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# NEWS

Ron J. Anderson, M.D. Robert Bernstein, M.D., F.A.C.P.  
Chairman Commissioner  
Texas Board of Health

### contents:

Diagnosis and Management of Mycobacterial Infection and Disease in Persons with Human T-Lymphotropic Virus Type III/Lymphadenopathy-Associated Virus Infection  
1986 Edition of Pediatric Red Book

Bureau of Epidemiology, 1100 West 49th Street, Austin, Texas 78756-3180 (512-458-7207)

## DIAGNOSIS AND MANAGEMENT OF MYCOBACTERIAL INFECTION AND DISEASE IN PERSONS WITH HUMAN T-LYMPHOTROPIC VIRUS TYPE III/LYMPHADENOPATHY-ASSOCIATED VIRUS INFECTION\*

In 1985, the number of new tuberculosis cases reported to CDC was essentially the same as that reported in 1984. In contrast, the average annual decline in morbidity during the past 32 years has been 5%. The failure of tuberculosis morbidity to decline as expected in 1985 is probably related to the occurrence of tuberculosis among persons with acquired immunodeficiency syndrome (AIDS) or human T-lymphotropic virus type III/lymphadenopathy-associated virus (HTLV-III/LAV)\*\* infection. Several reports have indicated that mycobacterial disease is common among AIDS patients and among persons at risk for AIDS. The most common mycobacterial species isolated from patients with diagnosed AIDS is *Mycobacterium avium* complex (MAC), although in some groups in which tuberculous infection is highly prevalent, disease caused by *M. tuberculosis* is more common. Even among groups in which MAC is the most common mycobacterial pathogen, *M. tuberculosis* accounts for a substantial proportion of the mycobacterial isolates. The association between mycobacterial disease and AIDS raises several important clinical and public health issues that are addressed below.

### DIAGNOSIS OF TUBERCULOSIS IN PATIENTS LIKELY TO HAVE HTLV-III/LAV INFECTION

Clinicians should consider the diagnosis of tuberculosis in patients with, or at risk of, HTLV-III/LAV infection, even if the clinical presentation is unusual. Available data indicate that extrapulmonary forms of tuberculosis, particularly lymphatic and disseminated (miliary), are seen much more frequently among patients with HTLV-III/LAV infection than among those without such infection. Pulmonary tuberculosis in patients with HTLV-III/LAV infection cannot readily be distinguished from other pulmonary infections, such as *Pneumocystis carinii* pneumonia, on the basis of clinical and radiographic findings. Patients with tuberculosis may have infiltrates in any lung zone, often associated with mediastinal and/or hilar lymphadenopathy. Cavitation is uncommon. Appropriate specimens to establish a culture-confirmed diagnosis of tuberculosis include respiratory secretions, urine, blood, lymph node, bone marrow, liver, or other tissue or body fluid that is indicated clinically. All tissue specimens should be stained for acid-fast bacilli and cultured for mycobacteria. In the presence of undiagnosed pulmonary infiltrates, bronchoscopy with lavage and transbronchial biopsy (if not contraindicated) may be needed to obtain material for both culture and histologic examination. A tuberculin skin test should be administered, but the absence of a reaction does not rule out the diagnosis of tuberculosis because immunosuppression associated with HTLV-III/LAV infection may cause false-negative results.

### TREATMENT OF MYCOBACTERIAL DISEASE IN A PATIENT WITH HTLV-III/LAV INFECTION

Chemotherapy should be started whenever acid-fast bacilli are found in a specimen from a patient with HTLV-III/LAV infection and clinical evidence of mycobacterial disease. Because it

\* Reprinted from: CDC, MMWR 1986;35:448-52.

\*\* The Human Retrovirus Subcommittee of the International Committee on the Taxonomy of Viruses has proposed the name human immunodeficiency virus (HIV) for this virus. (Science 1986;232:697).



87-126 NOV 24 1986

is difficult to distinguish tuberculosis from MAC disease by any criterion other than culture, and because of the individual and public health implications of tuberculosis, it is important to treat patients with a regimen effective against tuberculosis. With some exceptions, patients with tuberculosis and HTLV-III/LAV infection respond relatively well to standard antituberculosis drugs; however, their treatment should include at least three drugs initially, and treatment may need to be longer than the standard duration of 9 months. The recommended regimen is isoniazid (INH), 10-15 mg/kg/day, up to 300 mg/day; rifampin (RIF), 10-15 mg/kg/day, up to 600 mg/day; and either ethambutol (EMB), 25 mg/kg/day, or pyrazinamide (PZA), 20-30 mg/kg/day. The last two drugs are usually given only during the first 2 months of therapy. The addition of a fourth drug may be indicated in certain situations, such as central nervous system or disseminated disease or when INH resistance is suspected. An initial drug-susceptibility test should always be performed, and the treatment regimen revised if resistance is found to any of the drugs being used. The appropriate duration of treatment for patients with tuberculosis and HTLV-III/LAV infection is unknown; however, it is recommended that treatment continue for a minimum of 9 months and for at least 6 months after documented culture conversion. If INH or RIF is not included in the treatment regimen, therapy should continue for a minimum of 18 months and for at least 12 months following culture conversion. After therapy is completed, patients should be followed closely, and mycobacteriologic examinations should be repeated if clinically indicated.

Some clinicians would take a different approach to treatment than that outlined above, to cover the possibility of MAC disease. Although the clinical significance and optimal therapy of MAC disease in these patients is not well defined, and there are no definitive data on the efficacy of treatment, one regimen commonly used to treat MAC disease substitutes rifabutin (ansamycin LM 427) for rifampin, combined with INH, EMB, and clofazimine. Rifabutin and clofazimine are experimental drugs available to qualified investigators only under investigational new drug protocols. Rifabutin is distributed by the CDC Drug Service (telephone: [404] 329-3670), and clofazimine, by Ciba-Geigy (telephone: [201] 277-5787). If *M. tuberculosis* is isolated from a patient receiving this four-drug regimen, treatment should be switched to one of the three-drug regimens outlined above (INH, RIF, and EMB or PZA). If MAC is isolated from a patient who has been started on a three-drug regimen, the clinician may continue the three-drug regimen or switch to the four-drug regimen of INH, EMB, rifabutin, and clofazimine.

Although experience is very limited, patients with disease due to *M. kansasii* should respond to INH, RIF, and EMB. Some clinicians advocate the addition of streptomycin (SM), 1 gram twice weekly, for the first 3 months. Therapy should continue for a minimum of 15 months following culture conversion.

Monitoring for toxicity of antimycobacterial drugs may be difficult for patients who may be receiving a variety of other drugs and may have other concomitant conditions. Because hepatic and hematologic abnormalities may be caused by the mycobacterial disease, AIDS, or other drugs and conditions, the presence of such abnormalities is not an absolute contraindication to the use of the treatment regimens outlined above.

## INFECTION CONTROL

Recommendations for preventing transmission of HTLV-III/LAV infection to health-care workers have been published.<sup>1</sup> In addition, infection-control procedures applied to patients with HTLV-III/LAV infection who have undiagnosed pulmonary disease should always take the possibility of tuberculosis into account. This is especially true when diagnostic procedures, such as sputum induction or bronchoscopy, are being performed. Previously published guidelines for preventing tuberculosis transmission in hospitals should be followed.<sup>2</sup>

## CONTACT INVESTIGATION FOR TUBERCULOSIS

Patients with pulmonary tuberculosis and HTLV-III/LAV infection should be considered potentially infectious for tuberculosis, and standard procedures for tuberculosis contact



investigation should be followed. Specific data on the infectiousness of tuberculosis in patients with HTLV-III/LAV infection are not yet available.

#### EXAMINING HTLV-III/LAV-INFECTED PERSONS FOR TUBERCULOSIS AND TUBERCULOUS INFECTION

Individuals who are known to be HTLV-III/LAV seropositive should be given a Mantoux skin test with 5 tuberculin units of purified protein derivative as part of their clinical evaluation. Although some false-negative skin test results may be encountered in this setting as a result of immunosuppression induced by HTLV-III/LAV infection, significant reactions are still meaningful. If the skin test reaction is significant, a chest radiograph should be obtained, and if abnormalities are detected, additional diagnostic procedures for tuberculosis should be undertaken. Patients with clinical AIDS or other Class IV HTLV-III/LAV infections should receive both a tuberculin skin test and a chest radiograph because of the higher probability of false-negative tuberculin reactions in immunosuppressed patients.

#### EXAMINING PATIENTS WITH CLINICALLY ACTIVE TUBERCULOSIS OR LATENT TUBERCULOUS INFECTION FOR HTLV-III/LAV INFECTION

As part of the evaluation of patients with tuberculosis and tuberculous infection, risk factors for HTLV-III/LAV should be identified. Voluntary testing of all persons with these risk factors is recommended. In addition, testing for HTLV-III/LAV antibody should be considered for patients of all ages who have severe or unusual manifestations of tuberculosis. The presence of HTLV-III/LAV infection has implications regarding treatment (see above), alerts the physician to the possibility of other opportunistic infections, and allows for counselling about transmission of HTLV-III/LAV infection. Testing for HTLV-III/LAV antibody is especially important for persons over age 35 with *asymptomatic* tuberculous infection, because INH would not usually be indicated for persons in this age group unless they are also HTLV-III/LAV seropositive.

#### PREVENTIVE THERAPY

HTLV-III/LAV seropositivity in a person of any age with a significant tuberculin reaction is an indication for INH preventive therapy. Although it is not known whether INH therapy is as efficacious in preventing tuberculosis in HTLV-III/LAV-infected persons as in other groups, the usually good response of HTLV-III/LAV-infected persons with tuberculosis to standard therapy suggests that INH preventive therapy would also be effective. Before instituting preventive therapy, clinically active tuberculosis should be excluded.

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#### REFERENCE:

1. CDC. Recommendations for preventing transmission of infection with human T-lymphotropic virus type III/lymphadenopathy-associated virus in the workplace. MMWR 1985;34:681-95.
2. CDC. Guidelines for prevention of TB transmission in hospitals. Atlanta, Georgia: US Dept of Health and Human Services 1982: HHS publication no. (CDC) 82-8371.

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**1986 EDITION OF PEDIATRIC RED BOOK**

The American Academy of Pediatrics *Report of the Committee on Infectious Diseases*, commonly known as the *Pediatric Red Book*, 1986 edition, is now available. It is an excellent reference for health care professionals desiring the latest information on children's communicable diseases. New information in this edition includes: current guidelines on AIDS, infection control in day-care centers, and updated sections on Hemophilus influenza b vaccine and varicella zoster immune globulin. Copies are \$25.00 each and can be ordered from:

American Academy of Pediatrics  
Publications Department  
141 Northwest Point Boulevard  
PO Box 927  
Elk Grove Village, Illinois 60007

Toll-free information is available by telephone, 1-800-433-9016.


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