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Texas Preventable Disease NEWS

contents:

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AIDS UPDATE

As AIDS enters its fourth year as a major public health challenge, increased attention is being paid to four issues: 1) prevention, 2) long-term neurological complications (potentially as serious as the immune suppression), 3) difficulties in vaccine development (HTLV-III mutates rapidly), and 4) the development of an effective treatment.

Over 11,000 cases of AIDS have been reported to date in the United States. Half of those cases were reported between June 1981 and June 1984; the rest were reported during the last 12 months. Within the next two years, an additional 40,000 cases of AIDS are expected in the US. As of August 2, 1985, a total of 617 cases of AIDS had been reported in Texas.

An analysis by the Centers for Disease Control suggests the first 9,000 cases of AIDS cost an estimated $5.6 billion in direct medical costs and indirect costs such as lost earnings and productivity because of disability and premature death. In comparison, the direct and indirect costs of 910,000 cases of cancer diagnosed each year are estimated at $50 billion.

Serological surveys indicate the HTLV-III virus associated with AIDS is widespread in some populations.[1,2] CDC researchers report that gay men, intravenous drug users, Haitians living in the United States, and hemophiliacs have AIDS incidence rates between 18 and 3,000 times higher than the general population. The prevalence of antibody to HTLV-III among homosexual men seen at one San Francisco STD clinic rose from 25% in 1980 to 65% four years later. Even in cities where AIDS is reported less frequently, the virus has spread among high-risk groups. In Pittsburgh, for example, seropositive results of HTLV-III antibody testing increased to 28% last year from 10% in 1980. In Austin, studies have shown 16% of 176 gay men tested were seropositive for HTLV-III in 1982.

The cumulative mortality two years after the initial diagnosis of AIDS is approaching 80%. Since no successful therapies to restore immune function have been discovered as yet, public health officials in Texas and elsewhere emphasize prevention as a primary control measure. About 75% of all AIDS cases have developed in homosexual or bisexual men; in Texas, 90% of those reported have been homosexual or bisexual men. Thus, changing some sexual behaviors among gay men is a high priority. Given AIDS' two- to six-year incubation period, researchers conclude that the increasing incidence of HTLV-III and AIDS reflects transmission patterns that developed as long ago as the late 1970s.[3] Public health officials in major cities are hoping changes made now in sexual practices and drug habits will lessen the AIDS impact later. Preventive measures recommended by physicians and many gay organizations include greatly reducing the number of sexual partners and refraining from high-risk behaviors such as anal intercourse.

Reports from New York City, San Francisco, and Denver indicate that the incidence rate of anal gonorrhea is declining among homosexual men in those cities. The anal gonorrhea rates may be predictive of changes in gay sexual practices. However, because of the longer incubation period, a decline in AIDS cases will not be noted as quickly. Indeed, the prevalence of gay men with HTLV-III antibody increased steadily while anal gonorrhea rates declined.

Containment of AIDS by preventing large-scale spread of the virus to new population groups is also being urged. Heterosexual transmission of AIDS is common in Zaire, a central African country where HTLV-III first appeared a decade ago.[4] Prostitutes appear to be a major reservoir of the virus throughout central Africa. Cases of male-to-female and mother-to-infant transmission have occurred in the United States as well. Female sexual partners of IV drug abusers and of bisexual men in the United States have developed AIDS. These infected women have given birth to infants who become infected and later develop AIDS or a related collection of signs and symptoms (AIDS-Related Complex or ARC).

Exposure to HTLV-III does not always lead to the development of AIDS or even ARC. Five to 10% of those who have detectable antibodies to the virus will develop AIDS within five years of being infected.[5,6] A current CDC surveillance study of 361 health care workers exposed to the virus through sticks from hypodermic or surgical needles used on AIDS patients indicates that the virus has failed to produce antibody and, presumably, failed to infect all exposed persons. About 40% of these workers, (who do not fit into any known high-risk group) have been followed 12 months or longer, and none have developed AIDS. In Great Britain, a nurse developed antibody to HTLV-III ten weeks after a needle stick episode; she remains asymptomatic.

An asymptomatic person infected with HTLV-III may shed the virus via blood, semen, or other body fluid. Some people may be virus-positive and asymptomatic for up to six years, the longest period that such patients have been studied; there is concern that some persons may be long-term carriers.[7]

The long-term consequences of AIDS infection are poorly understood at this time. Neural deterioration, apparently caused when HTLV-III infects the central nervous system (CNS) or peripheral nerves, may be a consequence of AIDS as serious as the immune dysfunction. Neurosurgeons at the University of California-San Francisco have studied 370 AIDS patients seen there and found 178 to have significant neurological complications,[8,9] which were the initial complaints in 10% of the patients. The CNS-related diagnoses made so far in San Francisco include infections, tumors, and subacute encephalitis, a condition characterized at first by mild memory loss and inability to concentrate and progressing to severe cognitive impairment.

HTLV-III may produce both immune and neurological problems because T-lymphocytes and brain cells have common surface antigens. The San Francisco neurosurgeons have suggested that four of every ten AIDS patients may develop neurological complications. However, since reports of such complications are less than a year old, scientists have yet to develop a full clinical picture of this aspect of AIDS.

Controlling the spread of AIDS via immunization may be very difficult because the major exterior protein of HTLV-III, coded by the env gene, mutates rapidly. A research group at the National Institute of Cancer has found the gene sequence to have varied by at least 20% in HTLV-III and the AIDS-associated retrovirus (ARV) described by Jay Levy at the University of California at San Francisco.[10] To establish a beginning point for vaccine development, investigators are now attempting to determine whether any antigenic sequence of the envelope protein remains constant.

Of equal priority to vaccine development is the development of drugs that will lower the extremely high AIDS fatality rate. Efforts are being focused on six virostatic

drugs and three immune regulators.[11-15] Researchers are seeking a virostatic drug that will interrupt the HTLV-III infective cycle. HTLV-III is a retrovirus characterized by the enzyme "reverse transcriptase." Such RNA viruses are unique in nature because they use reverse transcriptase to form a negative DNA strand from RNA inside the infected T-helper cells. After a positive template of DNA is made from the negative strand, the two chains are incorporated into the host-cell DNA and replication begins. The new viral generation then spreads by budding from the infected T-helper cells.

Three of the six investigational drugs being tested against AIDS work as inhibitors of reverse transcriptase. Those drugs are suramin, used for 50 years to treat African trypanosomiasis; HPA23, being tested in France; and trisodium phosphonoformate, a non-competitive inhibitor of reverse transcriptase. Some investigators are especially interested in this last drug because it appears to have a major effect on visna virus, a retrovirus which causes CNS deterioration in sheep. Molecular geneticists and virologists who have sequenced HTLV-III say that it and visna virus have very similar nucleotide sequences. The three other investigational drugs include ribavirin, a guanosine analogue; anasamycin LM427, an inhibitor of DNA-dependant RNA polymerase that has been used against opportunistic organisms that infect after AIDS has developed; and α-interferon.

Other researchers are examining the molecular workings of the immune system to see why the T-helper cells become incapable of initiating and sustaining the body's immune response.[16] HTLV-III infection may produce a selective depletion of a specific subset of immune-system cells or cause dysfunction of those cells even when they are present in sufficient numbers. Bone marrow transplants and immune modulators, including interleukin-2 and other lymphokines, are being used experimentally in attempts to restore immune function by "reseeding" the immune system with new stem cells.

AIDS is a virulent disease with a case-fatality rate of at least 80% among those groups in which high incidence and prevalence rates have developed. Such groups, including homosexual men and intravenous drug abusers, must be aided by the development of therapy that can arrest or reverse the immune and neurological deterioration. However, because treatment efforts are in their infancy, every effort must be made to prevent further cases.

This report was prepared by Joann Schulte, Summer Intern, Texas Department of Health.

REFERENCES:

1. Hardy A, et al. The incidence rate of acquired immunodeficiency syndrome in selected populations. JAMA 1985;253:215-20.

2. Landesman S, et al. The AIDS epidemic. NEJM 1985;312:521-4.

3. Evatt B, et al. Coincidental appearance of LAV/HTLV-III antibodies in hemophiliacs and the onset of the AIDS epidemic. NEJM 1985;312:483-6.

4. Saxinger W, et al. Evidence for exposure to HTLV-III in Uganda before 1973. Science 1985;227:1036-8.

5. Lundberg G. The age of AIDS: a great time for defensive living. JAMA 1985;253:3440-1.

6. CDC. Provisional Public Health Service inter-agency recommendations for screening donated blood and plasma for antibody to the virus causing acquired immunodeficiency syndrome. MMWR 1985;34:1-5.

7. Salahuddin S, et al. HTLV-III in symptom-free seronegative persons. Lancet 1984;2:418-20.

8. Levy R, et al. Neurological manifestations of the acquired immunodeficiency syndrome (AIDS): experience at UCSF and review of the literature. Journal of Neurosurgery 1985;62:475-95.

9. Marwick C. Neurological complications appear often in AIDS. JAMA 1985;253: 3379-83.

10. Gonda M, et al. Sequence homology and morphologic similarity of HTLV-III and visna virus, a pathogenic lentivirus. Science 1985;227:173-7.

11. Rozenbaum W. A trial of antimoniotungstate (HPA23) in patients with AIDS or prolonged generalized lymphadenopathy. Presented at International Conference on Acquired Immunodeficiency, Atlanta, 1985, April 15.

12. Hirsch M. Prospects for therapy of AIDS virus infections. Presented at International Conference on Acquired Immunodeficiency Syndrome, Atlanta, 1985, April 16.

13. Getchell J. Ribavirin suppresses replication of lymphadenopathy-associated virus in cultures of human adult T-lymphocytes. Presented at International Conference on Acquired Immunodeficiency Syndrome, Atlanta, 1985, April 17.

14. Anand R. Ansamycin inhibits replication and infectivity of HTLV-III/LAV. Presented at International Conference on Acquired Immunodeficiency Syndrome, Atlanta, 1985, April 17.

15. Goldsmith M. "Not there yet, but 'on our way' in AIDS research", scientists say. JAMA 1985;253:3369-71, 3383-4.

16. Fauci A. Immunopathogenesis of AIDS. Presented at International Conference on Acquired Immunodeficiency Syndrome, Atlanta, 1985, April 16.

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