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## A Comparison of the Clinical Features of American and African Patients with AIDS

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The acquired immunodeficiency syndrome (AIDS) is a recently described immunoregulatory disorder that is characterized by multiple, progressive opportunistic infections and the occurrence of previously rare neoplasms such as Kaposi's sarcoma and primary intracranial lymphomas. Extensive epidemiological, clinical, serological and microbiological data has demonstrated that the putative agent is a retrovirus commonly referred to as human T-cell lymphotropic virus-III/lymphadenopathy-associated virus (HTLV-III/LAV). It is now recognized that AIDS is just one part of the spectrum of HTLV-III/LAV disease that includes asymptomatic carriage, transient immune defects, generalized lymphadenopathy, a diarrhea-wasting syndrome, multiple neuropathies and immune thrombocytopenia (3).

Since the first reported case in June, 1981, AIDS has reached epidemic proportions in the United States: there were 20,766 cases reported to the Centers for Disease Control (CDC) as of May 19, 1986 and it is now the leading cause of death in young men in Manhattan, New York and San Francisco, California. Since its recognition, the epidemiology of AIDS in the United States has remained remarkably constant. Among American adults, approximately 73% of cases appear in homosexual or bisexual men, 17% in intravenous drug users, 3% in blood transfusion recipients, 1% in heterosexual partners of AIDS patients, and 6% in patients who had recently immigrated from other AIDS endemic countries such as Haiti, or who denied any of the above risk factors.

It has now become distressingly apparent that there are an increasing number of cases in other parts of the world. According to information supplied by the Pan American Health Organization on May 29, 1986, in the Western Hemisphere, there have been 616 cases of AIDS in Haiti, 540 in Brazil, 435 in Canada, 34 in the Dominican Republic, 38 in the Bahamas, 33 in Mexico, 32 in Venezuela, and 191 in other Central American, South American and Caribbean nations.

AIDS is not just confined to the Western Hemisphere. As of March 31, 1986, 2,542 cases of AIDS had been reported to the World Health Organization (WHO) by the 26 European cooperating countries. Sixty percent of the cases have occurred in France, Great Britain and West Germany. Similar to the American patients, 69% of cases occurred in

homosexual or bisexual men, 6% in IV drug abusers and 4% in blood product recipients. Of particular interest was the fact that many of the patients diagnosed in Europe were of African origin (2). Indeed, during a 3 week period in 1983, 38 patients with AIDS were identified ratio was 1.1:1, and homosexuality, intravenous drug abuse, and blood transfusion did not appear to be risk factors for the transmission of the AIDS virus (7).

We have had a particular interest in the epidemiology of AIDS in different parts of the world. As part of these studies, we have noticed that the clinical manifestations of AIDS varies according to the geographic area. The purpose of this review is to compare the specific differences in the clinical features of AIDS between American patients and African patients.

The data on the African patients were accumulated from a prospective study of AIDS in Kinshasa, Zaire (5). Kinshasa, the most populous city in Central Africa with approximately 2.5 million inhabitants, is located on the Zaire River approximately 350 km from the Atlantic Ocean. The study was a cooperative effort of Project SIDA under the auspices of the Ministry of Health of Zaire, the Centers for Disease Control and National Institute of Allergy and Infectious Diseases in the U.S., and the Institute of Tropical Medicine in Belgium. The clinical features of the first 200 patients from this study were used for comparison. The clinical data on the American patients with AIDS were gathered from 100 patients we have seen at the National Institutes of Health and The Johns Hopkins Hospital.

American patients were identified according to current CDC criteria (1); essentially, this requires the presence of Kaposi's sarcoma or an opportunistic infection that is at least moderately predictive of a defect in cell-mediated immunity, that occurs in a patient with no known underlying cause for immunodeficiency. Due to practical limitations and restricted resources for diagnosing malignancies and infections in Zaire, the following case definition for AIDS in Zaire was employed (all four criteria were required):

- (1) At least one of the following three clinical criteria:
  - (a) A syndrome with profound weight loss (greater than 10% of normal body weight) plus either chronic diarrhea (lasting at least 2 months) or chronic fever and asthenia (lasting 1+ months);
  - (b) An opportunistic infection included in the CDC definition of AIDS (1). Restricted resources essentially limited recognized opportunistic infections to candidal esophagitis, cryptococcal meningitis, and chronic ulcerated herpes infection;
  - (c) Disseminated Kaposi's sarcoma, with histopathologic evidence of visceral invasion.
- (2) Anergy to intradermal tuberculin at 48-72 hours.

- (3) Both of the following lymphocyte subset criteria:
- (a) Absolute number of OKT4<sup>+</sup> cells < 400 per mm;<sup>3</sup>
  - (b) OKT4<sup>+</sup>/OKT8<sup>+</sup> ratio < 0.9.
- (4) Absence of conditions that might explain the patient's clinical or immunologic status, such as:
- (a) Cancer, severe malnutrition, or an immunodeficiency disease;
  - (b) Immunosuppressive therapy during the 2-month period before onset of illness or during the present illness.

During the eight months of the study, 332 cases of AIDS fulfilled the above definition, for an estimated annual incidence rate for adults of 380 cases/million population or 38/100,000. This is much higher than the overall U.S. annual incidence rate of 1.43/100,000. It is comparable, however, to the rate among high risk groups: 204.5/100,000 among single men in San Francisco, 113/100,000 among IV drug users, and 82/100,000 among recent Haitian entrants into the U.S. (4).

As in the previous study of AIDS in Zaire (7), the male:female ratio was 1.1:1. In the U.S., 93% of adult AIDS patients are men (male:female 13:1). The African male patients were also significantly older (37.4 vs 30.0 years) than the female patients. This feature, in addition to the nearly one-to-one sex distribution and evidence of clustering of cases among sexual partners, is quite typical of sexually transmitted diseases, implying that the disease may be transmitted by heterosexual intercourse. Another possibility is that since Africans with AIDS had a larger number of other sexually transmitted diseases and the syringes and needles used for treatment are poorly sanitized, the disease may have been transmitted by the percutaneous route. Further studies are underway to clarify this important concept.

A comparison of the presenting symptoms in 100 U.S. and 200 African patients with AIDS is given in the following table:

Table I

## PRESENTING SYMPTOMS

	<u>U.S.</u>	<u>African</u>
Mean duration (range)	5 (1-48) mon.	8 (1-78) mon.
Fever	93%	69%*
Weight loss	70%	98%*
Dyspnea	66%	10%*
Diarrhea	42%	73%*

\* p < 0.001, Chi-square

Thus, while in the U.S. patients, fever is the most common presenting symptom, in African patients, weight loss is the most common (Table I). The large number of Zairian patients with weight loss may be artifactual, since it was included as one of the criteria for the case definition of AIDS. Nevertheless, weight loss is a significant feature in African patients with AIDS, averaging approximately 30% of total body weight. The higher frequency of diarrhea was not entirely unexpected, and may be due to the larger parasitic burden carried by Africans. Weight loss and diarrhea are also the most common presenting symptoms of patients with AIDS in Haiti (6), another tropical, developing country.

The presenting signs of U.S. and African patients with AIDS also demonstrated significant differences as shown in Table II:

Table II

## PRESENTING SIGNS

	<u>U.S.</u>	<u>African</u>
Oral Thrush	40%	72%*
Lymphadenopathy	40%	32%*
Skin lesions	8%	70%*

\*  $p < 0.001$ , Chi-square

The most notable difference between the two groups is the large number of African patients with skin lesions. Some of these lesions were herpes simplex virus (HSV), but most were a rather distinctive pruritic, maculopapular rash. Biopsy of the lesions revealed changes consistent with leukocytoclastic vasculitis. The etiology of this rash remains unknown.

Table III presents the laboratory data of the patients.

Table III

## LABORATORY DATA

	<u>U.S.</u>	<u>African</u>
Lymphocyte count	1391/mm <sup>3</sup>	1072/mm <sup>3</sup>
OKT4 <sup>+</sup> cells	291/mm <sup>3</sup>	97/mm <sup>3</sup>
OKT8 <sup>+</sup> cells	472/mm <sup>3</sup>	633/mm <sup>3</sup>
OKT4 <sup>+</sup> /OKT8 <sup>+</sup> ratio	0.41	0.17
Anergy	100%	100%

Even though these findings make it appear that the African patients have more severe in vitro compromise of their immune status, these data are skewed since anergy, a reversed helper/suppressor ratio, and a reduction in the absolute number of helper T-cells were required for the diagnosis of AIDS in the African patients. In further studies, 330/332 (99.4%) of the African patients had sera that were repeatedly positive for HTLV-III/LAV on two separate ELISA assays; 99/100 ELISA positive sera were also positive by Western blot (5).

Opportunistic infections differed markedly in the two groups.

Table IV

OPPORTUNISTIC INFECTIONS

	<u>U.S.</u>	<u>African</u>
Mean number	3.0	1.5
<u>Pneumocystis carinii</u>	73%	2%
Candidiasis	71%	86%
Cytomegalovirus	40%	-
<u>M. avium-intracellulare</u>	23%	-
<u>M. tuberculosis</u>	0%	11%
Progressive HSV	17%	5%
Cryptosporidiosis	10%	6%
CNS cryptococcosis	8%	15%
Toxoplasmosis	5%	-
Disseminated KS	15%	6%

Even though P. carinii pneumonia is the most common infection of AIDS patients in the U.S. - accounting for 43% of reported opportunistic infections - it is rare in African patients. Part of this discrepancy may be due to the lack of facilities to make the diagnosis in Zaire, but the fact that only 10% of the Africans complained of dyspnea (Table I) also suggests that P. carinii pneumonia is uncommon in Kinshasa. In our series, no American had tuberculosis while 11% of African patients did. Tuberculosis is declining in incidence in the U.S., but it should be noted that none of our U.S. patients were of Haitian descent. Tuberculosis appears to be common among Haitian emigrants to the U.S. (8). Finally, the larger mean number infections diagnosed in the U.S. is probably due to the comprehensive diagnostic facilities present in the U.S.

In summary, the signs and symptoms of AIDS are not due to infection with HTLV-III/LAV itself, but rather reflect the underlying opportunistic pathogens that are present in populations from diverse areas. Even though initial infections may be successfully treated with various antibiotics, the persisting lack of immunocompetence leads to a succession of increasingly severe infections and the ultimate demise of the infected patient.

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