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## A MEDICAL REVIEW OF AIDS

*Marc J. Sicklick, M.D.\* and Arye Rubinstein, M.D.\*\**

### CASE DEFINITION

AIDS<sup>1</sup> is defined by the Centers for Disease Control (CDC) as an acquired immune deficiency syndrome in association with evidence of exposure to the Human T-cell lymphotropic retrovirus type III (HTLV-III) in a person who is not otherwise at risk for developing an immune deficiency syndrome.<sup>2</sup> This definition excludes any immune deficiencies accompanying malignancies or immune deficiencies which are induced by immunosuppressive medications (such as those given to organ transplant recipients).<sup>3</sup>

Certain disease symptoms must be documented in order to support a diagnosis of AIDS.<sup>4</sup> These symptoms include: opportunistic infection (infection with an organism that does not usually cause disease); *Kaposi's sarcoma* (a malignant skin lesion that is normally not found in young individuals); non-Hodgkin's lymphoma of high grade pathogenicity; or, in children under age thirteen, a lymphocytic (white blood cell) infiltrative process in the lung.<sup>5</sup>

The CDC case definition was established primarily for an epidemiologic survey.<sup>6</sup> However, physicians recognize many patients as being HTLV-III infected who do not fit the CDC criteria for AIDS, and who, therefore, are not included in published statistical and de-

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1. AIDS is the abbreviation for acquired immune deficiency syndrome.

2. Selik, Haverkos & Curran, *Acquired Immune Deficiency Syndrome (AIDS) Trends in the United States, 1978-1982*, 76 AM. J. MED. 493 (1984).

3. Jaffe, Bregman & Selik, *Acquired Immune Deficiency Syndrome in the United States: The First 1,000 Cases*, 148 J. INFECTIOUS DISEASES 339 (1983).

4. Selik, Haverkos & Curran, *supra* note 2, at 499.

5. *Id.*

6. *Revision of the Case Definition of Acquired Immunodeficiency Syndrome for National Reporting—United States*, 34 MORBIDITY & MORTALITY WEEKLY REP. 373 (June 28, 1985).

mographic CDC reports.<sup>7</sup> As a result, the original case definition of AIDS is modified as the disease is better understood and as new clinical patterns evolve.<sup>8</sup>

For the nonepidemiologist, it is helpful to think of AIDS as a spectrum of HTLV-III diseases ranging from HTLV-III infection in a healthy person, to recurrent nonopportunistic infections, to full blown AIDS as it is currently defined.<sup>9</sup> Any disease associated with HTLV-III infection that does not fall far enough into the spectrum to be classified as AIDS is called AIDS-related complex (ARC).<sup>10</sup>

#### HISTORICAL EVOLUTION OF THE DISEASE

The origin of AIDS is unclear. The disease probably surfaced in Africa in the 1960's, although isolated cases may have existed earlier.<sup>11</sup> In retrospect, we (the authors) probably saw our first case of AIDS in 1977 when we treated an intravenous drug user for a disseminated atypical mycobacterium infection (an opportunistic infection now commonly associated with AIDS). A few years later, in 1981, a clustering of *Kaposi's sarcoma* cases in young homosexuals was first noted in the United States,<sup>12</sup> while at the same time a disease process with persistent, generalized lymphadenopathy (swollen glands) was also documented in homosexuals.<sup>13</sup> In addition, it was

7. *Id.*

8. *Id.* at 373-74.

9. Blattner, Biggar, Weiss, Melbye & Goedert, *Epidemiology of Human T-Lymphotropic Virus Type III and the Risk of the Acquired Immunodeficiency Syndrome*, 103 *ANNALS INTERNAL MED.* 665, 668 (1985).

10. For a technical definition of ARC, see Redfield, Markham, Salahuddin, Wright, Sarngadharan & Gallo, *Heterosexually Acquired HTLV-III/LAV Disease (AIDS-Related Complex and AIDS)*, 254 *J. A.M.A.* 2094 (1985). ARC is also discussed in Jason, McDougal, Dixon, Lawrence, Kennedy, Hilgartner, Aledort & Evatt, *HTLV-III/LAV Antibody and Immune Status of Household Contacts and Sexual Partners of Persons With Hemophilia*, 255 *J. A.M.A.* 212 (1986).

11. See Williams, Stretton & Leonard, *AIDS in 1959?*, *LANCET*, Nov. 12, 1983, at 1136 (discussing the possibility that a patient diagnosed with cytomegalic inclusion disease and *Pneumocystis carinii* infection may in fact have died from AIDS). See also Selik, Haverkos & Curran, *supra* note 1, at 494 (noting two early cases: a Haitian man in Brooklyn, N.Y., in whom *Pneumocystis carinii pneumonia* was diagnosed in 1959; a woman in Louisiana in whom *Pneumocystis carinii pneumonia* was diagnosed in 1975).

12. *A Cluster of Kaposi's sarcoma and Pneumocystis carinii Pneumonia among Homosexual Male Residents of Los Angeles and Orange Counties, California*, 31 *MORBIDITY & MORTALITY WEEKLY REP.* 305 (June 18, 1982).

13. *Persistent, Generalized Lymphadenopathy among Homosexual Males*, 31 *MORBIDITY & MORTALITY WEEKLY REP.* 249 (May 21, 1982). Reports of this disease were made by physicians in major metropolitan areas in the United States. Of 57 patient records reviewed by the CDC, the mean age of the patients was 33 years. All were male, 81% were white, 15% were black, and 4% were Hispanic; 83% were single, 6% were married, and 11% divorced; 86%

not until 1983 that the existence of AIDS in children was generally accepted,<sup>14</sup> although we saw our first pediatric case three years earlier.

### EPIDEMIOLOGY

The AIDS-causing virus has been isolated from blood, semen, vaginal fluids, breast milk, saliva, and tears.<sup>15</sup> However, the presence of the virus cannot be equated with its risk of transmission. Although the AIDS virus may exist in saliva or tears, transmission via these sources has not been documented.<sup>16</sup>

The homosexual and bisexual populations constitute the largest risk group to develop AIDS or ARC.<sup>17</sup> Recently, however, incidences of the disease have become more noticeable among intravenous drug users.<sup>18</sup> Only a small number of patients fall into other known risk groups, such as recipients of blood products<sup>19</sup> and sexual partners of high risk group members.<sup>20</sup> A small but constant percentage of patients have no apparent risk factor.<sup>21</sup> The pediatric patients usually acquire the disease from their HTLV-III infected mothers,<sup>22</sup> or, less

were homosexual and 14% were bisexual. *Id.*

14. *Update: Acquired Immunodeficiency Syndrome—United States*, 35 MORBIDITY & MORTALITY WEEKLY REP. 17, 19 (Jan. 17, 1986) [hereinafter cited as *Update: United States*]. See also, Rubinstein, Sicklick, Gupta, Bernstein, Klein, Rubinstein, Spigland, Fruchter, Litman, Lee & Hollander, *Acquired Immunodeficiency with Reversed T4/T8 Ratios in Infants Born to Promiscuous and Drug-Addicted Mothers*, 249 J. A.M.A. 2350 (1983); Gupta, Sicklick, Bernstein, Rubinstein & Rubinstein, *Recurrent Infections, Interstitial Pneumonia, Hypergammaglobulinemia, and Reversed T4/T8 Ratio in Children With High Antibody Levels to Epstein Barr Virus*, Proceedings of the American Academy of Pediatrics (1982).

15. *Summary: Recommendations for Preventing Transmission of Infection with Human T-Lymphotropic Virus Type III/Lymphadenopathy-Associated Virus in the Workplace*, 34 MORBIDITY & MORTALITY WEEKLY REP. 681, 682 (Nov. 15, 1985) [hereinafter cited as *Preventing Transmission of Virus Type III*]; Selwyn, *AIDS: What is Now Known*, HOSP. PRAC., May 15, 1986, at 67, 73.

16. Selwyn, *supra* note 15, at 73; *Recommendations for Preventing Possible Transmission of Human T-Lymphotropic Virus Type III/Lymphadenopathy-Associated Virus from Tears*, 34 MORBIDITY & MORTALITY WEEKLY REP. 533, 534 (Aug. 30, 1985).

17. *Update: United States*, *supra* note 14, at 19.

18. *Id.* Homosexual and bisexual males and intravenous drug abusers account for 90% of the reported adult cases. Selwyn, *supra* note 15, at 69.

19. *Update: United States*, *supra* note 14, at 19. Transfusion-recipient cases account for 1% to 2% of all reported cases. Selwyn, *supra* note 15, at 69.

20. *Update: United States*, *supra* note 14, at 19.

21. *Id.* There is no identified risk in 3% to 4% of all reported cases. Selwyn, *supra* note 15, at 69.

22. See *Preventing Transmission of Virus Type III*, *supra* note 15, at 682.

frequently, through a blood transfusion.<sup>23</sup> In one case, transmission through breast milk was postulated.<sup>24</sup>

There is compelling evidence that the disease is not transmitted through casual contact.<sup>25</sup> The CDC, therefore, does not recommend routine screening for HTLV-III infection in high risk groups, and individuals infected with AIDS should not be restricted from work unless they have another infection or illness which would warrant such restriction.<sup>26</sup>

### CLINICAL PRESENTATION

The majority of adults seen with AIDS present with either opportunistic infections,<sup>27</sup> chronic diarrhea, recurrent pneumonias, or unexplained weight loss. Others exhibit generalized lymphadenopathy, encephalitis, or recurrent, frequent, nonopportunistic infections, such as common bacterial infections. As the disease progresses, the patient becomes more debilitated, experiences significant weight loss and loss of appetite, and usually acquires additional infections. Since some of these infections do not respond to known therapy, ultimately they may be the cause of death of the AIDS patient.

The pediatric AIDS patients present in a similar but somewhat different way. While adult patients display massive weight loss, pediatric patients present as failures to thrive; these children are abnormally small in both height and weight for their age. Children also exhibit recurrent infections, interstitial pneumonia, and chronic

23. *Possible Transfusion-Associated Acquired Immune Deficiency Syndrome (AIDS)*—California, 31 MORBIDITY & MORTALITY WEEKLY REP. 652 (Dec. 10, 1982).

24. Ziegler, Cooper, Johnson & Gold, *Postnatal Transmission of AIDS-Associated Retrovirus from Mother to Infant*, LANCET, April 20, 1985, at 896. The child of a previously healthy woman was delivered by caesarean section. Because of significant blood loss during the operation, the woman received a blood transfusion. She breast fed the infant for six weeks. Thirteen months later the blood donor developed AIDS. The antibody to the AIDS virus was identified in the infant. Since the mother was transfused after delivery, the baby was presumed to have been infected via the mother's breast milk or some other form of close contact with his mother. *Id.*

25. *Preventing Transmission of Virus Type III*, *supra* note 15, at 682. "There is currently no evidence of spread of LAV/HTLV-III by casual social contact even within households." *World Health Organization Workshop: Conclusions and Recommendations on Acquired Immunodeficiency Syndrome*, 253 J. A.M.A. 3385, 3385 (1985).

26. *Preventing Transmission of Virus Type III*, *supra* note 15, at 681.

27. Opportunistic infections are those "which occur due to the opportunity afforded by the altered physiological state of the host. Thus when certain antibiotics or adrenal cortical steroids are given for long periods, certain microorganisms which would otherwise be nonpathogenic become pathogenic." C. TABER, *TABER'S CYCLOPEDIA MEDICAL DICTIONARY* 0-19 (13th ed. 1977).

diarrhea.

In addition to the infections and malignancies that accompany the disease, significant neurological impairment often occurs. Adults can develop either peripheral neuropathies (damage to the noncentral nervous system) or dementia (another sign of central nervous system involvement). Children are often developmentally delayed and on a CAT scan may show cortical atrophy (shrinking of the gray matter of the brain).

#### DIAGNOSTIC TESTS

Until 1984, the diagnosis of AIDS was made by nonspecific clinical and immunological tests.<sup>28</sup> Currently, the most frequently utilized tests are those used to determine whether a person has antibodies to HTLV-III.<sup>29</sup> These tests only document exposure to the virus, not the presence of disease caused by the AIDS virus.<sup>30</sup> Although these tests have no prognostic value, they remain useful as a screening test for blood products.

The AIDS antibody tests may yield false positive or false negative results. Tests will be negative early in the course of the disease, before the infected person can mount an antibody response. Thus, a person may be infected with the disease in its early stages and nevertheless test negatively. If there is suspicion that the test result does not fit the clinical course of the patient, the Western blot test<sup>31</sup> should be performed. This is a more exact and more expensive test that can be used as a backup in patient evaluation. It fingerprints the virus and shows certain typical findings found in the HTLV-III virus. Detailed evaluation of the immune system, together with a thorough physical examination, is necessary before a definitive diagnosis

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28. The nonspecific clinical and immunological tests included assays for the ratio of helper to suppressor cells. Initially, there was widespread publicity about the reversal of this ratio when a greater number of suppressor cells were present because this reversal was thought to be responsible for the immune system shutting off. It has subsequently been learned that this ratio reversal occurs in many clinical findings, ranging from AIDS to conditions as simple as minor respiratory infections. Thus, it is no longer considered a viable diagnostic test for AIDS and only serves in screening the immune system. It was not until 1984 that R. C. Gallo, at the National Cancer Institute, made discoveries which allowed definition of the HTLV-III virus. Selwyn, *supra* note 15, at 73. Other studies followed, which confirmed the link between HTLV-III and AIDS. *Id.*

29. HTLV-III antibodies are "a reliable marker for the presence of live, infective virus," unlike virus antibodies which generally serve a protective function. *Id.*

30. *Id.*

31. For a description of Western blot analysis, see Jason, McDougal, Dixon, Lawrence, Kennedy, Hilgartner, Aledort & Evatt, *supra* note 10, at 213.

can be established.<sup>32</sup> However, it is important to realize that at the present time, no definitive test to determine the presence of AIDS exists.

#### THERAPY

No cure for AIDS has been found.<sup>33</sup> Therapeutic attempts have included the boosting of the body's own immune system and the use of antiviral agents.<sup>34</sup> To date, however, the best weapon to stem the spread of the disease is avoidance of high risk situations. The long-term prognosis of presently healthy individuals in whom other infection with HTLV-III has been documented remains unclear. It is uncertain how many will progress to ARC or to full-blown AIDS. Several million people today are HTLV-III antibody positive, and, as such, remain a potential reservoir for this infectious agent. Currently, AIDS is primarily restricted to high-risk groups; only the future will tell how this disease will affect individuals outside those groups. The AIDS virus can change and thus affect its clinical course for the better or for the worse.

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32. Another method for evaluating the immune system is growing the lymphocytes (white blood cells) of a patient in a test tube with nonspecific stimulants that ordinarily cause the cells to proliferate. If these cells fail to proliferate properly when a radioactive tag is added, it is compatible with the findings caused by the presence of the AIDS virus.

33. Selwyn, *supra* note 15, at 67, 82.

34. See Lawrence, *The Immune System in AIDS*, SCI. AM., Dec. 1985, at 84, 93.