ISSN 0125-7447

รายงานการเฝ้าระวังโรคประจำสัปดาห์

WEEKLY EPIDEMIOLOGICAL SURVEILLANCE REPORT

VOLUME 16 NUMER 16

APRIL 26, 1985

บทความ

AIDS Information for Health Professionals

Clinicians Guide to Evaluation of HTLV-III Antibody Positive Individuals

The Virus that Causes AIDS

The etiologic agent of the acquired immunodeficiency syndrome (AIDS) is human T-cell lymphotropic virus type III (HTLV-III), also known as LAV and ARV. This distinctive class of RNA virus shares some features with retroviruses previously linked to various disorders in animals, including leukemias, neurologic diseases, and immunodeficiency disorders and to a human virus, HTLV-I, linked to an unusual form of human leukemia. HTLV-III has a cytotoxic effect on T-lymphocytes of the helper type. The diverse infections and tumors which are the ultimate cause of death for AIDS patients result from the fact that the virus renders the immune system incompetent.

Clinical Significance of HTLV-III Seropositivity

Over 90% of patients with full-blown AIDS are positive for HTLV-III antibodies in the screening test, and with the application of additional research techniques close to 100% of such individuals are virus-positive. Among seropositive persons, the risk for developing frank AIDS may vary depending upon risk group and possibly other factors such as additional environmental exposures and genetic background. Preliminary estimates in cohorts of homosexual men followed prospectively for two to five years indicate that between 5% and 20% of persons with detectable HTLV-III antibodies may go on to develop AIDS. However, information that pertains to one risk group may not directly translate to other risk groups. The lack of precise data

on the clinical significance of HTLV-III antibody positivity for an individual patient coupled with the fact that many persons in high-risk groups have detectable HTLV-III antibodies, creates a dilemma for the physician confronted with evaluating and counseling such antibody-positive patients. If this virus follows patterns seen in other viruses, the majority of exposed individuals will remain clinically healthy. However, this is a new class of human virus and the long-term implications of exposure to the health of an individual are unknown. Furthermore, the implications of seropositivity in the individual to the potential for transmitting the virus to others are unknown. Epidemiologic data do document that homosexual and probably heterosexual sexual relations, needle sharing, blood transfusion and transplacental and/or perinatal exposure are modes of transmission. Finally, it should be emphasized that the current antibody test is licensed as a blood bank screening and not a diagnostic tool. In this regard, the absence of antibody in a high-risk person does not necessarily mean that the patient is virus negative, since the virus has been isolated from a few at-risk individuals who were antibody negative. Conversely, as with all antibody tests of this type, a few biologic false positives will be detected due to antibodies to non-HTLV-III cross-reactive antigens.

Dynamics of HTLV-III Infection

Seroconversion generally antedates the development of clinical or subclinical laboratory signs of viral infection by several years, necessitating extended follow-up. The first sign of subclinical infection may be a laboratory perturbation associated with HTLV-III seropositivity.

The laboratory parameter most frequently linked to HTLV-III infection is a depressed number of peripheral blood lymphocytes bearing the helper T-cell phenotype. Other laboratory parameters which have been associated with this process include elevated immunoglobulin levels; high titers to a variety of viral agents (particularly Epstein Barr virus and cytomegalovirus); and elevated beta-2 microglobulin, thymosin, and acid-labile alpha interferon. Although these various observations are of some research interest and reflect the variety of laboratory perturbations which result from fundamental virus-associated immunodeficiency, their relevance in the clinical setting is not sufficiently well-defined to be of practical diagnostic benefit. These are currently a focus of ongoing research studies.

Range of Clinical Manifestations

Another condition recognized as being associated with HTLV-III infection is the lymphadenopathy syndrome, a medical complex characterized by the occurrence of persistent, unexplained lymph node enlargement in several extra-inguinal lymph node groups. The relationship of the lymphadenopathy syndrome to progression to overt clinical AIDS is uncertain but probably is as high as 10%.

Another lesser manifestation is the AIDS related complex (ARC), a clinical and laboratory syndrome characterized by minor conditions clinically associated with immunosuppression

(e.g., oral thrush) and laboratory evidence of immunosuppression. In addition, unexplained idiopathic thrombocytopenia is probably associated with HTLV-III infection, as are a variety of non-life-threatening fungal, viral, and bacterial infectious processes which probably represent manifestations of virus-induced immunologic perturbation. These manifestations are sometimes termed lesser AIDS.

The clinical presentation of clinical AIDS, as originally defined, follows four major patterns:

1) A febrile prodrome of weeks to months followed by opportunistic infection.
2) Abrupt onset of opportunistic infection.
3) Presentation with Kaposi's sarcoma.
4) Progression from the AIDS-related complex.

Approach to Clinical Evaluation

AIDS and its diverse related clinical disorders challenge the diagnostic acumen of physicians in all branches of medicine. The prospective clinical evaluation of HTLV-III seropositive individuals who may be at risk for AIDS requires a careful multisystem approach to evaluate signs and symptoms. Clearly, it is important to take a careful medical and social history and perform thorough physical examinations on these individuals. Listed below is a broad overview of recognized clinical signs and symptoms. A more thorough review of the published literature is strongly recommended (see Background Reading).

Medical History: Possible source of exposure, identification of risk group exposure, blood transfusion, acupuncture, tattoos, needle stick exposure, foreign travel, and sexual history.

Dermatologic: Kaposi's sarcoma (purple or reddish nodules), which may appear anywhere in the skin and on mucocutaneous surfaces (e.g., mouth and rectum), infectious processes (e.g., Herpes simplex or zoster), seborrheic dermatitis, unexplained diffuse hyperpigmentation, alopecia.

Ophthalmologic: Ocular lesions (retinitis due to cytomegalovirus or toxoplasmosis), cottonwool spots, retinal hemorrhages.

Hematopoietic: Fluctuating adenopathy associated with aching discomfort. Variable lymph node size and consistency. Soft, moderately enlarged spleen. Large, firm spleen and/or very large lymph nodes are suggestive of intracellular infections (e.g., mycobacterium avium), lymphoma or Kaposi's sarcoma.

Gastrointestinal: Oral thrush, candida esophagitis associated with xerostomia and pharyngitis or odynophagia. Watery diarrhea due to various protozoan infestations and lower GI pain due to herpes proctitis.

Pulmonary: Non-productive cough and dyspnea (associated with *Pneumocystis carinii* or viral pneumonitis), productive cough linked to bacterial or other etiology.

Musculoskeletal: Diffuse arthralgias and myalgias associated with febrile prodrome suggestive of vasculitis, autoimmune and rheumatologic diseases.

(ต่อหน้า 197)

AIDS Information for Health Professionals (ต่อจากหน้า 191)

Neurologic: Persistent headache, memory loss, ataxia, confusion, irrational behavior, personality change, focal neurologic signs, and seizure.

General: Fatigue, asthenia, night sweats or sweating, decreased libido, withdrawal and other signs of depression, fever including Pel-Ebstein fever pattern.

Laboratory tests that could be helpful in evaluating antibody positives include a complete blood count, differential and platelet count, VDRL, tests of hepatitis B infection, and baseline routine chemistries, including gamma globulin levels. Additional, specific tests should be directed by the clinical findings.

Therapeutic Intervention

Therapeutic interventions that are specific for the virus or for the immunodeficiency do not yet exist, although there is considerable research being done attempting to develop such modalities. However, rapid diagnostic evaluation and intervention with appropriate antimicrobials in specifically documented illnesses may be lifesaving. Some clinicians have advocated use of prophylactic therapy to prevent common protozoan and fungal diseases (i.e., trimethoprim-sulfamethoxazole and ketoconazole), but there is also a substantial amount of drug-related dermatologic and hematologic toxicity for some of these agents and implementation of such therapy without consulting a specialist would not be recommended.

What to Tell the Seropositive Patient

From a clinical perspective, counseling a seropositive, clinically healthy individual presents a challenge since the risk of clinical disease is not well characterized. The possibility that the test reactivity represents a biologic false positive should be discussed particularly in the patients without definable risk exposure. It is inevitable that substantial psychological stress will derive from the knowledge of antibody positivity, and judicious reassurance is supported by the current data which suggests that the vast majority of antibody positives are clinically well. However, given the fact that clinical problems may take some years to become manifest clinically, *long-term follow-up with careful assessment of symptomatology* as described above are in order. HTLV-III has also been linked to hematologic and neurologic disorders, a focus of active investigation. With this in mind, clinical symptoms in antibody-positive persons should be pursued vigorously to assure optimal care. The risk for an antibody-positive individual being infectious for another person is not quantified. As summarized above, certain factors (e.g., sexual contact, needle sharing, pregnancy) are linked to virus transmission and may serve as the basis for tailoring recom-

mendations to the antibody positive individual to decrease the likelihood of transmission of the virus.

Summary

The practicing physician encountering an HTLV-III antibody-positive person must deal with incomplete knowledge about the natural history of the disease. Preventive measures and practical advice to the individual are summarized in attached documents. Clinical long-term follow-up of antibody-positive persons should be a commitment for physicians confronted with such patients. Careful monitoring of the fast-moving medical literature concerning this condition is important to provide optimal care. Where feasible, consideration of referral to a center organized to follow such patients may be appropriate.

Background Reading

AIDS, Devita, V.T., Jr., Hellman, Rosenberg, A. (Eds.), Lippincott, Philadelphia, 1985.

AIDS. A Basic Guide for Clinicians, Ebbesen, P., Biggar, R.J., Melbye, M. (Eds.), Munksgaard/Saunders, Philadelphia, 1984.

Advances in Host Defense Mechanisms: Acquired Immunodeficiency Syndrome (AIDS), Gallin, J.I., Fauci, A.S., Raven Press, New York, 1985.

Reprinted from AIDS Information for Health Professionals, Food and Drug Administration, U.S. Public Health Service.