Acquired Immune Deficiency Syndrome (AIDS)

During June and July 1981, the U.S. Centers for Disease Control (CDC) reported to the medical community an unprecedented occurrence of Kaposi's sarcoma and *Pneumocystis carinii* pneumonia among apparently previously healthy homosexual men. One and a half years later, over 1,000 individuals with a similar illness characterized by unusual rare malignancies and opportunistic infections have been reported to CDC. Multiple detailed reports have appeared in the literature clearly documenting this unique pattern of disease, and the number of cases continues to increase at approximately three cases per day in the United States with increasing case reports throughout Europe, Africa, and Haiti. Since a common denominator in all of these patients appears to be the development of a profound immunosuppressed state, the disease has been referred to as the acquired immune deficiency syndrome (AIDS). CDC defines a case of AIDS as a disease, at least moderately predictive of a defect in cell-mediated immunity, occurring in a person with no known cause for diminished resistance to that disease. The disease may manifest as Kaposi's sarcoma, *P. carinii* pneumonia, and other serious opportunistic infections listed below.

As of 9 February 1983, CDC has received notification of 1,051 cases of AIDS in the United States as reported from 34 states. CDC also has information on 70 additional cases which have occurred in 15 other countries. The incidence of AIDS in the United States has roughly doubled every six months since the second half of 1979. Analysis of cases of AIDS reported to CDC shows that 50 per cent had *P. carinii* pneumonia, a rare protozoan pulmonary infection which previously was a major infection only in severely immunosuppressed patients, such as bone marrow transplant patients or patients undergoing chemotherapy (Table 1). A total of 28 per cent of AIDS patients had Kaposi's sarcoma, an extremely rare, malignant neoplasm seen previously only in elderly men or in individuals immunosuppressed due to organ transplantation or steroid therapy. Unlike the limited radiosensitive Kaposi's sarcoma seen in this latter group, Kaposi's sarcoma in AIDS patients is typically radiation and chemotherapy insensitive and frequently disseminates to a lymphadenopathic form resulting in the death of the patient within two years. Prior to the recognition of AIDS, this lymphadenopathic form of Kaposi's was occasionally seen in Equatorial Africa affecting primarily young men. An additional 8 per cent of the 1,051 cases of AIDS have had both Kaposi's sarcoma and *P. carinii* infection, a combination of diseases which had never been recognized in the past. The remaining 14 per cent of AIDS patients had other opportunistic infections which again are only seen in immunosuppressed patients. These infections include pneumonia, meningitis, or encephalitis due to one of the following: *Aspergillus, Candida, Cryptococcus,* cytomegalovirus, *Nocardia, Strongyloides, Toxoplasma, Zygomycoses,* or atypical *Mycobacteria;* esophagitis due to *Candida,* cytomegalovirus, or herpes simplex virus; progressive multifocal leukoencephalopathy; chronic enterocolitis (more than four weeks) due to *Cryptosporidia;* or unusually extensive mucocutaneous herpes simplex infection of more than five weeks duration. None of the above patients had a history of having received any immunosuppressive therapy such as corticosteroids. Patients with Hodgkins' disease and other lymphomas were excluded for epidemiological purposes.

Table 1. Distribution of AIDS cases, according to clinical reports, notified in the United States of America, up to 9 February 1983.*

Disease	Number	Total cases	Fatality percentage
Kaposi's sarcoma	295	28	21
Pneumocystis carinii pneumonia	527	50	44
Both	86	8	51
Other opportunistic infections	143	14	46
Total	1,051	100	39

*Information provided by U.S. Centers for Disease Control (CDC), Atlanta, Georgia.

Approximately 80 per cent of the cases reported in the U.S. have been concentrated in six metropolitan areas: New York City (46 per cent), San Francisco (11 per cent), Los Angeles (6 per cent), Newark (5 per cent), Miami and Houston (4 per cent) (Table 2). Of the total cases, 73 per cent occurred among homosexually or bisexually active men, 16 per cent among heterosexual intravenous drug abusers, 5 per cent among Haitian immigrants residing in the U.S., and 1 per cent among hemophiliacs receiving lyophilized concentrates of Factor 8 (Table 3). Over the past year other categories of patients have developed AIDS which include patients who have received routine blood transfusions, children of AIDS patients, heterosexual partners of AIDS

Table 2. Percentage distribution of AIDS cases by area of residence, United States of America, up to 9 February 1983.*

Residence	Percentage of total
New York State	50
New York City	46
California	21
San Francisco	11
Los Angeles	6
Florida	6
Miami	4
New Jersey	6
Newark	5
Other States (30)	17

*Information provided by CDC.

Table 3. Percentage distribution of AIDS cases, by risk categories, United States of America, up to 9 February 1983.*

Category	Per cent
Homosexual/bisexual men	73
Heterosexual IV drug abusers	16
Haitian immigrants	5
Hemophiliacs	1
Others:	5
Patients receiving blood transfusions	
Children of AIDS patients	
Heterosexual partners of AIDS patients	
Prison inmates	

*Information provided by CDC.

Table 4. Percentage distribution of AIDS cases by race, United States of America, up to 9 February 1983.*

Race	Percentage of total
White	59.9
Black	21.0
Hispanic	12.7
Haitian	5.4
Native American	0.2
Asian	0.2
Unknown	0.6
Total	100.0

*Information provided by CDC.

Table 5. Percentage distribution of AIDS cases according to age, United States of America, up to 9 February 1983.*

Age	Percentage of total
Under 20	0.4
20-24	4.3
25-29	17.4
30-34	27.5
35-39	20.3
40-49	22.6
Over 50	7.2
Unknown	0.3
Total	100.0

*Information provided by CDC.

patients, and prison inmates who state that they do not belong in the above risk categories. The racial and age distribution of AIDS cases in the U.S. are shown in Tables 4 and 5.

Occurrence of AIDS among hemophiliacs, those receiving blood transfusions, and heterosexual intravenous drug abusers has suggested that the syndrome, or the etiologic agent of the syndrome may be transmitted through blood products, analogous to hepatitis B virus or non-A or non-B hepatitis. In addition, the frequent occurrence among homosexually active men and among the heterosexual partners of AIDS patients also suggests the sexual transmissibility of this syndrome. Clustering of cases and analysis of contacts of patients with AIDS have also shown that many patients may be asymptomatic carriers of this syndrome.

The overall case fatality rate for the 1,051 cases has been 38.6 per cent. However, for cases that were diagnosed two years ago the mortality rate exceeds 70 per cent. It is estimated that the five year mortality rate will exceed 90-95 per cent. The fatality rate for cases of *P. carinii* pneumonia without Kaposi's sarcoma was 44 per cent and for Kaposi's sarcoma without *P. carinii*, 21 per cent. Cases with both *P. carinii* pneumonia and Kaposi's sarcoma had a fatality rate of 51 per cent. Those with other opportunistic infections had a mortality rate of 46 per cent.

The common denominator in these patients appears to be a profound immunosuppressed state, particularly among the patients with severe opportunistic infections. Typically, patients present lymphopenia (total lymphocyte count less than 1,500 cells per mm) and anergy to all skin tests. There is an absolute depression of helper T lymphocytes resulting in a decreased ratio of helper T-cells to suppressor T-lymphocytes (usually less than 1.0; normal is greater than 1.0). In addition,

diminished proliferative responses to most mitogens are observed in vitro. In addition to defective natural killer cell activity, B cell function appears to be slightly abnormal with polyclonal hypergammaglobulin and increased immune complexes. The latter have been associated with autoimmune thrombocytopenic purpura and autoimmune hemolytic anemia in patients. As a consequence of the immunosuppressed cell-mediated response, patients with AIDS will typically develop infections with fungal, viral, and parasitic infections. Since neutrophil function remains intact, bacterial infections other than mycobacteria are not a major problem in these patients.

Although immunologic dysfunction is the common factor among all AIDS patients, the clinical spectrum of disease has been quite variable. From epidemiological studies the incubation period appears to be between 6-12 months. There is usually a 3-6 month symptomatic period commonly referred to as the prodromal period of AIDS, characterized by unexplained fever, night sweats, chills, diarrhea, fatigue, diminished libido and impotency, depression, apathy, and generalized lymphadenopathy. The syndrome is then typically diagnosed with the appearance of either Kaposi's sarcoma or disseminated opportunistic infections.

Treatment of patients with AIDS has been challenging because they often have multiple opportunistic infections which tend to present themselves. Whether treatment is initially successful for an opportunistic infection or for improvement in Kaposi's sarcoma, the immunologic defect is persistent and the patient frequently has occurrence of malignancy or opportunistic infection. Treatment modalities in addition to specific treatment for the identified infections have included interferon, interleukin, thymosin, and bone marrow transplantation. In all instances there is an attempt to avoid treatment with immunosuppressive drugs. Infections with *Mycobacterium avium-intracellulare* or with cryptosporidiosis have proven to be highly resistant to treatment and the efficacy of new investigative drugs is being studied.

From the studies on the epidemiology of AIDS, the data highly support the hypothesis that this syndrome is caused by an infective agent transmissible through blood, blood products, or sexual activities. The appearance of AIDS in children born to mothers with AIDS also suggests either transplacental transmission or transmission through maternal-fetal blood transfer at time of birth. Thus far, all investigative efforts have failed to identify a cause of this disease. Until an etiologic factor is identified or successful treatment is developed, it is likely that the number of cases of AIDS will continue to increase in epidemic numbers within the United States and in other countries, and if the fatality rate continues unabated, the lethal effects of this disease will eventually be felt throughout the world.

Note:

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.

The National Hemophilia Foundation has made specific recommendations for management of patients with hemophilia.[1]

The interim recommendation requesting that high-risk persons refrain from donating plasma and/or blood is especially important for donors whose plasma is recovered from plasmapheresis centers or other sources and pooled to make products that are not inactivated and may transmit infections, such as hepatitis B. The clear intent of this recommendation is to eliminate plasma and blood potentially containing the AIDS agent from the supply. Since no specific test is known to detect AIDS at an early stage in a potential donor, the recommendation to discourage donation must encom-

[1] Medical and Scientific Advisory Council Recommendations to prevent AIDS in patients with hemophilia. New York: National Hemophilia Foundation, January 14, 1983.

pass all members of groups at increased risk for AIDS, even though it includes many individuals who may be at little risk of transmitting AIDS.

As long as the cause remains unknown, the ability to understand the natural history of AIDS and to undertake preventive measures is somewhat compromised. However, the above recommendations are prudent measures that should reduce the risk of acquiring and transmitting AIDS.

(*Source:* Thomas C. Quinn, M.D., Senior Investigator, National Institutes of Allergy and Infectious Diseases, National Institutes of Health (USA), and MMWR32 (8): 102-103, March 1983.)

The Cuban *Aedes aegypti* Campaign: a Year Later

The *Epidemiological Bulletin* Vol. 3, No. 1 (1982) reported on the program for dengue elimination and *Aedes aegypti* eradication following the 1981 epidemic of dengue when 344,203 cases and 158 deaths were reported in Cuba. Dengue was declared eliminated from Cuba on 16 November 1981 and, at that time, the premises index had been reduced from 35 and greater before the epidemic to 0.09.

On 5 October 1981 the consolidation phase of the eradication program began. The initial strategy was to do treatment cycles at two month intervals and verification cycles every one or two months depending on the area. During November 1982, a team from PAHO accompanied staff from the National *Aedes aegypti* Eradication Program to several areas in Cuba where statistical information of the first year of the consolidation phase was analyzed.

The technical information obtained from the intensive control measures that are being directed against *A. aegypti* in Cuba and the flexibility to combat technical difficulties inherent in many programs have prompted a follow-up of the original report. The information presented may guide other member countries in seeking solutions for some of their control problems.

The program completed seven cycles on 11 December 1982. Table 1 gives the cycle schedule, number of positive premises, and the premises index. As anticipated, the index did not vary greatly between cycles due to the fact that it is fairly easy to bring about a rapid reduction when the index is high but as the index of infestation approaches zero, the expenditure of effort greatly increases. Consequently, without increases in staff and supplies, any campaign may expect a static period before eradication is completed. Considering that the Cuban campaign is only 16 months old and covers approximately 2.5 million houses, the progress is remarkable.

Several factors account for the continued presence of positive premises despite the intensity of the campaign. By the third cycle, it was evident that the problem of control had shifted from an urban to a rural environment (Table 2). At the same time it became necessary to place a greater priority on treatment of schools, factories, and other nonresidential structures. Rural and industrial areas were identified as a cause for continued positivity at the beginning of the rainy season. Rains caused an increase of natural containers (tree holes, bamboo, coconut shells, etc.) serving as *A. aegypti* breeding sites and aggravated logistical problems because of dispersed premises in treatment and evaluation. Despite the logistical problem, the cycle schedule was maintained and in some risk areas, the number of evaluations actually increased.

Closed houses, a problem in many programs, has not caused concern in Cuba. The goal of 100 per cent coverage was almost met in every cycle. For example, only 0.9 per cent of the houses were closed in the second cycle, 0.2 per cent in the third, 0.3 per cent in the fourth, and

Table 1. Premises found positive for *Aedes aegypti* and premises index, by treatment cycle, Cuba, 1982.

Cycle	Dates	Number of positive premises	Premises index
1	5 Oct. -12 Dec. 1981	504	0.020
2	14 Dec. -23 Jan. 1982	294	0.013
3	25 Jan. -20 Mar. 1982	501	0.019
4	22 Mar.-22 May 1982	497	0.020
5	24 May - 6 Aug. 1982	470	0.018
6	16 Aug.-16 Oct. 1982	298	0.012
7*	18 Oct. -11 Dec. 1982	117	0.005

*Data incomplete.