



June 25, 1993 / Vol. 42 / No. RR-9

MMWR

*Recommendations
and
Reports*

MORBIDITY AND MORTALITY WEEKLY REPORT

**Recommendations for Counseling
Persons Infected with Human
T-Lymphotropic Virus, Types I and II**

**Recommendations on Prophylaxis and
Therapy for Disseminated
Mycobacterium avium Complex for
Adults and Adolescents Infected with
Human Immunodeficiency Virus**

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Centers for Disease Control
and Prevention (CDC)
Atlanta, Georgia 30333



The *MMWR* series of publications is published by the Epidemiology Program Office, Centers for Disease Control and Prevention (CDC), Public Health Service, U.S. Department of Health and Human Services, Atlanta, Georgia 30333.

SUGGESTED CITATION

Centers for Disease Control and Prevention. Recommendations for counseling persons infected with human T-lymphotrophic virus, types I and II. Recommendations on prophylaxis and therapy for disseminated *Mycobacterium avium* complex for adults and adolescents infected with human immunodeficiency virus. *MMWR* 1993;42(No. RR-9): [inclusive page numbers].

Centers for Disease Control and Prevention William L. Roper, M.D., M.P.H.
Director

The material in this report was developed by:

National Center for Infectious Disease James M. Hughes, M.D.
Director

Division of HIV/AIDS Harold W. Jaffe, M.D.
Director

Division of Viral and Rickettsial Diseases Brian W. J. Mahy, Ph.D., ScD.
Director

The production of this report as an *MMWR* serial publication was coordinated in:

Epidemiology Program Office Barbara R. Holloway, M.P.H.
Director

Richard A. Goodman, M.D., M.P.H.
Editor, MMWR Series

Scientific Information and Communications Program

Recommendations and Reports Suzanne M. Hewitt, M.P.A.
Managing Editor

Ava W. Navin, M.A.
Project Editor

Rachel J. Wilson
Writer-Editor

Morie M. Higgins
Visual Information Specialist

Contents

Recommendations for Counseling Persons Infected with Human T-Lymphotropic Virus, Types I and II	1
Introduction	1
HTLV-I	2
HTLV-II	4
Serologic Tests for HTLV-I and HTLV-II	5
Notification and Deferral of Blood Donors	6
Recommendations for Counseling	7
Recommendations on Prophylaxis and Therapy for Disseminated <i>Mycobacterium avium</i> Complex for Adults and Adolescents Infected with Human Immunodeficiency Virus	13

Use of trade names is for identification only and does not imply endorsement by the Public Health Service or the U.S. Department of Health and Human Services.

Single copies of this document are available from the Centers for Disease Control and Prevention, National AIDS Clearinghouse, P.O. Box 6003, Rockville, MD 20850. Telephone: (800) 458-5231.

Copies can be purchased from Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402-9325. Telephone: (202) 783-3238.

**Centers for Disease Control and Prevention and U.S.
Public Health Service Working Group for
Recommendations for Counseling Persons Infected
with Human T-Lymphotropic Virus, Types I and II**

Rima F. Khabbaz, M.D.
Keiji Fukuda, M.D.
Jonathan E. Kaplan, M.D.
Division of Viral and Rickettsial Diseases
National Center for Infectious Diseases
Centers for Disease Control and
Prevention
Atlanta, GA

Cielso Bianco, M.D.
Maria Rios
New York Blood Center
New York, NY

William A. Blattner, M.D.
National Cancer Institute
Rockville, MD

Michael Busch, M.D., Ph.D.
Irwin Memorial Blood Centers
San Francisco, CA

Roger Dodd, M.D.
Alan E. Williams, Ph.D.
Marian Sullivan, M.S., M.P.H.
American Red Cross
Rockville, MD

Jay Epstein, M.D.
Food and Drug Administration
Bethesda, MD

Ronald Gilcher, M.D.
Oklahoma Blood Institute
Oklahoma City, OK

Craig Jackson, Ph.D.
Reagents Applications, Inc.
San Diego, CA

Louis Katz, M.D.
Mississippi Valley Regional Blood Center
Davenport, IA

Steven Kleinman, M.D.
University of California at Los Angeles
Medical Center
Los Angeles, CA

Edward L. Murphy, M.D.
University of California
San Francisco, CA

George Nemo, Ph.D.
Elaine Sloand, M.D.
National Heart, Lung, and Blood Institute
Bethesda, MD

Bernard J. Poiesz, M.D.
State University of New York Health
Science Center
Syracuse, NY

Recommendations for Counseling Persons Infected with Human T-Lymphotropic Virus, Types I and II*

Summary

The human T-lymphotropic viruses, type I (HTLV-I) and type II (HTLV-II), are closely related but distinct retroviruses that can infect humans. They are different from the human immunodeficiency viruses that cause acquired immunodeficiency syndrome. Screening of the U.S. blood supply for HTLV-I/II, which began in 1988, identifies HTLV-I- and HTLV-II-infected persons who should be counseled regarding their infections. This document summarizes current information about HTLV, types I and II, and presents recommendations developed by CDC and a U.S. Public Health Service working group for counseling HTLV-I- and HTLV-II-infected persons.

INTRODUCTION

Human T-lymphotropic viruses, type I (HTLV-I) and type II (HTLV-II), were the first human retroviruses discovered (1,2). Both belong to the oncovirus subfamily of retroviruses and can transform human lymphocytes so that they are self-sustaining in vitro. They are only distantly related to the human immunodeficiency viruses (HIV-1 and HIV-2), which belong to the lentivirus subfamily of retroviruses and which cause acquired immunodeficiency syndrome (AIDS). Infections with HTLV-I and HTLV-II are most easily detected serologically. The presence of antibodies to HTLV-I or HTLV-II indicates that a person is infected with the virus.

In November 1988, the Food and Drug Administration (FDA) recommended that blood donation centers screen the U.S. blood supply for HTLV-I (3). Since then, all donations of whole blood and blood components in the United States have been screened for antibodies to HTLV-I. The screening tests that were licensed, as well as the investigational supplementary tests used to confirm seroreactivity (Western immunoblot and radioimmunoprecipitation assay), do not reliably differentiate between antibodies to HTLV-I and the closely related HTLV-II. In addition, the licensed screening tests, which use HTLV-I antigens, vary in their sensitivity to detect antibodies to HTLV-II (4,5).

Approximately 2,000 HTLV-I/II-infected volunteer blood donors were identified in the first year of screening in the United States; testing, after amplification by polymerase chain reaction, indicated that approximately half were infected with HTLV-I and half with HTLV-II (6). Such donors are counseled and permanently deferred from donating blood. Because the polymerase chain-reaction test is not routinely available, many donors and other persons positive by serologic assays have been told that they are infected with HTLV-I/II. The uncertainty regarding the identity of the infecting virus and the differing epidemiologic and clinical correlates of HTLV-I and HTLV-II infections have complicated counseling of HTLV-I/II-infected persons.

*This report was previously published in *Annals of Internal Medicine* (Vol. 118, No. 6, March 15, 1993) and is printed here as a service to the *MMWR* readership.

Until recently, the only reliable way to differentiate HTLV-I from HTLV-II infection was by polymerase chain reaction (7). Within the past 2 years, investigational peptide- and recombinant protein-based serologic assays that can more easily differentiate the antibodies to HTLV-I and HTLV-II have been developed (8,9). Preliminary data suggest that these investigational tests are potentially useful for typing serum samples (8,9).

The recommendations for counseling HTLV-I-, HTLV-II-, and HTLV-I/II-infected persons included in this document are intended for use by health-care workers and public health officials in the United States. They may not be applicable in developing countries, where the need for breast-feeding may outweigh concerns about transmission of these viruses.

HTLV-I

Prevalence

HTLV-I infection is endemic in southwestern Japan (10), the Caribbean basin (11), Melanesia (12), and in parts of Africa (13-15). In some areas where HTLV-I infection is endemic, prevalence rates as high as 15% have been reported in the general population. Seroprevalence increases with age; in older age groups, rates are usually higher among women than men.

In the United States, HTLV-I/II seroprevalence rates among volunteer blood donors average 0.016% (6). Approximately half of HTLV-I/II-seropositive blood donors nationwide are infected with HTLV-I. HTLV-I-infected donors most often report a history of birth in HTLV-I-endemic countries or sexual contact with persons from the Caribbean or Japan. Smaller percentages report a history of either injecting drug use or blood transfusion. Clusters of HTLV-I infections have also been reported in blacks from the southeastern United States (16) and in immigrants from HTLV-I-endemic areas residing in Brooklyn, New York (17).

Transmission

Transmission of HTLV-I occurs from mother to child (18), by sexual contact (19), by blood transfusion (20), and by sharing contaminated needles. Mother-to-child transmission occurs primarily through breast-feeding (21); in HTLV-I-endemic areas, approximately 25% of breast-fed infants born to HTLV-I-seropositive mothers acquire infection. Recent studies suggest that transmission of HTLV-I by breast-feeding may be associated with the presence of maternal antibodies to the HTLV-I transactivating

TABLE 1. Clinical features of adult T-cell leukemia/lymphoma

Leukemia with circulating abnormal lymphocytes (flower cells)
Generalized peripheral lymphadenopathy
Hepatomegaly and abnormal liver function tests
Splenomegaly
Skin lesions
Bone lesions and hypercalcemia

protein, *tax* (22), or with elevated maternal titers of total antibodies to HTLV-I (23). However, the clinical usefulness of these markers has not been established. Intrauterine or perinatal transmission of HTLV-I does occur, but it appears to be less frequent than transmission by breast-feeding; approximately 5% of children born to infected mothers but not breast-fed acquire infection (24).

Sexual transmission of HTLV-I appears to be more efficient from males to females than from females to males. In one study of married couples in Japan, the efficiency of sexual transmission from males to females was estimated to be 60.8% over a 10-year period, compared with <1% from females to males (25). In another study, the presence of antibody to *tax* in the male partner was associated with sexual transmission to the female partner (26). In one study in Jamaica, genital ulcer disease in the male was identified as a risk for female-to-male sexual transmission (27). In the United States, approximately 25%–30% of sex partners of HTLV-I/II-seropositive blood donors are also seropositive (28,29).

Transmission of HTLV-I by blood transfusion occurs with transfusion of cellular blood products (whole blood, red blood cells, and platelets) but not with the plasma fraction or plasma derivatives from HTLV-I-infected blood. Seroconversion rates of 44% to 63% have been reported in recipients of HTLV-I-infected cellular components in HTLV-I endemic areas (20,30). Lower rates (approximately 20%) have been reported in recipients of contaminated cellular components in the United States (31). The probability of transmission by whole blood or packed red blood cells appears to diminish with greater duration of product storage; this finding has been ascribed to depletion of infected cells, presumably T-lymphocytes (30,32). Sharing blood-contaminated needles is the likely mode of transmission among injecting drug users.

HTLV-I is not transmitted by casual contact. Health-care workers caring for HTLV-I-infected persons need only be concerned about percutaneous exposure to HTLV-I-contaminated blood. One health-care worker who unintentionally inoculated himself with blood from an adult T-cell leukemia/lymphoma patient in Japan is reported to have seroconverted (33). However, no seroconversions occurred among 31 other laboratory and health-care workers exposed to HTLV-I via puncture wounds (34). Universal precautions, recommended for contact with all patients, are adequate to guard against HTLV-I transmission to health-care workers (35).

TABLE 2. Clinical features of HTLV-I-associated myelopathy/tropical spastic paraparesis

Slowly progressive chronic spastic paraparesis
Lower limb weakness
Urinary incontinence and impotence
Sensory disturbances such as tingling, pins and needles, and burning
Low back pain
Lower-extremity hyperreflexia with clonus and Babinski's sign
Impaired vibration sense

Diseases

Two diseases have been definitively associated with HTLV-I: adult T-cell leukemia/lymphoma (ATL) and a chronic degenerative neurologic disease, HTLV-I-associated myelopathy/tropical spastic paraparesis (HAM/TSP).

ATL is a malignancy of HTLV-I-infected CD4+ T-lymphocytes. The HTLV-I provirus is monoclonally integrated in the abnormal cell population. A spectrum of clinical and pathologic features has been described, including acute, chronic, lymphomatous, and smoldering forms (36,37). The acute form of ATL is characterized by infiltration of lymph nodes, viscera, and skin with malignant cells, resulting in a constellation of clinical features (Table 1). Circulating abnormal lymphocytes, called flower cells, are generally seen. Hypercalcemia, abnormal liver function values, and lytic bone lesions are common. Median survival is 11 months from diagnosis. Conventional chemotherapy is not curative, and relapses often occur quickly, although prolonged survival has been reported. ATL has been estimated to occur in 2%–4% of persons infected with HTLV-I in regions where HTLV-I is endemic and where early childhood infection is common (38,39). ATL occurs most frequently among persons 40–60 years of age, suggesting that a latent period as long as a few decades may be required for the disease to develop. One case of ATL in an immunocompromised patient has been reported in which the infection appears to have been transfusion acquired (40).

HAM/TSP is characterized by progressive, permanent lower-extremity weakness, spasticity, hyperreflexia, sensory disturbances, and urinary incontinence (Table 2). In patients with HAM/TSP, unlike those with multiple sclerosis, the signs and symptoms do not wax and wane, cranial nerves are not involved, and cognitive function is not affected. Antibodies to HTLV-I are characteristically found in the cerebrospinal fluid (41). Treatment with corticosteroids has been reported to be useful in some cases (42). Danazol, a synthetic androgen, reportedly improves symptoms, including bladder dysfunction (43,44). HAM/TSP develops in <1% of HTLV-I-infected persons (45), is believed to be immunologically mediated, and affects women more frequently than men. The latency period for HAM/TSP is shorter than that for ATL; cases of HAM/TSP have been associated with blood transfusion, with a median interval of 3.3 years between transfusion and development of HAM/TSP (46).

Recently, infective dermatitis, a chronic eczema associated with *Staphylococcus aureus* and beta-hemolytic streptococcus, has been reported in Jamaican children infected with HTLV-I (47).

The full spectrum of HTLV-I-associated diseases may include other disorders. Cases of polymyositis (48), chronic arthropathy (49), panbronchiolitis (50), and uveitis (51) have been reported in HTLV-I-infected patients.

HTLV-II

Prevalence

Until recently, partly because of the lack of serologic tests to differentiate HTLV-II from HTLV-I, no information was available regarding the seroepidemiology or modes of transmission of HTLV-II. HTLV-II is prevalent among injecting drug users in the United States and in Europe (52,53); more than 80% of HTLV-I/II seropositivity in drug users in the United States is due to HTLV-II infection (54). HTLV-II also appears to be

endemic in American Indian populations, including the Guaymi Indians in Panama (55) and North American Indians in Florida (56) and New Mexico (57). Approximately half of U.S. volunteer blood donors seropositive for HTLV-I/II are infected with HTLV-II. HTLV-II-infected blood donors most often report either a history of injecting drug use or a history of sexual contact with an injecting drug user (6,58). A smaller percentage report a history of blood transfusion.

Transmission

HTLV-II is presumed to be transmitted similarly to HTLV-I, but much less is known about the specific modes and efficiency of transmission of HTLV-II. One study of 20 non-breast-fed children born to HTLV-II-infected women in New York City failed to show evidence of transmission to the newborns (59). The HTLV-II provirus has been detected in breast milk from HTLV-II-infected mothers (60), but no data are available regarding transmission to breast-fed infants.

HTLV-II can be transmitted sexually (61); the most commonly reported risk factor among HTLV-II-infected female U.S. blood donors is sexual contact with an injecting drug user (6,58).

HTLV-II can be transmitted by transfusion of cellular blood products (whole blood, red blood cells, and platelets) (31,32). The probability of transmission from red blood cells appears to diminish with greater duration of product storage (31).

The high prevalence of HTLV-II among injecting drug users is likely due to sharing blood-contaminated needles or other injection paraphernalia (62).

Diseases

HTLV-II infection has not been clearly associated with any diseases. The virus was first isolated from two patients with hairy-cell leukemia (2,63), but no evidence of HTLV-II infection was found in 21 additional patients with hairy-cell leukemia (64). In one study, rates of lymphoproliferative illnesses were not found to be increased in New Mexico, where HTLV-II is present in American Indians (65). Rare cases of HAM/TSP-like neurologic illnesses (66) and of mycosis fungoides (67) and large granular lymphocyte leukemia (68) have been reported in HTLV-II-infected persons. Cases of erythrodermatitis and bacterial skin infections have been reported in HIV-1- and HTLV-II-coinfected persons (69).

SEROLOGIC TESTS FOR HTLV-I AND HTLV-II

Serum specimens are screened for antibody to HTLV-I by using licensed enzyme immunoassays prepared from HTLV-I whole-virus lysate antigens. These assays vary in their sensitivity to detect antibodies to HTLV-II (4,5). Initially reactive specimens are retested in duplicate to minimize the chance that reactivity is due to technical error. Specimens that are reactive in either of the duplicate tests are considered repeatedly reactive. Specimens that do not react in either of the duplicate repeat tests are considered nonreactive (3).

Additional tests, such as the Western immunoblot and the radioimmunoprecipitation assay, are needed to correctly interpret repeatedly reactive specimens. Such supplementary tests must be inherently capable of identifying antibodies to the core (*gag*) and the envelope (*env*) proteins of HTLV-I/II. Indirect fluorescent antibody test-

ing for HTLV-I/II has been used in some laboratories, but it does not distinguish antibodies to specific HTLV gene products. None of the supplementary tests have been licensed by the Food and Drug Administration, but they are available in research institutions, blood banks, some public health laboratories, and industrial laboratories, and as in-house tests in some diagnostic laboratories.

The following criteria for HTLV-I/II seropositivity were adopted by a U.S. Public Health Service (USPHS) working group in 1988 (3): a specimen that is repeatedly reactive by enzyme immunoassay must demonstrate immunoreactivity to both the *gag* gene product p24 and to an *env* gene product (gp46 and/or gp61/68) to be considered seropositive for HTLV-I/II. Reactive serum specimens that do not satisfy these criteria but do show immunoreactivity to at least one suspected HTLV gene product are designated "indeterminate." Both Western immunoblot and radioimmunoprecipitation may be required to determine whether a specimen is positive or indeterminate. Serum specimens with no immunoreactivity to any HTLV gene product in addition, more specific tests are considered false positive. Several studies involving provirus amplification have supported the accuracy of these diagnostic criteria; persons whose specimens satisfy the criteria for positivity are virtually always infected with HTLV-I or HTLV-II (7,70). In contrast, persons whose specimens are "indeterminate" are rarely infected with either virus; for those who are found to be infected, repeat serologic testing frequently demonstrates seropositivity (70,71). In rare instances, persons with reactivity to p19 and to an *env* gene product (gp46 and/or gp61/68) but without reactivity to p24 have been found to be infected with HTLV-I/II (72).

An important advance in HTLV serologic testing has been the development of a recombinant *env* protein, p21e. Reactivity to p21e (in either enzyme immunoassay or "spiked" Western immunoblot) has been found to be highly sensitive for HTLV-I/II infection, being observed in virtually 100% of infected persons (73). However, the specificity of the p21e reactivity has been questioned (74,75). For purposes of notification and counseling, the positivity of samples showing p21e serologically should be confirmed by tests that detect *env* reactivity, such as radioimmunoprecipitation or recombinant protein-based assays (76), or by polymerase chain reaction until further information is available concerning this test.

The supplementary serologic tests discussed thus far are incapable of differentiating antibodies to HTLV-I and HTLV-II. The relative intensity of the reactivity to the *gag* proteins p19 and p24 on the "spiked" Western immunoblot has been used to differentiate HTLV-I from HTLV-II (77), but such differentiation may be unreliable (78). Recently, several synthetic peptides and recombinant proteins have been developed for this purpose (8,9,79). As with the previously discussed supplementary tests, all these tests are available for research only. Preliminary data indicate that such assays can be highly specific in differentiating antibodies to HTLV-I and HTLV-II (8,9,79). Not all HTLV-I/II-positive serum specimens, however, can be typed as HTLV-I or HTLV-II by using these tests. In these cases, more sophisticated methods, such as provirus amplification or virus isolation, may be needed to differentiate HTLV-I from HTLV-II infection.

NOTIFICATION AND DEFERRAL OF BLOOD DONORS

In the United States, blood donors whose serum specimens are repeatedly reactive by the HTLV-I enzyme immunoassay and confirmed as seropositive for HTLV-I/II by the

additional specific tests discussed above are notified and permanently deferred from donating blood. This deferral policy includes donors confirmed positive with antibodies to HTLV-I, HTLV-II, or HTLV-I/II (if differentiation between the infections is not attempted or is unsuccessful). Blood donors with serum specimens repeatedly reactive on screening but not confirmed as seropositive for HTLV-I/II (a category that includes false-positive specimens and those indeterminate for HTLV) should also be notified and deferred if the same result is obtained on two separate donations. In some blood centers, such donors are deferred after the first such donation. Persons who are repeatedly reactive on screening but not confirmed as seropositive for HTLV-I/II should not be told that they are infected with HTLV-I or HTLV-II. The above policies for donor deferral are based on FDA recommendations. In addition, FDA recommendations regarding the use of blood components should be followed.

RECOMMENDATIONS FOR COUNSELING

In consideration of the information presented above, the following recommendations for counseling HTLV-seropositive persons have been issued. In instances in which viral typing is possible, counseling should be virus specific. As noted above, HTLV-I and HTLV-II are two different retroviruses with differing epidemiologies and disease associations. The specific recommendations for persons infected with HTLV-I or HTLV-II should therefore take these differences into account.

HTLV-I

Persons found to be seropositive for HTLV-I/II according to the USPHS criteria and positive for HTLV-I by additional testing should be informed that they are infected with HTLV-I. They should be told that HTLV-I is not the AIDS virus, that it does not cause AIDS, and that AIDS is caused by a different virus called HIV. They should be told that HTLV-I is a lifelong infection. They should be given information regarding modes and efficiency of transmission, disease associations, and the probability of developing disease.

In particular, persons infected with HTLV-I should be advised to:

- **Share the information with their physician**
- **Refrain from donating blood, semen, body organs, or other tissues**
- **Refrain from sharing needles or syringes with anyone**
- **Refrain from breast-feeding infants**
- **Consider the use of latex condoms to prevent sexual transmission**

If the HTLV-I-positive person is in a mutually monogamous sexual relationship, testing of the sex partner should be recommended to help formulate specific counseling advice. If the sex partner is also positive, no further recommendations are indicated. If the sex partner is negative, the couple should be advised that the use of latex condoms can help prevent transmission of HTLV-I to the negative partner, male or female. Male-infected, female-non-infected couples desiring pregnancy should be made aware of the finite risk of sexual transmission of HTLV-I during attempts at pregnancy and of the small risk for vertical

transmission from mother to infant unrelated to breast-feeding. Such couples might be advised to use latex condoms at all times except during the fertile period while they are attempting pregnancy. The use of latex condoms is strongly recommended for HTLV-I-positive persons with multiple sex partners or otherwise engaging in non-mutually monogamous sexual relationships. These persons should be reminded of the risk of acquiring other sexually transmitted infections, including HIV.

HTLV-II

Persons found to be seropositive for HTLV-I/II according to the USPHS criteria and positive for HTLV-II by additional testing should be informed that they are infected with HTLV-II. They should be told that HTLV-II is not the AIDS virus, that it does not cause AIDS, and that AIDS is caused by a different virus called HIV. They should be told that HTLV-II is a lifelong infection. They should be given information regarding possible modes of transmission and the lack of firm disease associations.

In particular, they should be advised to:

- **Share the information with their physician**
- **Refrain from donating blood, semen, body organs, or other tissues**
- **Refrain from sharing drug needles or syringes with anyone**
- **Refrain from breast-feeding infants**

Although the risks of transmission of HTLV-II by breast-feeding and of disease from HTLV-II are unknown, the theoretical risk of transmission and disease, as for HTLV-I, makes it prudent to recommend that HTLV-II-infected mothers refrain from breast-feeding when and where safe nutritional alternatives exist.

- **Consider the use of barrier precautions to prevent sexual transmission**

HTLV-II can be sexually transmitted, but the risks of disease are unknown. If the HTLV-II-positive person is in a mutually monogamous sexual relationship, testing of the sex partner should be recommended to help formulate specific counseling advice. If the sex partner is also positive, no further recommendations are indicated. If the sex partner is negative, the couple should be advised that the use of latex condoms can help prevent transmission of HTLV-II to the negative partner, male or female. The use of latex condoms is strongly recommended for HTLV-II-positive persons with multiple sex partners or otherwise engaging in non-mutually monogamous sexual relationships. These persons should be reminded of the risk of acquiring other sexually transmitted infections, including HIV.

HTLV-I/II

Persons found to be seropositive for HTLV-I/II according to the USPHS criteria but without differentiation of their infection should be informed they are positive for HTLV-I/II and that they are likely infected with either HTLV-I or HTLV-II. Because of the differences in the epidemiologic and clinical correlates of HTLV-I and HTLV-II, an effort to type the infection should be made. If such efforts are unsuccessful, these HTLV-I/II seropositive persons should be given information regarding possible modes and effi-

ciency of transmission of HTLV-I and HTLV-II, disease associations of HTLV-I, and the probability of developing disease. Specific counseling advice should be the same as for HTLV-I-infected persons (refer to HTLV-I section).

HTLV Indeterminate

Blood donors with serum specimens that are HTLV-indeterminate on two occasions at least 3 months apart should be advised that their specimens were reactive in a screening test for HTLV-I but that the results could not be confirmed by a second, more specific test. They should be reassured that "indeterminate" test results are only rarely caused by HTLV-I or HTLV-II infection. Persons testing "indeterminate" for HTLV-I/II on one occasion should be offered retesting to make sure they are not recently infected with HTLV-I or HTLV-II and in the process of seroconverting. If subsequent test results are the same, they should be reassured that they are unlikely to be infected with HTLV-I or HTLV-II.

HTLV False Positive

Blood donors with serum specimens that are repeatably reactive by HTLV-I enzyme immunoassay but negative by Western immunoblot on two occasions should be advised that their HTLV-I screening test is falsely positive and that it could not be confirmed by a second, more specific test. They should be reassured that they are not infected with HTLV-I or HTLV-II.

Medical Follow-up

A periodic medical evaluation of HTLV-I- or HTLV-II-infected persons by a physician knowledgeable about these viruses is recommended. This evaluation might include a physical examination, including a neurologic examination, and a complete blood count with peripheral smear examination. Medical evaluation of HTLV-II-infected persons should be considered optional.

References

1. Poiesz BJ, Ruscetti FW, Gazdar AF, Bunn PA, Minna JD, Gallo RC. Detection and isolation of type-C retrovirus particles from fresh and cultured lymphocytes of a patient with cutaneous T-cell lymphoma. *Proc Natl Acad Sci USA* 1980;77:7415-9.
2. Kalyanaraman VS, Sarngadharan MG, Robert-Guroff M, et al. A new subtype of human T-cell leukemia virus (HTLV-II) associated with a T-cell variant of hairy cell leukemia. *Science* 1982;218:571-3.
3. CDC. Licensure of screening tests for antibody to human T-lymphotropic virus type I. *MMWR* 1988;37:736-40,745-7.
4. Wiktor SZ, Pate EJ, Weiss SH, et al. Sensitivity of HTLV-I antibody assays for HTLV-II. *Lancet* 1991;338: 512-3.
5. Cossen C, Hagens S, Fukuchi R, Forghani B, Gallo D, Ascher M. Comparison of six commercial human T-cell lymphotropic virus type I (HTLV-I) enzyme immunoassay kits for detection of antibody to HTLV-I and -II. *J Clin Microbiol* 1992;30:724-5.
6. CDC. Human T-lymphotropic virus type-I screening in volunteer blood donors—U.S., 1989. *MMWR* 1990;39:915,921-4.
7. Ehrlich GD, Glaser JB, LaVigne K., et al. Prevalence of human T-cell leukemia/lymphoma virus (HTLV) type II infection among high-risk individuals: type-specific identification of HTLVs by polymerase chain reaction. *Blood* 1989;74:1658-64.
8. Lal RB, Heneine W, Rudolph DL, et al. Synthetic peptide-based immunoassays for distinguishing between human T-cell lymphotropic virus type I and type II infections in seropositive individuals. *J Clin Microbiol* 1991;29: 2253-8.

9. Lipka JJ, Miyoshi I, Hadlock KG, et al. Segregation of human T cell lymphotropic virus type I and II infections by antibody reactivity to unique viral epitopes. *J Infect Dis* 1992;165:268-72.
10. Hinuma Y, Komoda H, Chosa T, et al. Antibodies to adult T-cell leukemia-virus-associated antigen (ATLA) in sera from patients with ATL and controls in Japan: a nation-wide sero-epidemiologic study. *Int J Cancer* 1982;29:631-5.
11. Murphy EL, Figueroa JP, Gibbs W, et al. Human T-lymphotropic virus type I (HTLV-I) seroprevalence in Jamaica. I. Demographic determinants. *Am J Epidemiol* 1991;133:1114-24.
12. Yanagihara R, Jenkins CL, Alexander SS, Mora CA, Garruto RM. Human T lymphotropic virus type I infection in Papua New Guinea: high prevalence among the Hagahai confirmed by western analysis. *J Infect Dis* 1990;162:649-54.
13. Wiktor SZ, Piot P, Mann JM, et al. Human T-cell lymphotropic virus type I (HTLV-I) among female prostitutes in Kinshasa, Zaire. *J Infect Dis* 1990;161:1073-7.
14. Fleming AF, Maharajan R, Abraham M, et al. Antibodies to HTLV-I in Nigerian blood donors, their relatives and patients with leukemias, lymphomas, and other diseases. *Int J Cancer* 1986;38:809-13.
15. Lillo F, Varnier OE, Sabbatani S, Ferro A, Mendez P. Detection of HTLV-I and not HTLV-II infection in Guinea Bissau (West Africa). *J Acquir Immun Defic Syndr* 1991;4:541-2. (letter).
16. Blayney DW, Blattner WA, Robert-Guroff M, et al. The human T-cell leukemia-lymphoma virus in the southeastern United States. *JAMA* 1983;250:1048-52.
17. Dosik H, Denic S, Patel N, Krishnamurty M, Levine PH, Clark JW. Adult T-cell leukemia/lymphoma in Brooklyn. *JAMA* 1988;259:2255-7.
18. Hino S, Yamaguchi K, Katamine S, et al. Mother-to-child transmission of human T-cell leukemia virus type-I. *Jpn J Cancer Res (Gann)* 1985;76:474-80.
19. Tajima K, Tominaga S, Suchi T, et al. Epidemiological analysis of the distribution of antibody to adult T-cell leukemia virus-associated antigen: possible horizontal transmission of adult T-cell leukemia virus. *Jpn J Cancer Res (Gann)* 1982;73:893-901.
20. Okochi K, Sato H, Hinuma Y. A retrospective study on transmission of adult T cell leukemia virus by blood transfusion: seroconversion in recipients. *Vox Sang* 1984;46:245-53.
21. Kusuhara K, Sonoda S, Takahashi K, Tokugawa K, Fukushige J, Ueda K. Mother-to-child transmission of human T-cell leukemia virus type-I (HTLV-I): a fifteen-year follow-up study in Okinawa, Japan. *Int J Cancer* 1987;40:755-7.
22. Kashiwagi S, Kajiyama W, Hayashi J, et al. Antibody to p40^{tax} protein of human T cell leukemia virus 1 and infectivity. *J Infect Dis* 1990;161:426-9.
23. Hino S, Doi H, Yoshikuni H, et al. HTLV-I carrier mothers with high-titer antibody are at risk as a source of infection. *Jpn J Cancer Res (Gann)* 1987;78:1156-8.
24. Takahashi K, Takezaki T, Oki T, et al. Inhibitory effect of maternal antibody on mother-to-child transmission of human T-lymphotropic virus type I. *Int J Cancer* 1991;49:673-7.
25. Kajiyama W, Kashiwagi S, Ikematsu H, Hayashi J, Nomura H, Okochi K. Intrafamilial transmission of adult T-cell leukemia virus. *J Infect Dis* 1986;154:851-7.
26. Chen Y-MA, Okayama A, Lee T-H, Tachibana N, Mueller N, Essex M. Sexual transmission of human T-cell leukemia virus type I associated with the presence of anti-*tax* antibody. *Proc Natl Acad Sci USA* 1991;88:1182-6.
27. Murphy EL, Figueroa JP, Gibbs WN, et al. Sexual transmission of human T-lymphotropic virus type I (HTLV-I). *Ann Intern Med* 1989;111:555-60.
28. Williams AE, Sullivan MT, Fang CT, American Red Cross HTLV-I/II Study Group. HTLV-I/II infection in contacts of HTLV-I+ blood donors and recipients identified by lookback. Third Annual Retrovirology Conference, Hawaii, February 12-14, 1990. [abstract]
29. Kleinman S, Fitzpatrick L, Lee H. Transmission of HTLV-I/II from blood donors to their sexual partners. [abstract]. In: Program and Abstracts: International Society of Blood Transfusion/American Association of Blood Banks Joint Congress Meeting (Los Angeles). Arlington, VA: American Association of Blood Banks, 1990:129.
30. Manns A, Wilks RJ, Murphy EL, et al. A prospective study of transmission by transfusion of HTLV-I and risk factors associated with seroconversion. *Int J Cancer* 1992;51:886-91.
31. Sullivan MT, Williams AE, Fang CT, et al. Transmission of human T-lymphotropic virus types I and II by blood transfusion. *Arch Intern Med* 1991;151:2043-8.

32. Donegan E, Transfusion Safety Study (TSS) Group. Comparison of HTLV-I/II with HIV-1 transmission by component type and shelf storage before administration. *Transfusion* 1989;29:(38S). [abstract].
33. Kataoka R, Takehara N, Iwahara Y, et al. Transmission of HTLV-I by blood transfusion and its prevention by passive immunization in rabbits. *Blood* 1990;76:1657-61.
34. Amin RM, Jones B, Rubert M, et al. Risk of retroviral infection among retrovirology laboratory and health care workers. American Society for Microbiology 92nd General Meeting, New Orleans, Louisiana, May 26-30, 1992. [abstract T-20].
35. CDC. Recommendations for prevention of HIV transmission in health-care settings. *MMWR* 1987;36(2S):3s-18s.
36. Yamaguchi K, Kiyokawa T, Futami G, et al. Pathogenesis of adult T-cell leukemia from clinical pathologic features. In: Blattner WA, ed. *Human Retrovirology: HTLV*. New York: Raven Press 1990:163-71.
37. Shimoyama M, the Lymphoma Study Group (1984-87). Diagnostic criteria and classification of clinical subtypes of adult T-cell leukaemia-lymphoma. *Br J Haematol* 1991;79:428-37.
38. Kondo T, Nonaka H, Miyamoto N, et al. Incidence of adult T-cell leukemia-lymphoma and its familial clustering. *Int J Cancer* 1985;35:749-51.
39. Murphy EL, Hanchard B, Figueroa JP, et al. Modelling the risk of adult T-cell leukemia/lymphoma in persons infected with human T-lymphotropic virus type I. *Int J Cancer* 1989;43:250-3.
40. Chen Y-C, Wang C-H, Su I-J, et al. Infection of human T-cell leukemia virus type I and development of human T-cell leukemia/lymphoma in patients with hematologic neoplasms: a possible linkage to blood transfusion. *Blood* 1989;74:388-94.
41. Gessain A, Caudie C, Gout O, et al. Intrathecal synthesis of antibodies to human T-lymphotropic virus type I and the presence of IgG oligoclonal bands in the cerebrospinal fluid of patients with endemic tropical spastic paraparesis. *J Infect Dis* 1988;157:1226-34.
42. Osame M, Igata A, Matsumoto M, et al. HTLV-I associated myelopathy (HAM): treatment trials, retrospective survey and clinical and laboratory findings. *Hematol Rev* 1990; 3:271-4.
43. Harrington W, Sheramata W, Cabral L, Toussaint MR. Treatment of HTLV-I associated myelopathy (HAM) with danazol. Proceedings of the Fifth International Conference on Human Retrovirology; HTLV. Kumamoto, Japan, May 11-13, 1992. [abstract #W-14A]
44. Bartholomew C, Edwards J, Maharaj M. A trial of danazol in TSP patients in Trinidad. Proceedings of the Fifth International Conference on Human Retrovirology; HTLV. Kumamoto, Japan, May 11-13, 1992. [abstract #W-14B].
45. Kaplan JE, Osame M, Kubota H, et al. The risk of development of HTLV-I-associated myelopathy/tropical spastic paraparesis among persons infected with HTLV-I. *J Acquir Immun Defic Syndr* 1990;3:1096-1101.
46. Osame M, Janssen R, Kubota H, et al. Nationwide survey of HTLV-I-associated myelopathy in Japan: association with blood transfusion. *Ann Neurol* 1990;28:50-6.
47. LaGrenade L, Hanchard B, Fletcher V, Cranston B, Blattner W. Infective dermatitis of Jamaican children: a marker for HTLV-I infection. *Lancet* 1990;336:1345-7.
48. Morgan OStC, Mora C, Rogers-Johnson P, Char G. HTLV-I and polymyositis in Jamaica. *Lancet* 1989;2:1184-7.
49. Nishioka K, Maruyama I, Sato K, Kitajima I, Nakajima Y, Osame M. Chronic inflammatory arthropathy associated with HTLV-I. *Lancet* 1989;1:441.
50. Sugimoto M, Nakashima H, Kawano O, Ando M, Araki S. Bronchoalveolar T-lymphocytosis in HTLV-I-associated myelopathy. *Chest* 1989;95:708. (letter)
51. Shirao M, Yoshimura K, Mochizuki M, Araki S, Miyata N, Yamaguchi K. A seroepidemiologic study of HTLV-I uveitis. Proceedings of the Fifth International Conference on Human Retrovirology; HTLV. Kumamoto, Japan, May 11-13, 1992. [abstract #P-24].
52. Lee HH, Weiss SH, Brown LS, et al. Patterns of HIV-1 and HTLV-I/II in intravenous drug abusers from the middle Atlantic and central regions of the USA. *J Infect Dis* 1990;162:347-52.
53. Zella D, Mori L, Sala M, et al. HTLV-II infection in Italian drug abusers. *Lancet* 1990;336:575-6. (letter)
54. Khabbaz RF, Onorato IM, Cannon RO, et al. Seroprevalence of HTLV-I and HTLV-II among intravenous drug users and persons in clinics for sexually transmitted diseases. *N Engl J Med* 1992;326:375-80.

55. Heneine W, Kaplan JE, Gracia F, et al. HTLV-II endemicity among Guaymi Indians in Panama. *N Engl J Med* 1991;324:565 (letter)
56. Levine PH, Jacobson S, Elliott R, et al. HTLV-II infection in Florida Indians. *AIDS Res Hum Retroviruses* 1993;9:123-7.
57. Hjelle B, Scalf R, Swenson S. High frequency of human T-cell leukemia-lymphoma virus type II infection in New Mexico blood donors: determination by sequence-specific oligonucleotide hybridization. *Blood* 1990;76:450-4.
58. Lee HH, Swanson P, Rosenblatt JD, et al. Relative prevalence and risk factors of HTLV-I and HTLV-II infection in U.S. blood donors. *Lancet* 1991;337:1435-9.
59. Kaplan JE, Abrams E, Schaffer N, et al. Low risk of mother-to-child transmission of human T-lymphotropic virus type II in non-breast-fed infants. *J Infect Dis* 1992;166:892-5.
60. Heneine W, Woods T, Green D, et al. Detection of HTLV-II in breastmilk of HTLV-II infected mothers. *Lancet* 1992;340:1157-8. (letter).
61. Hjelle B, Cyrus S, Swenson SG. Evidence for sexual transmission of human T-lymphotropic virus type II. *Ann Intern Med* 1992;116:90-1.
62. Feigal E, Murphy E, Vranizan K, et al. Human T-cell lymphotropic virus types I and II in intravenous drug users in San Francisco: risk factors associated with seropositivity. *J Infect Dis* 1991; 164:36-42.
63. Rosenblatt JD, Golde DW, Wachsmann W, et al. A second isolate of HTLV-II associated with atypical hairy-cell leukemia. *N Engl J Med* 1986;315:372-7.
64. Rosenblatt JD, Gasson JC, Glaspy J, et al. Relationship between human T-cell leukemia virus-II and atypical hairy cell leukemia: a serologic study of hairy cell leukemia patients. *Leukemia* 1987;1:397-401.
65. Hjelle B, Mills R, Swenson S, Mertz G, Key C, Allen S. Incidence of hairy cell leukemia, mycosis fungoides, and chronic lymphocytic leukemia in first known HTLV-II-endemic population. *J Infect Dis* 1991;163:435-40.
66. Hjelle B, Appenzeller O, Mills R, et al. Chronic neurodegenerative disease associated with HTLV-II infection. *Lancet* 1992;339:645-6.
67. Zucker-Franklin D, Hooper WC, Evatt BL. Human lymphotropic retroviruses associated with mycosis fungoides: evidence that human T-cell lymphotropic virus type II (HTLV-II) as well as HTLV-I may play a role in the disease. *Blood* 1992;80:1537-45.
68. Loughran TP Jr, Coyle T, Sherman MP, et al. Detection of human T-cell leukemia/lymphoma virus, type II, in a patient with large granular lymphocyte leukemia. *Blood* 1992;80:1116-9.
69. Kaplan MH, Hall WW, Susin M, et al. Syndrome of severe skin disease, eosinophilia, and dermatopathic lymphadenopathy in patients with HTLV-II complicating human immunodeficiency virus infection. *Am J Med* 1991;91:300-9.
70. Khabbaz RF, Heneine W, Grindon A, Hartley TM, Shulman G, Kaplan J. Indeterminate HTLV serologic results in U.S. blood donors: are they due to HTLV-I or HTLV-II? *J Acquir Immun Defic Syndr* 1992;5:400-4.
71. Kwok S, Lipka JJ, McKinney N, et al. Low incidence of HTLV infections in random blood donors with indeterminate Western blot patterns. *Transfusion* 1990;30:491-4.
72. Donegan E, Pell P, Lee H, Shaw GM, Moseley JW, Transfusion Safety Study Group. Transmission of human T-lymphotropic virus type I by blood components from a donor lacking anti-p24: a case report. *Transfusion* 1992;32:68-71.
73. Lillehoj EP, Alexander SS, Dubrule CJ, et al. Development and evaluation of a human T-cell leukemia virus type I serologic confirmatory assay incorporating a recombinant envelope polypeptide. *J Clin Microbiol* 1990;28:2653-8.
74. Hartley TM, Malone GE, Khabbaz RF, Lal RB, Kaplan JE. Evaluation of a recombinant human T-cell lymphotropic virus type I (HTLV-I) p21E antibody detection enzyme immunoassay as a supplementary test in HTLV-I/II antibody testing algorithms. *J Clin Microbiol* 1991;29:1125-7.
75. Lal RB, Brodine S, Kuzura J, et al. Sensitivity and specificity of a recombinant transmembrane glycoprotein (rgp21)-spiked Western immunoblot for serologic confirmation of human T-cell lymphotropic virus type I and type II infection. *J Clin Microbiol* 1992;30:296-9.
76. Roberts BD, Fong SKH, Lipka JJ, et al. Evaluation of an immunoblot assay for serologic confirmation and differentiation of human T-cell lymphotropic virus types I and II. *J Clin Microbiol* 1993;31:260-4.

77. Wiktor SZ, Alexander SS, Shaw GM, et al. Distinguishing between HTLV-I and HTLV-II by Western blot. *Lancet* 1990;335:153-34. (letter).
78. Lal RB, Brodine SK, Coligan JE, Roberts CR. Differential antibody responsiveness to p19 *gag* results in serological discrimination between human T-lymphotropic virus type I and type II. *J Med Virol* 1991;35:232-6.
79. Chen, Y-MA, Lee T-H, Wiktor SZ, et al. Type-specific antigens for serological discrimination of HTLV-I and HTLV-II infection. *Lancet* 1990;336:1153-5.

**Recommendations on Prophylaxis and Therapy
for Disseminated *Mycobacterium avium*
Complex for Adults and Adolescents Infected
with Human Immunodeficiency Virus**

**U.S. Public Health Service Task Force on
Prophylaxis and Therapy for
Mycobacterium avium Complex**

Members of Task Force

Henry Masur, M.D., Chair
National Institutes of Health
Bethesda, MD

David L. Cohn, M.D.
Denver Disease Control
Denver, CO

Michael H. Cynamon, M.D.
Veterans Administration Medical Center
Syracuse, NY

Lawrence R. Deyton, M.D., M.S.P.H.
National Institute of Allergy and
Infectious Diseases
Rockville, MD

Robin J. Edison, M.D.
Food and Drug Administration
Rockville, MD

Robert W. Eisinger, Ph.D.
National Institutes of Health
Bethesda, MD

Jerrold J. Ellner, M.D.
Case Western Reserve University
Cleveland, OH

Judith Feinberg, M.D.
Johns Hopkins Hospital
Baltimore, MD

Mark J. Goldberger, M.D.
Food and Drug Administration
Rockville, MD

Charles Jeff Goodgame, M.D.
Maitland, FL

Fred M. Gordin, M.D.
Veterans Administration Medical Center
Washington, D.C.

Mark Harrington
ACT-UP/New York
New York, NY

Diane V. Havlir, M.D.
University of California at San Diego
San Diego, CA

C. Robert Horsburgh, Jr., M.D.
Centers for Disease Control
and Prevention
Atlanta, GA

Clark B. Inderlied, Ph.D.
Children's Hospital
Los Angeles, CA

Carol A. Kemper, M.D.
Santa Clara Valley Medical Center
San Jose, CA

Joyce A. Korvick, M.D.
National Institute of Allergy and
Infectious Diseases
Rockville, MD

Linda L. Lewis, M.D.
National Cancer Institute
Bethesda, MD

Abe M. Macher, M.D.
Health Resources Services
Administration
Bethesda, MD

Brent G. Petty, M.D.
Johns Hopkins Hospital
Baltimore, MD

Michael A. Polis, M.D., M.P.H.
National Institute of Allergy and
Infectious Diseases
Bethesda, MD

Fred R. Sattler, M.D.
University of Southern California Medical
Center
Los Angeles, CA

Members of Task Force — Continued

Elaine Sloand, M.D.
National Heart, Lung, and Blood Institute
Bethesda, MD

Richard J. Wallace, Jr., M.D.
University of Texas Health Center
Tyler, TX

Consultants

Constance A. Benson, M.D.
Rush-Presbyterian-St.Luke's Medical
Center
Chicago, IL

Leonard B. Heifets, M.D., Ph.D.
National Jewish Center for Immunology
and Respiratory Medicine
Denver, CO

Richard E. Chaisson, M.D.
Johns Hopkins University
Baltimore, MD

Recommendations On Prophylaxis and Therapy for Disseminated *Mycobacterium avium* Complex for Adults and Adolescents Infected with Human Immunodeficiency Virus

Summary

Mycobacterium avium complex (MAC) causes disseminated disease in up to 40% of patients with advanced human immunodeficiency virus (HIV) disease in the United States. A U.S. Public Health Service Task Force convened to address the prophylaxis and therapy of MAC recommends that patients with HIV infection and <100 CD4+ T-lymphocytes/ μ L be administered prophylaxis against MAC. The recommended regimen is rifabutin, 300 mg by mouth daily, for the patient's lifetime. If disseminated MAC develops, a treatment regimen containing clarithromycin or azithromycin and at least one other agent is recommended. Diagnosis, therapy, and prophylaxis for HIV-infected children follow similar guidelines.

INTRODUCTION

Mycobacterium avium complex (MAC) causes disseminated disease in up to 40% of patients with human immunodeficiency virus (HIV) in the United States, producing fever, sweats, weight loss, and anemia (1–3). Disseminated MAC characteristically affects patients with advanced HIV disease and peripheral CD4+ T-lymphocyte counts <100 cells/ μ L. Effective prevention and therapy of MAC has the potential to contribute substantially to improved quality of life and duration of survival for HIV-infected persons.

Two randomized, placebo-controlled, multicenter studies were recently conducted to study the use of rifabutin for the prevention of disseminated MAC, as defined by positive blood culture. In these studies, rifabutin was shown to reduce the frequency of MAC bacteremia by approximately 50% (48 of 566 patients receiving rifabutin developed MAC, compared with 102 of 580 patients receiving placebo, $p<0.001$) (4,5).

On December 23, 1992, the Food and Drug Administration issued the first approval for a prophylactic drug targeted against MAC. Data collected in published and unpublished studies (1–3) suggest that health-care providers may utilize and their patients may benefit from recommendations for prevention and management provided by a panel of experts drawn from government agencies, universities, practicing clinicians, and the community. The U.S. Public Health Service Task Force on Prophylaxis and Therapy for *Mycobacterium avium* Complex was convened in Bethesda, Maryland, on December 7–8, 1992, and issued the recommendations in this report.

Indications for Prophylaxis

Patients with HIV infection and <100 CD4+ T-lymphocytes/ μ L should be administered prophylaxis against MAC. Prophylaxis should be continued for the patient's

lifetime unless multiple drug therapy for MAC becomes necessary because of the development of MAC disease.

Clinicians must weigh the potential benefits of MAC prophylaxis against the potential for toxicities and drug interactions, the cost, the potential to produce resistance in a community with a high rate of tuberculosis, and the possibility that the addition of another drug to the medical regimen may adversely affect patients' compliance with treatment. Because of these concerns, therefore, in some situations rifabutin prophylaxis should not be administered.

Evaluation before Beginning Prophylaxis

Before prophylaxis is administered, patients should be assessed to ensure that they do not have active disease due to MAC, *M. tuberculosis*, or any other mycobacterial species. This assessment may include a chest radiograph and tuberculin skin test.

Prophylactic Regimens

Rifabutin, 300 mg by mouth daily, is recommended for the patient's lifetime unless disseminated MAC develops, which would then require multiple drug therapy (4,5). Although other drugs, such as azithromycin and clarithromycin, have laboratory and clinical activity against MAC, none has been shown in a prospective, controlled trial to be effective and safe for prophylaxis. Thus, in the absence of data, no other regimen can be recommended at this time.

The 300-mg dose of rifabutin has been well tolerated (4,5). Adverse effects included neutropenia, thrombocytopenia, rash, and gastrointestinal disturbances.

Diagnosis of MAC

Disseminated MAC is most readily diagnosed by one positive blood culture (6). Blood cultures should be performed in patients with symptoms, signs, or laboratory abnormalities compatible with mycobacterium infection. Blood cultures are not routinely recommended for asymptomatic persons, even for those who have CD4+ T-lymphocyte counts <100 cells/ μ L.

Therapy of Disseminated MAC

Although studies have not yet identified an optimal regimen or confirmed that any therapeutic regimen produces sustained clinical benefit for patients with disseminated MAC, the Task Force concluded that the available information indicated the need for treatment of disseminated MAC (7-14). The Public Health Service therefore recommends that regimens be based on the following principles:

- Treatment regimens outside a clinical trial should include at least two agents.
- Every regimen should contain either azithromycin or clarithromycin; many experts prefer ethambutol as a second drug. Many clinicians have added one or more of the following as second, third, or fourth agents: clofazimine, rifabutin, rifampin, ciprofloxacin, and in some situations amikacin. Isoniazid and pyrazinamide are not effective for the therapy of MAC.

- Therapy should continue for the lifetime of the patient if clinical and microbiologic improvement is observed.

Monitoring Patients Receiving Therapy for Disseminated MAC

- Clinical manifestations of disseminated MAC—such as fever, weight loss, and night sweats—should be monitored several times during the initial weeks of therapy. Microbiologic response, as assessed by blood culture every 4 weeks during initial therapy, can also be helpful in interpreting the efficacy of a therapeutic regimen.
- Most patients who ultimately respond show substantial clinical improvement in the first 4–6 weeks of therapy. Elimination of the organisms from blood cultures may take somewhat longer, often requiring 4–12 weeks.

Recommendations for HIV-Infected Children

HIV-infected children <12 years of age also develop disseminated MAC. Some age adjustment is necessary when clinicians interpret CD4+ T-lymphocyte counts in children <2 years of age. Diagnosis, therapy, and prophylaxis should follow recommendations similar to those for adolescents and adults.

References

1. Horsburgh CR. *Mycobacterium avium* complex infection in the acquired immunodeficiency syndrome. N Engl J Med 1991;324:1332-8.
2. Chaisson RE, Moore RD, Richman DD, Keruly J, Creagh T, the Zidovudine Epidemiology Study Group. Incidence and natural history of *Mycobacterium avium* complex infection in patients with advanced HIV disease treated with zidovudine. Am Rev Respir Dis 1992;146:285-9.
3. Havlik JA, Horsburgh CR, Metchock B, Williams P, Fann SA, Thompson SE. Disseminated *Mycobacterium avium* complex infection: clinical identification and epidemiologic trends. J Infect Dis 1992;165:577-80.
4. Gordin F, Nightingale S, Wynne B, et al. Rifabutin monotherapy prevents or delays *Mycobacterium avium* complex bacteremia in patients with AIDS (abstract no. B100). In: Program and Abstracts of the VIII International Conference on AIDS/Third STD World Congress (Amsterdam). Amsterdam: Harvard University/Dutch Foundation, 1992.
5. Cameron W, Sparti P, Pietroski N, et al. Rifabutin therapy for the prevention of *M. avium* complex bacteremia in patients with AIDS and CD4 <200 (abstract no. We54). In: Program and Abstracts of the VIII International Conference on AIDS/Third STD World Congress (Amsterdam). Amsterdam: Harvard University/Dutch Foundation, 1992.
6. Evans KD, Nakasome AS, Sutherland PA, de la Maza LM, Peterson EM. Identification of *Mycobacterium tuberculosis* and *Mycobacterium avium-M. intracellulare* directly from primary Bactec^R cultures by using acridinium-ester labeled DNA probes. J Clin Microbiol 1992;30:2427-31.
7. Kemper C, Havlir D, Haghghat D, et al. Effect of ethambutol, rifampin, or clofazimine, given singly, on *Mycobacterium avium* bacteremia in AIDS. VIII International Conference on AIDS: Amsterdam, The Netherlands, July 19-24, 1992:PoB 3087.
8. Chaisson RE, Benson CA, Dube M, et al. Clarithromycin therapy for disseminated *Mycobacterium avium*-complex (MAC) in AIDS. Abstracts of the 32nd Interscience Conference on Antimicrobial Agents and Chemotherapy, Anaheim, California, 1992;891.
9. Dautzenberg B, Truffot C, Legris S, et al. Activity of clarithromycin against *Mycobacterium avium* infection in patients with the acquired immune deficiency syndrome: a controlled clinical trial. Am Rev Respir Dis 1992;144:564-9.
10. Young LS, Wiviott L, Wu M, Kolononski P, Bolan R, Inderlied CB. Azithromycin for treatment of *Mycobacterium avium-intracellulare* complex infection in patients with AIDS. Lancet 1991;338:1107-9.

11. Kemper CA, Meng TC, Nussbaum J, et al. Treatment of *Mycobacterium avium* complex bacteremia in AIDS with a four-drug oral regimen: rifampin, ethambutol, clofazimine and ciprofloxacin. *Ann Intern Med* 1992;116:466-72.
12. Agins BD, Berman DS, Spicehandler D, El-Sadr W, Simberkoff MS, Rahal J. Effect of combined therapy with ansamycin, clofazimine, ethambutol, and isoniazid for *Mycobacterium avium* infection in patients with AIDS. *J Infect Dis* 1989;159:784-787.
13. Hoy J, Mijch A, Sandland M, Grayson L, Lucas R, Dwyer B. Quadruple-drug therapy for *Mycobacterium avium* bacteremia in AIDS patients. *J Infect Dis* 1990;161:801-5.
14. Horsburgh CR, Havlik JA, Metchock BG, Thompson SE. Oral therapy of disseminated *Mycobacterium avium* complex infection in AIDS relieves symptoms and is well tolerated. *Am Rev Respir Dis* 1991;143:A115.

MMWR

The *Morbidity and Mortality Weekly Report (MMWR)* Series is prepared by the Centers for Disease Control and Prevention (CDC) and is available on a paid subscription basis from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402; telephone (202) 783-3238.

The data in the weekly *MMWR* are provisional, based on weekly reports to CDC by state health departments. The reporting week concludes at close of business on Friday; compiled data on a national basis are officially released to the public on the succeeding Friday. Inquiries about the *MMWR* Series, including material to be considered for publication, should be directed to: Editor, *MMWR* Series, Mailstop C-08, Centers for Disease Control and Prevention, Atlanta, GA 30333; telephone (404) 332-4555.