopathy by a mean of 29 months.

Abrams has conducted small, placebo-controlled clinical trials of interferon and Isoprinosine; he has also investigated the use of the antiviral drug suramin. Results of the trials are still pending.

At the recent UCSF conference on the mental health issues related to AIDS, Abrams expressed hesitancy to conduct extensive clinical trials with his study subjects until more is known of the natural history of the syndrome.

"I wonder if it's appropriate for all my lymphadenopathy patients to embark on anti-viral therapies. Perhaps their systems are already responding appropriately."

ETHICAL DILEMMAS

Everyday the news media reports another clash between AIDS public health policies and civil liberties concerns. City halls, health departments, school districts, and private businesses across the country struggle to cope with both the rational and the irrational fears of AIDS. There may be some help on the way.

The Hastings Center Institute of Society, Ethics, and the Life Sciences has embarked on an ambitious project to study the social conflicts that accompany the AIDS epidemic and to propose practical resolutions. Carol Levine, co-director of the "AIDS: Public Health and Civil Liberties" project, recently outlined the effort during an interview with the *Journal of the American Medical Association* (November 8, 1985).

"What differentiates our study from other attempts to look at the ethical implications for society of AIDS is that we will make every effort to look beyond the immediate AIDS crisis and consider it in the larger perspective of the interaction of social and political forces and disease," said Levine.

The AIDS researcher said she and co-director Ronald Bayer, PhD will assemble two dozen experts in various fields of human behavior, such as public health and epidemiology, medicine, law, history, ethics, and the social sciences to discuss possible responses with practical applications. Representatives from gay civil rights groups will also participate. The group will issue interim reports geared to the needs of public policy makers.

The Hastings Center had already entered the controversial territory of AIDS policies when it proposed practical solutions to the problems that faced blood banks and blood donors before the HTLV-3 antibody test became available.

This new undertaking received funding from the Field Foundation, the Crowe Family Foundation, and the AIDS Medical Foundation.

The amount of research information now appearing in the medical and lay press staggers most AIDS health care and service providers. This newsletter represents an attempt to place much of the data and press reports in a context that will prove meaningful and useful to its readers. Suggestions and comments are welcome and encouraged. Please address correspondence to Editor, AIDS Health Project, 333 Valencia Street, 4th Floor, San Francisco, CA 94103.

NEXT MONTH

"AIDS is a mental health crisis as well as a public health crisis," asserted Michael Gottlieb, MD, director of the UCLA AIDS Center. Gottlieb echoed the sentiments of most speakers at the recent special conference entitled "AIDS: Policy, Administrative, and Clinical Issues of Mental Health."

Another speaker, Deane Wolcott, MD, from the UCLA Department of Psychiatry, presented preliminary data from studies conducted in San Francisco and New York.

"During their lifetimes 40% of people with AIDS and people with ARC will develop neurological disorders: 10% will develop these disorders as the first symptom of AIDS and ARC." Wolcott delivered a special message to his mental health colleagues, "One of the great problems with AIDS is that psychiatric problems are not treated seriously and are not treated with therapies."

In the January issue of FOCUS, Jeffrey Mandel, PhD, MPH, coordinator of the UCSF Biopsychosocial AIDS Project, will present an assessment of the psychosocial issues faced by people with AIDS. In addition, Samuel Tucker, MD, Assistant Clinical Professor of Psychiatry, UCSF, will evaluate the appropriate therapies for central nervous system disorders.