Key Epidemiologic Questions About AIDS and Infection with HTLV-III/LAV

Foreword

The Epidemiology and Prevention Workgroup of the PHS Executive Task Force on AIDS developed the following list of key epidemiologic questions about AIDS and HTLV-III/LAV infection as part of the followup to the "Public Health Service Plan for the Prevention and Control of Acquired Immune Deficiency Syndrome" (1). The workgroup's purpose in developing this list was to provide a framework to help ensure that studies designed to answer the most important such questions were completed, under way, or initiated as soon as possible. The list is published in Public Health Reports *to encourage consideration of these questions by laboratory and clinical workers and by applied epidemiologists who plan investigations of AIDS or HTLV-III/LAV infection.*

Donald R. Hopkins, MD, MPH
Chairperson, Epidemiology and Prevention Workgroup,
PHS Executive Task Force on AIDS

A. SURVEILLANCE AND PREVALENCE

1. What are the prevalences and trends of HTLV-III/LAV infection in various American cities among:
   a. Intravenous (IV) drug abusers?
   b. Gay men?
   c. Hemophiliacs?
   d. Heterosexuals with multiple sexual contacts (males and females)?
   e. Blood donors, sperm donors, organ or tissue donors?
   f. Military recruits?
   g. Random population?
2. What are the prevalences and trends of HTLV-III/LAV infection in prostitutes in various American cities and what is their role in transmission?
3. What are the risks to:
   a. Health care professionals who have needlestick injuries or mucous membrane exposures to patients infected by HTLV-III/LAV, including patients who do not meet the AIDS surveillance definition?
   b. Other persons caring for HTLV-III/LAV seropositive patients; for example, developmentally disabled individuals, young children, and others?
   c. Members of the households of individuals infected with HTLV-III/LAV—does the risk vary by the clinical status of the index person?
   d. School children, staff members, or children attending day care centers with classmates who are seropositive or culture positive for HTLV-III/LAV?

B. NATURAL HISTORY OF INFECTION

1. What proportion of seropositive persons will develop AIDS, AIDS-related complex (ARC), or other outcomes, or remain asymptomatic?
2. What is the long-term prognosis for someone:
   a. With HTLV-III/LAV antibody?
   b. With viral infection with or without lymphadenopathy or constitutional symptoms?
   c. With viral and immunological abnormality?
3. Can the clinical, pathological, and laboratory aspects of infection with HTLV-III/LAV virus, including the factors which determine clinical outcome, be delineated, characterized, and described?
4. Are cofactors, including age, sex, ethnicity, demographic status, chemical or drug exposures (including nitrites), other infections (for example, hepatitis B, cytomegalovirus), and HLA type important in:
   a. Infection with HTLV-III/LAV?
   b. Determination of the infection's outcome?
   c. Occurrence of Kaposi's sarcoma?
   d. Occurrence of opportunistic infections?
   e. Establishing or eliminating the carrier state?
5. What are the consequences of repeated exposures to or infections with HTLV-III/LAV? Do different strains of HTLV-III/LAV play a role in pathogenesis of the infection?
6. What is the role of infection with HTLV-I in drug-abusing populations and others (interaction of retroviruses)?
7. How and for how long does infection persist in different patients? How long does it persist

("incubate") before physiological and biochemical changes are detectable?

8. What is the clinical and epidemiologic significance of the virus-positive, antibody-negative state?
9. What are the clinical manifestations at various stages of infection with HTLV-III/LAV?
   a. Which of the earliest symptoms are predictive for AIDS?
   b. What is the course and prognosis of the lymphadenopathy syndrome?
   c. What is the time range before clinical illness appears, and what determines variations in the incubation period?
   d. Are there other effects of HTLV-III/LAV? What and when?
10. Do immunological manifestations vary in different persons?
   a. Cellular—
      (1) In which cells and for how long is virus expressed?
      (2) What cells are damaged and how quickly?
   b. Humoral—in which body fluids does viral antigen circulate?
   c. What types and amounts of antibody develop? How and for how long are they detectable? In which fluids and secretions?
   d. Are any immunological resources protective?
11. How is Kaposi's sarcoma related to HTLV-III/LAV infection?
12. Other neoplasms—which lymphoreticular and other neoplasms are related to AIDS, to HTLV-III/LAV infection? How are they related?
13. Does the natural history of HTLV-III/LAV infection vary in different populations, for example:
   a. Hemophiliacs?
   b. Gay men?
   c. Transfusion recipients?
   d. IV drug abusers?
   e. Persons in central Africa?
14. Do variations in *in vivo* virus titer and antibody levels vary over time in an infected individual, and are these variations predictive of clinical outcome or infectiousness or both? Do outcomes vary with inoculum size?
15. Do variations in factors such as nutritional status of the mother affect the incidence or natural history of HTLV-III/LAV infection in infants and young children?
16. Is HTLV-III/LAV in the drug-using community related to patterns of intravenous and nonintravenous drug abuse, including the use of beverage alcohol?
17. What, if any, are the immunosuppressive effects of beverage alcohol, heroin, marijuana, and nitrites on individuals who have been infected with HTLV-III/LAV and on those who have not?
18. What is the effect of HTLV-III/LAV infection on safety and efficacy of live, killed, or attenuated vaccines, and on the outcomes of exposure to infectious agents such as *Mycobacterium tuberculosis* and varicella?
19. Does HTLV-III/LAV infection have an effect on susceptibility to or on the natural history of other infections such as tuberculosis, malaria, measles, and so forth? Does prior history of these or other illnesses predispose one to HTLV-III/LAV infection?
20. What is the significance of low-titer HTLV-III/LAV antibody in children with Burkitt's lymphoma in Uganda?

C. MODES OF TRANSMISSION

1. Can HTLV-III/LAV transmission occur through routes other than sexual contact, needle-sharing, perinatal transmission from mother to child, or receipt of blood, its components, or clotting factor concentrate? If so, how?
2. What is the quantitative risk of transmission from an infected individual to another person through:
   a. Insertive or receptive penile-rectal intercourse?
   b. Insertive or receptive penile-vaginal intercourse?
   c. Insertive or receptive penile-oral intercourse?
   d. Which specific sexual practices are associated with transmission of or protection from HTLV-III/LAV infection?
   e. Does likelihood of sexual transmission, and likelihood of acquisition, vary with the presence of clinical conditions associated with lymphocytic exudate such as chronic cervicitis, or chronic diarrhea (for example, does chronic diarrhea in an infected partner increase chances of spread through anal intercourse? Does chronic diarrhea in an uninfected person increase chances of acquiring infection through anal intercourse with an infected person)?
3. What is the biological, clinical, and public health significance of HTLV-III/LAV presence (if any) in:
   a. Saliva?
   b. Semen?

c. Cervical secretions, vaginal specimens, and menstrual blood?
d. Feces?
e. Sweat?
f. Respiratory secretions, sneeze droplets?
g. Other (tears, urine, breast milk, fomites)?

4. How does the presence of antibody to HTLV-III/LAV or isolatable virus in blood correlate with infectivity by various routes of transmission?
5. What are the risk factors for HTLV-III/LAV infection among Haitians, residents of central Africa, and other populations, and what proportions of infection in infants, children, and adults can be attributed to these risk factors?
6. What is the quantitative risk of HTLV-III/LAV from infected mother to newborn according to:
   a. Trimester of pregnancy?
   b. Clinical, immunological, and virologic status of mother?
   c. Risk factors?
7. What is the quantitative risk to recipients of infected blood products in relation to:
   a. Type of product?
   b. Inoculum size?
   c. Cofactors?
8. What is the significance of persons who are known to have been exposed to HTLV-III/LAV repeatedly and yet remain seronegative?
9. Are arthropods (or other insects) potential vectors for HTLV-III/LAV transmission?
10. What are the relative risks of IV drug abuse and sexual contact for acquisition and dissemination of HTLV-III/LAV infection by addicted female prostitutes?
11. What, if any, is the risk for infection through casual contact?

D. EFFECTIVENESS OF CONTROL AND PREVENTION MEASURES

1. How effective are prevention efforts?
   a. In increasing understanding of the modes of transmission and safer sex practices among target groups?
   b. In sexual behavior change among gay men and heterosexual men and women?
   c. In reducing IV drug abuse and needle-sharing?
   d. In deferral of pregnancy in women known to be HTLV-III/LAV positive?
   e. In encouraging voluntary testing?
   f. In blood and plasma donor deferral?
   g. In increasing use of condoms in target groups?
2. What is the evidence of effectiveness of heat treatment in the prevention of HTLV-III/LAV transmission through clotting factor concentrates?
3. Do condoms, diaphragms, spermicides, IUDs, douches, or birth control pills diminish person-to-person spread of HTLV-III/LAV? Is there a significant difference in the protective effect of condoms made of different materials? In their use in vaginal insertive versus oral or rectal insertive sex?
4. What means are effective in preventing HTLV-III/LAV transmission in prisons and other custodial institutions?
5. How efficacious is providing HTLV-III/LAV antibody test results (negative and positive) as part of a counseling program to prevent HTLV-III/LAV transmission and acquisition among gay men? High-risk heterosexual men and women? How effective are providing test results and counseling in preventing infection among pregnant women and newborns?
6. What is the efficacy of providing IV drug abusers with sterile needles and syringes as part of a program to reduce the risk of HTLV-III/LAV transmission and acquisition? Of methadone substitution?
7. What is the efficacy of contact tracing in preventing transmission?
8. What is the effectiveness of educational programs aimed at sexually active populations?
   a. High school?
   b. College?
   c. Young adult (including military)?
   d. Developing countries?
9. What determinants (levels of knowledge, attitudes, values, beliefs, perceptions, skills, resources-services, and supports) are associated with behavior identified as increasing or decreasing the risk of HTLV-III/LAV infection?
10. What is the quantitative effect of screening blood donors for HTLV-III/LAV infection on the safety of blood supply?
11. Can the effect on transmission of HTLV-III/LAV that is presumed to follow from closing or regulating commercial or public sites catering to high-risk behaviors be demonstrated? If so, what is the evidence?

E. DIRECTLY RELATED LABORATORY PROJECTS

1. Which test or combination of tests for antibody to HTLV-III/LAV are the most sensitive and specific, as judged by the best available

epidemiologic, clinical, and other laboratory data?

2. What is the reproducibility and predictive value of these tests in screening settings, diagnostic settings?
3. Can rapid diagnostic tests for the presence of HTLV-III/LAV or viral antigens be developed?
4. Can viral subtyping systems be developed?
5. What is the qualitative (and quantitative) ability, compared to blood, to recover HTLV-III/LAV from:
   a. Cervical secretions, menstrual blood, and vaginal specimens?
   b. Urine?
   c. Feces?
   d. Sweat?
   e. Saliva?
   f. Semen?
   g. Respiratory secretions?
   h. Fomites?
   i. The environment?
   j. Animals and insects?
6. What is the relationship between simian T-lymphotropic virus, type III, and similar viruses in primates and HTLV-III/LAV in humans?
7. Under what conditions may HTLV-III/LAV be inactivated by drying, heating, ultraviolet light, commonly used chemical germicides (including those not yet tested as well as those that have been tested under uncontrolled conditions), and in-use disinfection and decontamination procedures, including use of appropriate medical devices?
8. Can results of studies of the natural history of nonhuman primate viruses be applied to understanding manifestations of HTLV-III/LAV infections?

Reference

1. Public Health Service plan for the prevention and control of acquired immune deficiency syndrome (AIDS). Public Health Rep 100: 453–455, September-October 1985.

LETTER TO THE EDITOR

Gynecomastia Among Ethiopian Jews

We have read with interest the article by Sattin and coworkers in *Public Health Reports* (99: 504–510, September-October 1984), "Epidemic of Gynecomastia Among Illegal Haitian Entrants."

Their article prompted us to investigate another immigrant population, one that had experienced severe starvation in Ethiopia before being brought to Israel in the "Moses Operation" early in 1985. Once in Israel, these Ethiopian Jews received markedly improved nutrition and medical care.

In a pilot study at the Romema Health Center in Haifa, 16 male refugees, aged 10–60, were examined. Eight had bilateral gynecomastia of grade 1 to grade 3 according to the classification of Nydick and coworkers (*1*); one had unilateral gynecomastia; none had breast sensitivity or secretion. The examinations were carried out about 4 months after their arrival. Among an age-matched comparison group of Romema residents, there was no bilateral gynecomastia and only one case of unilateral gynecomastia in a 14-year old boy.

This statistically significant increased prevalence of gynecomastia among refed Ethiopians is not explained either by a response to INH therapy for tuberculosis or by age effects such as delayed adolescence. We suggest that this may be another example of refeeding gynecomastia in another refugee population. We shall submit the data from this study for publication and plan to extend this study to a larger population of immigrant Ethiopian Jews in the light of these findings.

S. Linn, MD, DrPH
Director, Epidemiology Unit
Rambam Medical Center
Haifa, Israel
G. Almagor, MD, DPH
Head, Department of Family Medicine
Kupat Holim
Haifa, Israel
S. Lamm, MD, DTPH
President, Consultants in Epidemiology and Occupational Health, Inc.
Washington, DC

Reference

1. Nydick, M., Bustos, J., Dale, J. H., and Rawson, R. W.: Gynecomastia in adolescent boys. JAMA 178: 449–454, Nov. 4, 1961.