ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS)—A NEW EPIDEMIC: A REVIEW

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Abstract

Acquired Immunodeficiency Syndrome (AIDS) is a relatively new disease with a defect in cell-mediated immunity resulting in the victim becoming prey to cancers and infections. The retrovirus or human T-cell lymphoma virus, HTLV-III, is currently considered to be a likely etiologic agent. This disease, which most commonly affects homosexual men, intravenous drug users and Haitians carries a poor prognosis. An attempt is made in this paper to present a broad review of this entity. The epidemiology of the disease, etiology, signs and symptoms, laboratory investigations and the treatment of the disease are discussed.

With new cases being reported every day in different parts of the country, there is a mass hysteria about the Acquired Immunodeficiency Syndrome, AIDS. This relatively new medical malady, also called the "gay plague," has acquired the status of being the most virulent epidemic of the century. The most worrisome aspect of the disease is that after three years of intensive investigations, its precise cause remains a matter of speculation. It is very important for the public to have all known facts about this deadly disease, through physicians, so that there is rational thinking about it and cooperation in the areas of early detection or prevention of the disease. This review is based on the study of papers published in 1982-84.[1-16]

Key Words: AIDS, Acquired Immunodeficiency Syndrome.

What is AIDS and What Causes It?

A case of AIDS is defined by the Centers for Disease Control, CDC, as "a disease, at least moderately predictive of a defect in cell-mediated immunity, occuring in a person with no known cause for diminished resistance to that disease."

AIDS causes a nearly complete breakdown of a person's natural immune system. When the immune system breaks down, the victim becomes prey to cancers and infections that a normal, healthy individual would be able to fight off. Several opportunistic infections have been reported in patients with AIDS. Pneumonia, meningitis or encephalitis have been caused by aspergillosis, candidiasis, cryptococosis, cytomegalovirus (CMV), nocardiosis, pneumocytosis, strongyloidosis, toxoplasmosis, zygomycosis, atypical mycobacteriosis. Esophagitis has been caused by candidiasis, CMV and herpes simplex virus. The JC Virus, a new human papovavirus has caused progressive multifocal leukoencephalopathy, cryptosporidiosis has caused chronic enterocolitis and herpes simplex virus has also caused extensive mucocutaneous disease. Several recent papers have discussed in detail the role of these infecting agents. Perhaps the most important of all the infections is the Pneumocystis carinii pneumonia.

A rare type of malignancy often seen in the victims of AIDS is Kaposi's Sarcoma. Several reports have detailed current outbreaks of Kaposi's Sarcoma in cases of AIDS. Until recently this was a rare tumor. Severe immunologic deficiencies have been detected in cases of Kaposi's Sarcoma in homosexual men and Haitians. The immunologic parameters which have been studied include serum immunoglobulin levels, enumeration of B cell, T cells, T-cell subsets and quantitation of lymphocyte responsiveness to phytohemagglutinin (PHA) and pokeweed mitogen (PWM). Sites of disease include skin, lymph nodes, gastrointestinal tract, spleen and lung.

CMV antibodies have been found in 80 to 95 per cent of AIDS patients compared with 50 per cent in the general population. CMV has been cultured from

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the urine of homosexual men but not from the urine of heterosexual men. There is also evidence suggesting that CMV infections can be transmitted sexually. The Epstein-Barr Virus, EBV, has also been implicated. Antibodies for EBV have been found in very high concentrations in a group of AIDS patients.

The current concept of an etiologic agent is the retrovirus of human T-cell lymphoma virus, HTLV-III, which is an RNA virus with an inherent reverse transcriptase. HTLV-III has been isolated from 18 of 21 patients with lymphadenopathy syndrome and 26 of 72 adults and juveniles with AIDS. It has not been isolated from 115 healthy heterosexuals. Antibody to this virus has been isolated from serum samples of 88% of AIDS patients and 79% of patients with lymphadenopathy syndrome. Only 1 of 64 healthy patients had this antibody. The antibody appears to be directed against a viral envelope protein. French investigators isolated a virus in the same family of viruses which may be the identical organism and has been referred to as a lymphadenopathy virus (LAV). They have defined a code protein of this agent which can also be used for serologic evaluation. A third retrovirus isolate has been found in hemophiliacs, referred to as immunodeficiency associated virus (IDAV), it appears to be quite similar if not identical with the other two.

Transmission of AIDS

Transmission of the disease is probably through sexual contacts (anal, vaginal or oral), blood transfusions, use of contaminated needles (by drug users), intimate family contacts (skin infections), saliva, semen or urine, and possibly transmitted by the mother to the fetus in her womb. This pattern of transmission parallels that of hepatitis B virus infection.

Enormity of the Problem

The first reports on isolated cases of AIDS were published by the CDC in the summer of 1979. As of November 26, 1984 physicians and health departments in the United States had reported 6,993 patients meeting the surveillance definition for acquired immunodeficiency syndrome. More than 86% of the adult patients with AIDS and 82% of the pediatric patients have been reported since January 1983. Three thousand three hundred and forty-two (48%) of all reported patients are known to have died (48% of the adults and 69% of the children), including 73% of patients diagnosed before January 1983.

Epidemiologists predict that the chance of survival beyond 5 years will be less than 35 per cent. The gravity of these predictions is evident in the fact that before the days of vaccination even small pox killed only 25 per cent of the victims.

Incubation Period

The incubation period for AIDS is thought to be 6 to 8 months and possibly as long as 2 years. That means, a person who has recently been infected with a virus causing AIDS may not develop symptoms for many months and thus remain in the dark about the existence of this fatal disease for up to 2 years.

The Most Likely Victims

The analysis of cases in the United States allows identification of several groups that are at increased risk for developing AIDS. The high-risk groups are:

(a) Homosexual men—with multiple sexual partners
(b) Intravenous drug users
(c) Haitians
(d) Patients with hemophilia
(e) Female partners of drug users
(f) Women who are steady sexual partners of men with AIDS
(g) Women who are sexual partners of men in high risk groups
(h) Infants born to mothers from groups at high-risk for AIDS
(i) Recipients of blood donated inadvertently by victims of AIDS.

The homosexuals form by far, the largest group, accounting for 71 per cent of all of the 6,993 reported cases. The drug abusers rank second with 17 per cent of all cases of AIDS. It is a mystery as to why Haitians have emerged as a high-risk group. Five per cent of AIDS cases are Haitian men and women, especially those who came to the U.S. within the past few years. AIDS is the second leading cause of death in hemophiliacs, ranking second to uncontrollable bleeding. Eleven cases of unexplained infections and immune deficiency have been diagnosed in patients with hemophilia in recent months. Patients receiving blood or blood product transfusion have also been know to contract AIDS. There have been 13 such cases. Instances of AIDS in previously healthy women also have been recorded.

In addition to the patients in the high risk group, Chamberland et al reported 201 cases of the acquired immunodeficiency syndrome in persons who could not be classified into a group identified to be at increased risk for this syndrome. Thirty-five had received transfusion of single donor blood components in the 5 years preceding diagnosis of the syndrome and 30 were sexual partners of persons belonging to a high risk group. However, information was incomplete for most remaining patients, but because many of these patients are demographically similar to populations recognized to be at increased risk for the syndrome, previously identified risk factors may have been present but not reported for some of them. Additionally, a few persons who meet the

case definition for the syndrome probably had other reasons for the opportunistic disease and did not have the acquired immunodeficiency syndrome. The slow emergence of the acquired immunodeficiency syndrome in new populations is consistent with transmission mediated through sexual contact or parental exposure to blood.

Symptoms and signs of AIDS

The most common symptoms are fatigue (in 70 per cent), fever (in 40 per cent) and night sweats (in 44 per cent). These symptoms persist for weeks or months. Some patients (28 per cent) lose weight. Diarrhea is also a frequent complaint.

In cases of Pneumocystis Carinii pneumonia fever is usually associated with shortness of breath. If the victim has Kaposi's Sarcoma, he may have dark blue or purple-brown plaques or nodules in the skin. These are most commonly seen on lower extremities but may occur on any part of the body. Some patients experience headaches, loss of appetite and difficulty in swallowing and rarely they suffer from seizures and other neurological abnormalities.

A common feature of the disease is the enlargement of lymph glands in the neck or groins. In about 26 per cent of the patients, there is also enlargement of liver and the spleen. Fungal infections and thrush are sometimes seen.

In children with immune deficiency the clinical picture consists of anemia (hypochromic mycrocytic), infections, failure to thrive, hepatosplenomegaly, recurrent febrile episodes, thrush and eczema-like rash.

Prevention and Control of AIDS

Several organizations such as the National Gay Task Force, the National Hemophilia Foundation, the American Red Cross, the American Association of Blood Banks, and the American Association of Physicians for Human Rights have issued statements on prevention and control of AIDS. All organizations, physicians, public and the press should share responsibility in disseminating available information on AIDS. The following recommendations should be followed by persons or organizations concerned. These will greatly help in controlling and preventing AIDS:

1. A person experiencing symptoms of AIDS should seek medical advice as soon as possible so that the physician can take a full history, perform a complete examination, carry out laboratory tests, and render appropriate advice.
2. Individuals in high-risk groups should realize that multiple sexual partners tend to increase the probability of developing AIDS.
3. Sexual contacts with persons known or suspected to have AIDS should be avoided.
4. The high-risk persons should refrain from donating blood and/or plasma.
5. Physicians should adhere strictly to medical indications for transfusions.
6. Blood collection centers should adopt strict screening procedures to eliminate donors with a probability of transmitting AIDS.
7. Infants born to mothers from groups at high-risk for AIDS should be carefully screened by physicians.
8. Every proven or suspected case of AIDS should be reported to CDC.
9. Additional recommendations made by the CDC, The Public Health Service or the U.S. Department of Health and Human Services and the National Hemophilia Foundation should be sought and carefully implemented.
10. Male homosexuals involved in extensive sexual activity should use condoms during sexual activity.

Treatment

There is a natural concern in the minds of those who are afflicted and even the ones who are not as to the effectiveness of treatment. It must be stressed at the outset that the disease has been resistant to treatment and response has been poor to various aggressive medications.

Most treatments aim at reversing the abnormality of immune deficiency, fighting cancer or fighting the virus.

Dr. Allan L. Goldstein of the George Washington University School of Medicine has shown that thymosin, a group of hormones secreted by thymus gland activates the immune system. Therefore, it is possible that thymosin can be useful in the treatment of AIDS if it is caused by malfunction of the thymus gland.

Dr. Bihan Safai, at Sloan Kettering Cancer Center, has tried interferon with good results. He has treated Kaposi's Sarcoma with this drug. Of the 12 patients who have completed treatment, 3 have no evidence of cancer and their immune systems has improved. Some cases of Kaposi's Sarcoma have responded to treatment with an experimental drug (VP-16-213) developed to treat leukemia. Results of responses to Chemotherapy with single agents such as Vinblastine, Actinomycin D., Rozaxone, Bleomycin, Cytoxan, DTIC and combinations of agents Actinomycin D with Vincristine, Actinomycin D with Vincristine and DTIC, Vinblastine with Bleomycin, Methyl CCNU with Adriamycin have been recorded.

A drug called pentamidine, available through CDC, has been tried for Pneumocystis Carinii pneumonia with good results.

In general, the results of treatments are disappointing. There is no promise of cure on the horizon. The prospects are well summarized by Dr. Henry Masur of the National Institute of Health who has said,

"since patients with AIDS are susceptible to such a wide range of devastating infections and neoplasms (growths), real progress in this syndrome will probably be made by elucidating the mode of transmission of AIDS and the mechanisms of immunosuppression."

What Can a Physician Do For His Patient?

Every physician should familiarize himself with all aspects of AIDS. He should be able to render advice to the patient on symptoms of the disease, prevention of the syndrome and most importantly, conduct an examination to identify some of the signs such as enlarged glands, enlarged liver and spleen and skin changes. He should carry out investigations that may throw additional light on the possibility of the existence of this disease. For instance, he could order Anti-HBc test to detect possible AIDS infectivity in blood. This blood test is positive in 90 per cent of the victims of AIDS and in only 5 per cent of the general population. Other investigations may include chest x-ray, biopsy of skin lesions, virologic and fungal studies and immunologic tests. A summary of abnormal laboratory tests is presented in Table 1. The physician should refer the patient to an appropriate place for further investigations if his office is not equipped to carry out the investigations. A great deal of compassion will be needed in dealing with the patients of AIDS.

TABLE 1
ABNORMAL LABORATORY TESTS IN AIDS

LABORATORY TEST	RESULT
T Helper Cells (T4)	↓↓↓
T4/T8 Ratio	↓↓
Total Cells (T11)	↓
IgG	↑
CMV, E.B. and herpes antibody titer	↑
Hepatitis B core AB (anti-HBc)	+
Skin tests for PPD, histo, candida, dermotophytin, mumps	↓↓
Lymphoblastic transformation PHA, Con A and PWM	↓↓
Natural killer cell cytotoxicity	↓
Circulation immune complexes	Normal or ↑
Total hemolytic complement activity	↑

Social Impact of the Disease

The epidemic proportions of the disease, lack of knowledge of its cause, far from satisfactory treatments, poor prognosis and high fatality rates have created a disastrous impact on the society:

1. The *healthy* population is concerned about the spread of the disease.
2. The *contacts* of the high-risk population are anxious about their involvement.
3. The *high-risk groups* are developing a psychiatric syndrome of anxiety, depression, loss of self-respect and fear of contracting the disease.
4. Those who are known to suffer from the disease are fearful of death. They are carrying the social stigma of the disease. They are becoming "untouchables." They are raising cries of discrimination — social discrimination, job discrimination, medical discrimination. The fright is so overwhelming that the AIDS victims are shunned by their communities, their fellow workers, and sometimes by their friends and families. In New York, even funeral directors are wary of handling AIDS victims. The homosexual community and the Haitians are outraged at such reactions.

Conclusions

HTLV-III/LAV is currently the best viral candidate for the etiologic agent of AIDS, and proof of this causal role will probably come from either disease eradication by a vaccine or production of the disease by the agent in an animal model. Also we should soon be hearing about one or more sensitive and specific diagnostic tests for detecting the presence of the infection through the measurement of specific antibody to the virus and serum or the identification of a product associated with virus replication. Such a test will allow us to determine when the infection-as opposed to the disease occurs and in particular to prevent transmission by contaminated blood or blood products. Furthermore, specific public health and personal measures needed to diminish the spread of AIDS from direct human contact will become obvious with this information. Even those serious efforts to treat chronic viral infection are only just beginning, there are several obvious lessons we can learn from what has already been done. For example, the first need is for accurate data on natural history. If this virus is like most persistent viruses, there is a stage in the normal host that is associated with either minor or asymptomatic disease, and this probably constitutes the bulk of infections. It is even possible that an infection by other agents acts as a cofactor or that multiple human retroviral infections are required for the development of the severest form of the infection, full blown AIDS. For example, in recipients of organ allografts, in whom most of the same infectious and neoplastic complications occur, although less frequently, cytomegalovirus infections have a cofactor role with the clinically required immunosuppressant drugs in causing enhanced susceptibility. Of course, the ultimate test of our

understanding will be whether we can control this agent in human beings. Undoubtedly, the benefits will not come soon enough for all but an apparatus capable of attacking this problem rationally is currently in place. Furthermore, previous experience with persistent viral infections suggests that there is much work ahead. Experienced investigators know that the fact that vaccines can be produced does not mean that the whole problem can be dealt with quickly. Instead, we will most probably need a combination of effective diagnostic tools, vaccines, and antiviral or immunoenhancing therapy (or both) to provide disease control for all who are at risk.

REFERENCES

1. Drew WL, Mintz L, Miner RC, Sands M, and Ketterer B: Prevalence of Cytomegalovirus Infection in Homosexual Men. J. of Infectious Diseases 143: 2, 1981.
2. Follansbee SE, Busch DF, Wofsy CB, Coleman DL, Gullet J, Aurigemma GP, Ross T, Hadley KW, and Drew WL: An Outbreak of Pneumocystis carinii Pneumonia in Homosexual Men. Ann of Int Med 96: 1, 1982.
3. Friedman-Kien AE, Laubenstein LJ, Rubinstein P, Buimovici-Klein E, Marmor N, Stahl R, Spigland I, Kim KS, and Zolla-Pazner S: Disseminated Kaposi's Sarcoma in Homosexual Men. Ann of Int Med 96: 1, 1982.
4. CDC-Update: Acquired Immunodeficiency Syndrome. J.A.M.A. 252: 3355-3356, 1984.
5. Oleske JM, Minnefor AB: Acquired Immune Deficiency Syndrome in Children. Pediatric Infectious Disease 2:2, 1983.
6. Overby LR: AIDS: A New and Deadly Disease, Hepatitis Forum. Abbott Laboratories Diagnostics Division, March, 1983.
7. Physicians' Washington Report, Volume 6, No 12, June 1983.
8. Pitchenik AE, Fischl MA, Dickinson GM, Becker DM, Fournier AM, O'Connell MT, Colton RM, and Spine TJ: Opportunistic Infections and Kaposi's Sarcoma Among Haitians: Evidence of a New Acquired Immunodeficiency State. Ann of Int Med 98:3, 1983.
9. Poon MC, Landay A, Prasthofer EF, and Stagno S: Acquired Immunodeficiency Syndrome with Pneumocystis carinii Pneumonia and Mycobacterium avium-intracellulare Infection in a Previously Healthy Patient with Classic Hemophilia. Ann of Int Med 98:3, 1983.
10. Rubinstien A, Sicklick M, Gupta A, Bernstein L, Klein N, Rubinstein E, Spigland I, Fruchter L, Litman N, Lee H and Hollander M: Acquired Immunodeficiency Syndrome. J.A.M.A. 249:17, 1983.
11. Small CB, Klein RS, Friedland GH, Moll B, Emeson EE, and Sprigland I: Community-Acquired Opportunistic Infections and Defective Cellular Immunity in Heterosexual Drug Abusers and Homosexual Men. American J of Med 64: March 1983.
12. Sonnabend J, Witkin SS, and Purtilo DT: Acquired Immunodeficiency Syndrome, Opportunistic Immunodeficiency syndrome, Opportunistic Infections, and Malignancies in Male Homosexuals. J.A.M.A. 249: 17, 1984.
13. Stahl RE, Friedman-Kien A, Dubin R, Marmor M, and Zolla-Pazner S: Immunologic Abnormalities in Homosexual Men: Relationship to Kaposi's Sarcoma. American J of Med 73: Aug. 1982.
14. Viera J, Frank E, Spira TJ, and Landesman SH: Acquired Immune Deficiency in Haitians: Opportunistic Infections in Previously Healthy Haitian Immigrants. New Eng J Med 308:3, 1983.
15. Volberding P, Conant MA, Sitticker RB, Lewis BJ: Chemotherapy in Advanced Kaposi's Sarcoma: Implications for Current Cases in Homosexual Men. American J of Med 74: April 1983.
16. The Infection Reporter, Volume 1, No. 2, February, 1984.
17. Chamberland ME, Castro KG, Haverkos HW et al: Acquired Immunodeficiency Syndrome in the United States: An Analysis of Cases Outside High-Incidence Groups. Ann of Int Med 101: 617-623, 1984.
18. Broder S, Gallo RC: A Pathogenic Retrovirus (HTLV-III) Linked to AIDS. New Eng J Med 311:1292, 1984.
19. Merigan TC: What are we going to do about AIDS and HTLV-III/LAV infections? New Eng J Med 311:1311, 1984.