VIRGINIA
EPIDEMIOLOGY BULLETIN

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Prevention and Treatment of Tuberculosis Among Patients Infected with Human Immunodeficiency Virus:

Principles of Therapy and Revised Recommendations

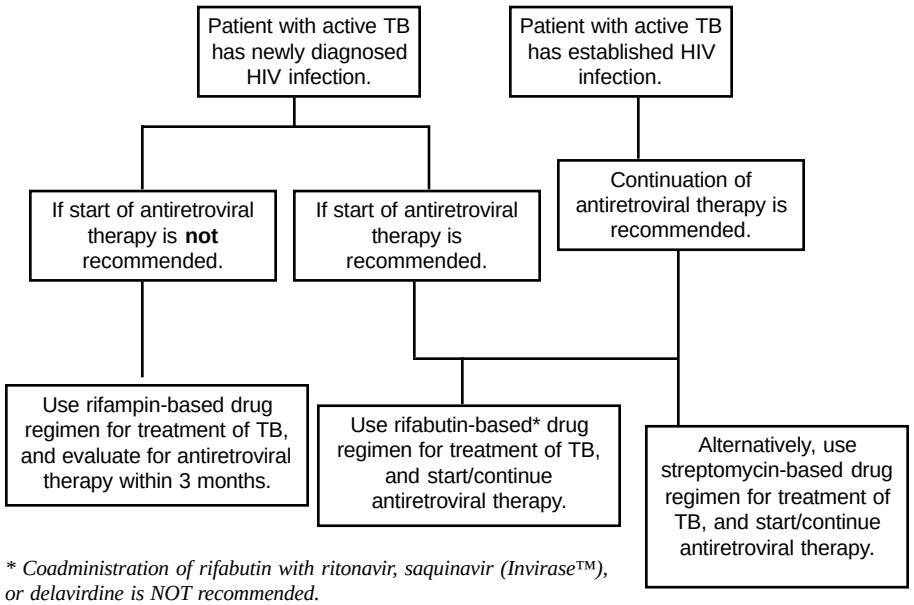
Summary

The following article includes excerpts from the MMWR article with the above title (1998:47[No. RR-20]:1-58). This report summarizes the recommendations of a panel of expert consultants convened by the Centers for Disease Control and Prevention (CDC) in September 1997 and is intended to update previous recommendations for the diagnosis, treatment, and prevention of tuberculosis (TB) among adults and children coinfected with human immunodeficiency virus (HIV) in the United States. In developing these guidelines, the panel considered the findings of recent and past clinical trials in addition to the cumulative experiences of panel members. Because alternatives to the use of rifampin for antituberculosis treatment are now available, the previously recommended practice of stopping protease inhibitor therapy to allow the use of rifampin for TB treatment is no longer recommended for patients with HIV-related TB. In addition to CDC's current recommendations for administering isoniazid preventive therapy to HIV-infected persons who were exposed to patients with infectious TB, this report also describes in detail the use of new short-course (i.e., 2-month) multidrug regimens (e.g., a rifamycin, such as rifampin or rifabutin, combined with pyrazinamide) to prevent TB in persons with HIV infection. If you would like a copy of the entire MMWR article, you may call the Office of Epidemiology at 804/786-6261 or visit the CDC web site, http://www.cdc.gov.

Introduction

Management of human immunodeficiency virus (HIV)-related tuberculosis (TB) disease is complex, and clinical and public health consequences associated with treatment failure are serious. Health-care professionals need to be familiar with these new guidelines to ensure the use of the most effective management strategies for TB patients infected with HIV while concurrently promoting optimal antiretroviral therapy for these patients. A recommended management strategy is shown in the Figure. When possible, the treatment of TB in HIV-infected persons should be directed by or done in consultation with a physician with extensive experience in the care of patients with TB and HIV disease. Part I of this report contains an extensive review of background information about HIV-related TB in the United States and the scientific principles of therapy for both diseases. The recommendations of the expert panel contained in Part II are based upon this review.

Figure. Recommended management strategies for TB patients with HIV infection



** Coadministration of rifabutin with ritonavir, saquinavir (Invirase™), or delavirdine is NOT recommended.*

In This Issue:

PART I. BACKGROUND AND SCIENTIFIC RATIONALE

Frequency of Coexisting TB and HIV Infection and Disease in the United States

In the United States, epidemiologic evidence indicates that the HIV epidemic contributed substantially to the increased number of TB cases in the late 1980's and early 1990's. Although limited by incomplete reporting of HIV status for persons with TB, a recent national survey suggested that 14% of persons with TB in 1993-1994 (27% among those aged 25-44 years) were coinfected with HIV.

In prospective epidemiologic studies, investigators have estimated that the annual rate of TB disease among untreated tuberculin skin-test (TST)-positive, HIV-infected persons in the United States ranges from 1.7 to 7.9 TB cases per 100 person-years, a rate 4-26 times higher than the rate among comparable HIV-infected, TST-negative persons, and 200-800 times higher than the rate of TB estimated for the U.S. population overall. Therefore, activities to control and eliminate TB in the United States must include aggressive efforts to identify HIV-infected persons with latent TB infection and to provide them with therapy to prevent progression to active TB disease. In addition, persons with HIV are more likely to have drug-resistant tuberculosis than are those without HIV-infection. This increased risk for TB drug resistance might reflect a higher proportion of TB disease resulting from recently acquired *Mycobacterium tuberculosis* infection.

TB Therapy Outcomes among Patients with HIV-Related TB

When TB disease develops in an HIV-infected person, the prognosis is often poor, though it depends on the person's degree of immunosuppression and response to appropriate antituberculosis therapy. The 1-year mortality rate for treated, HIV-related tuberculosis ranges from 20% to 35% and shows little variation between cohorts from industrialized and developing countries. The observed mortality rate for HIV-infected persons with TB is approximately four times greater than the rate for TB patients not infected with HIV. Epidemiologic data also suggest that active TB accelerates the natural progression of HIV infection.

Among patients treated for TB, early clinical response to therapy and the time in which *M. tuberculosis* sputum cultures convert from positive to negative appear to be similar for those with or without HIV infection. In three studies, investigators found that 6-month rifamycin-containing TB regimens were associated with a clinically acceptable (less than or equal to 5.4%) TB relapse rate. The expert consultants who reviewed the available data agreed that short-course (i.e., 6-month) regimens should be used for the treatment of HIV-related pansusceptible TB (i.e., susceptible to all first-line antituberculosis drugs) in the United States, where patients are usually treated with directly observed therapy (DOT) and where response to antituberculosis drugs can be monitored. However, the experts recommended that clinicians treating TB in patients with HIV infection should consider the factors that increase a person's risk for a poor clinical outcome (e.g., lack of adherence to TB therapy, delayed conversion of *M. tuberculosis* sputum cultures from positive to negative, and delayed clinical response) when deciding the total duration of TB therapy.

Paradoxical Reactions Associated with Initiation of Antiretroviral Therapy During the Course of TB Therapy

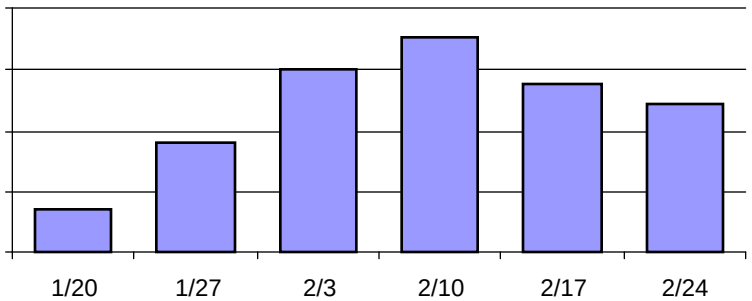
The temporary exacerbation of TB symptoms and lesions after initiation of antituberculosis therapy — known as a paradoxical reaction — has been reported among patients with HIV-related TB. These reactions appear to be related more often to the concurrent administration of antiretroviral and antituberculosis therapy and occur with greater frequency than do paradoxical reactions associated primarily with the administration of antituberculosis therapy. Patients with paradoxical reactions can have hectic fevers, lymphadenopathy that may be severe, worsening of chest radiographic manifestations of TB (e.g., miliary infiltrates, pleural effusions), and worsening of original tuberculous lesions (e.g., cutaneous and peritoneal). However, these reactions are not associated with changes in *M. tuberculosis* bacteriology (i.e., no change from negative to positive culture and smear), and patients generally feel well and have no signs of toxicity.

Considerations for TB Therapy for HIV-Infected Patients Treated with Antiretroviral Agents

Protease inhibitors (saquinavir, indinavir, ritonavir, and nelfinavir) and NNRTIs (nevirapine, delavirdine, and efavirenz) have substantive interactions with the rifamycins (rifampin, rifabutin, and rifapentine). These drug interactions principally result from induction or inhibition of the hepatic cytochrome CYP450 enzyme system. For example, if protease inhibitors are administered with rifampin (a potent CYP450 inducer), blood concentrations of the protease inhibitors decrease markedly. For this reason, the use of rifampin to treat active TB in a patient who is taking a protease inhibitor or an NNRTI is always contraindicated. Conversely, if ritonavir (a potent CYP450 inhibitor) is administered with rifabutin, blood concentrations of rifabutin increase markedly. Rifabutin is a less potent inducer of the CPY450 cytochrome enzymes than is rifampin and, when used in appropriately modified doses, might

Flu Corner

Influenza activity in Virginia has been characterized as widespread since January 20, 1999. Laboratory-confirmed cases of influenza type A have been reported from each of the health planning regions and laboratory-confirmed cases of influenza type B have been reported from the northwest and eastern health planning regions. Twenty-three nursing homes from across the state have reported outbreaks of influenza-like illness, nine of which have been laboratory-confirmed as influenza type A. Isolates from seven of these nursing home outbreaks have been further subtyped as A/Sydney/5/97, the H3N2 component of the 1998/99 vaccine.



not be associated with a clinically significant reduction of protease inhibitors or nevirapine. As an alternative to the use of rifamycin for the treatment of TB, the use of streptomycin-based regimens that do not contain rifamycin can be considered for the treatment of TB in patients undergoing antiretroviral therapy with protease inhibitors or NNRTIs. In contrast to the protease inhibitors and the NNRTIs, the other class of antiretroviral agents available, nucleoside reverse transcriptase inhibitors (NRTIs) (zidovudine, didanosine, zalcitabine, stavudine, and lamivudine) are not metabolized by CYP450. No contraindication exists for the use of NRTIs, NNRTIs, and protease inhibitors with isoniazid, pyrazinamide, ethambutol, or streptomycin.

Use of Rifabutin-Based Regimens for the Treatment of HIV-Related TB

The inclusion of rifampin in regimens to treat HIV-related TB was supported by data collected from approximately 90 controlled clinical trials conducted from 1968 to 1988. Excluding rifampin from the TB treatment regimen was not recommended because regimens not containing rifampin a) had not been proven to have acceptable efficacy and b) require prolonging duration of therapy from 6 months to 12-15 months. Presently, available data suggest that rifabutin in short-course (i.e., 6-month) multidrug regimens to treat TB provides the same benefits as the use of rifampin. In addition: a) observations suggest that rifabutin might be more reliably absorbed than rifampin in patients with advanced HIV disease; b) the use of rifabutin appears to be better tolerated in patients with rifampin-induced hepatotoxicity; and c) the use of rifabutin might lessen the possibility of interactions with other medications commonly prescribed for patients with HIV infection.

Use of Alternative TB Treatment Regimens that Contain Minimal or No Rifamycin

TB treatment regimens that contain no rifamycins have been proposed as an alternative for patients who take protease inhibitors or NNRTIs. Most studies demonstrated high relapse rates when regimens not containing streptomycin were used and when the duration of therapy was less than 9 months. Thus, the expert consultants who developed these guidelines concluded that treatment of TB without rifamycin always requires longer-duration (at least 9 months) regimens that include streptomycin or an injectable antituberculosis drug such as capreomycin, amikacin, or kanamycin.

Scientific Rationale for the Treatment of Latent *M. tuberculosis* Infection in Patients with HIV Infection

Treatment for HIV-infected persons who are latently infected with *M. tuberculosis* is an important part of the United States strategy for the elimination of TB and is also an important personal health intervention because of the serious complications associated with active TB in HIV-infected persons. Four studies of HIV-infected persons have evaluated 6-month and 12-month regimens of daily isoniazid. In summary, these data indicate that a) the optimal duration of isoniazid preventive therapy should be greater than 6 months to provide the maximum degree of protection against TB; b) therapy for 9 months appears to be sufficient; c) therapy for greater than 12 months does not appear to provide additional protection; and d) the available data suggest that the protection obtained from isoniazid preventive therapy regimens should be the same whether the drug is administered daily or twice a week. Isoniazid preventive therapy has not been found to be useful or cost-effective in preventing TB when administered to TST-negative or anergic HIV-infected persons.

Short-Course Multidrug Regimens for TB Preventive Therapy

Four clinical trials conducted among HIV-infected populations have evaluated courses of preventive therapy that are shorter than 6 months and that include rifampin in combination with isoniazid or pyrazinamide. Available data indicate that in the United States, a regimen of rifampin and pyrazinamide administered daily for 2 months is a reasonable treatment option for HIV-infected adults with latent *M. tuberculosis* infection. Available data do not permit CDC to make a definitive statement regarding the intermittent (i.e., twice a week) administration of a 2-month regimen of rifampin and pyrazinamide.

PART II. RECOMMENDATIONS

This section of the report provides clinicians with recommendations for diagnosing, treating, and preventing TB among persons coinfected with HIV while concurrently promoting optimal antiretroviral care for these patients.

Active Tuberculosis

Prompt initiation of effective antituberculosis treatment rapidly renders patients noninfectious, reducing the risk of disease transmission, increasing the chance of cure, and minimizing risk of TB-related mortality.

Optimal management of HIV-related tuberculosis is based on the following principles:

- Rule out active tuberculosis in all HIV-infected persons with TB-like symptoms.
- Recognize that typical signs of TB, including classic chest X-ray findings, may be absent and atypical signs are common in HIV-infected patients with active TB.
- Evaluate thoroughly all HIV-infected patients with positive TST's to exclude active TB.
- Initiate multidrug antituberculous chemotherapy in all HIV-infected persons in whom active tuberculosis is suspected and evaluation is in progress.
- Treat all persons with HIV and tuberculosis with DOT.
- Counsel and offer HIV testing to all patients with tuberculosis.
- Evaluate for antiretroviral therapy all HIV-infected patients undergoing treatment for TB.

Treatment Options for Patients with HIV Infection and Drug-Susceptible Pulmonary TB

The currently recommended treatment regimens for patients with HIV infection and drug-susceptible pulmonary TB are shown in Table 1. Recommended dosages for each of the drugs are shown in Table 2.

The final decision on the duration of therapy should consider the patient's response to treatment. For patients with delayed response to treatment, the duration of rifamycin-based regimens should be prolonged from 6 months to 9 months (or to 4 months after culture conversion is documented).

The minimum duration of nonrifamycin, streptomycin-based TB treatment regimens is 9 months. For patients with delayed response to treatment, the duration of streptomycin-based regimens should be prolonged from 9 months to 12 months (or to 6 months after culture conversion is documented).

Latent *M. tuberculosis* Infection

When caring for persons with HIV infection, clinicians should make aggressive efforts to identify those who also are infected with *M. tuberculosis*. Because the reliability of the TST can diminish as the CD4+ T-cell count declines, TB screening with TST should be performed as soon as possible after HIV infection is diagnosed. Because the risk of infection and disease with *M. tuberculosis* is

Table 1. Treatment regimen for HIV-related TB

Induction Phase		Continuation Phase		Considerations for HIV Therapy	Comments
Drugs	Interval and Duration	Drugs	Interval and Duration		
Six-month RFB-based therapy (may be prolonged* to 9 months)					
•INH •RFB •PZA† •EMB†	Daily for 2 months (8weeks)	•INH •RFB	Daily or 2 times/week for 4 months (18 weeks)	RFB should not be used concurrently with ritonavir, hard-gel saquinavir (Invirase™), or delavirdine. A 20%-25% increase in the dose of protease inhibitors or NNRTIs might be necessary. The patient should be monitored carefully for RFB drug toxicity (arthalgia, uveitis, leukopenia) if RFB is used concurrently with protease inhibitors or NNRTIs. Evidence of decreased antiretroviral drug activity should be assessed periodically with HIV RNA levels. No contraindication exists for the use of RFB with NRTIs.	If the patient also is taking indinavir, nelfinavir, or amprenavir, the daily dose of RFB is decreased from 300mg to 150mg. The twice weekly dose of RFB (300mg) remains unchanged if the patient is also taking these protease inhibitors. If the patient also is taking efavirenz, the daily or twice weekly dose of RFB is increased from 300mg to 450mg. Three-times-a-week administration of RFB used in combination with antiretroviral therapy has not been studied.
	or		or		
•INH •RFB •PZA† •EMB†	Daily for 2 weeks and then 2 times/week for 6 weeks	•INH •RFB	2 times/week for 4 months (18 weeks)		
Nine-month SM-based therapy (may be prolonged* to 12 months)					
•INH •SM •PZA •EMB	Daily for 2 months (8 weeks)	•INH •SM •PZA	2-3 times/week for 7 months (30 weeks)	Can be used concurrently with antiretroviral regimens that include protease inhibitors, NRTIs, and NNRTIs.	SM is contraindicated for pregnant women. Every effort should be made to continue administering SM for the total duration of treatment. When SM is not used for the recommended 9 months, EMB should be added to the regimen and the treatment duration should be prolonged from 9 months (38 weeks) to 12 months (52 weeks).
	or		or		
•INH •SM •PZA •EMB	Daily for 2 weeks and then 2-3 times/week for 6 weeks	•INH •SM •PZA	2-3 times/week for 7 months (30 weeks)		
Six-month RIF-based therapy (may be prolonged* to 9 months)					
•INH •RIF •PZA§ •EMB§ (or SM)	Daily for 2 months (8 weeks)	•INH •RIF	Daily or 2-3 times/week for 4 months (18 weeks)	Protease inhibitors or NNRTIs should not be administered concurrently with RIF. NRTIs can be administered concurrently with RIF. If appropriate, patients should be assessed every 3 months to evaluate the decision to initiate antiretroviral therapy. A 2-week "P-450 induction washout" period may be necessary between the last dose of RIF and the first dose of protease inhibitors or NNRTIs.	SM is contraindicated for pregnant women.
	or		or		
•INH •RIF •PZA§ •EMB§ (or SM)	Daily for 2 weeks and then 2-3 times/week for 6 weeks	•INH •RIF	2-3 times/week for 4 months (18 weeks)		
	or		or		
•INH •RIF •PZA •EMB (or SM)	3 times/week for 2 months (8 weeks)	•INH •RIF •PZA •EMB (or SM)	3 times/week for 4 months (18 weeks)		

EMB=ethambutol; INH=isoniazid; PZA=pyrazinamide; RFB=rifabutin; RIF=rifampin; SM=streptomycin.
NNRTI=nonnucleoside reverse transcriptase inhibitor; NRTI=nucleoside reverse transcriptase inhibitor.

*Duration of therapy should be prolonged for patients with delayed response to therapy. Criteria for delayed response should be assessed at the end of the 2-month induction phase and include a) lack of conversion of the *Mycobacterium tuberculosis* culture from positive to negative or b) lack of resolution or progression of signs or symptoms of TB.
†Continue PZA and EMB for the total duration of the induction phase (8 weeks).
§Continue PZA for the total duration of the induction phase (8 weeks). EMB can be stopped after susceptibility test results indicate *Mycobacterium tuberculosis* susceptibility to INH and RIF.

Table 2. Antituberculosis medications: doses, toxicities, and monitoring requirements

Drug	Dose in mg/kg *(maximum dose)* Route of Administration						Adverse Reactions	Monitoring	Comments
	Daily		Two times/week*		Three times/week*				
	Children	Adults	Children	Adults	Children	Adults			
INH	10-20 *(300 mg)* PO or IM	5 *(300 mg)* PO or IM	20-40 *(900 mg)* PO or IM	15 *(900 mg)* PO or IM	20-40 *(900 mg)* PO or IM	15 *(900 mg)* PO or IM	• Rash • Hepatic enzyme elevation • Hepatitis • Peripheral neuropathy • Mild central nervous system effects • Drug interactions resulting in increased phenytoin (Dilantin) or disulfram (Antabuse) levels	Liver function tests Repeat measurements if • baseline results are abnormal • patient is pregnant or at high risk for adverse reactions • patient has symptoms of adverse reactions	Hepatitis risk increases with age and alcohol consumption. Pyridoxine (Vitamin B_6) might prevent peripheral neuropathy and central nervous system effects.
RIF	10-20 *(600 mg)* PO or IV	10 *(600 mg)* PO or IV	10-20 *(600 mg)* PO or IV	10 *(600 mg)* PO or IV	10-20 *(600 mg)* PO or IV	10 *(600 mg)* PO or IV	• Rash • Hepatitis • Fever • Thrombocytopenia • Flu-like symptoms associated with intermittent dosing • Orange-colored body fluids (secretions, urine, tears)	Complete blood count, platelets, and liver function tests Repeat measurements if • baseline results are abnormal • patient has symptoms of adverse reactions	RIF use contraindicated for patients taking PIs or NNRTIs. Decreases levels of many drugs (e.g., methadone, dapsone, ketoconazole, hormonal contraceptives). Might permanently discolor soft contact lenses.
RFB†	10-20 *(300 mg)* PO or IV or NA§ *(150 mg)* PO or IV or NA¶ *(450 mg)* PO or IV	5 *(300 mg)* PO or IV or NA§ *(150 mg)* PO or IV or NA¶ *(450 mg)* PO or IV	10-20 *(300 mg)* PO or IV or 10-20§ *(300 mg)* PO or IV or NA¶ *(450 mg)* PO or IV	5 *(300 mg)* PO or IV or 5§ *(300 mg)* PO or IV or NA¶ *(450 mg)* PO or IV	Not known Not known Not known	Not known Not known Not known	• Rash • Hepatitis • Fever • Thrombocytopenia • Orange-colored body fluids (secretions, urine, tears) With increased levels of RFB: • Severe arthalgias • Uveitis • Leukopenia	Complete blood count, platelets, and liver function tests Repeat measurements if • baseline results are abnormal • patient has symptoms of adverse reactions Use adjusted daily dose of RFB,§ and monitor for decreased antiretroviral activity and for RFB toxicity if RFB taken concurrently with PIs or NNRTIs.	RFB is contraindicated for patients taking ritonavir, saquinavir (Inverase™), or delavirdine. Reduces levels of many drugs (e.g., PIs, NNRTIs, methadone, dapsone, ketoconazole, hormonal contraceptives). Might permanently discolor soft contact lenses.
PZA	15-30 *(2.0 g)* PO	15-30 *(2.0 g)* PO	50-70 *(3.5 g)* PO	50-70 *(3.5 g)* PO	50-70 *(2.5 g)* PO	50-70 *(2.5 g)* PO	• Gastrointestinal upset • Hepatitis • Rash • Arthralgias • Hyperuricemia • Gout (rare)	Liver function tests and uric acid Repeat measurements if • baseline results are abnormal • patient has symptoms of adverse reactions	Treat hyperuricemia only if patient has symptoms. Might make glucose control more difficult in persons with diabetes.
EMB	15-25 *(1600 mg)* PO	15-25 *(1600 mg)* PO	50 *(4000 mg)* PO	50 *(4000 mg)* PO	25-30 *(2000 mg)* PO	25-30 *(2000 mg)* PO	• Optic neuritis (decreased red-green color discrimination), decreased visual acuity • Rash	Baseline and monthly tests of visual acuity and color vision	Optic neuritis might be unilateral; check each eye separately.
SM	20-40 *(1 g)* IM or IV	15 *(1 g)* IM or IV	25-30 *(1.5 g)* IM or IV	25-30 *(1.5 g)* IM or IV	25-30 *(1.5 g)* IM or IV	25-30 *(1.5 g)* IM or IV	• Ototoxicity (hearing loss or vestibular dysfunction) • Nephrotoxicity	Baseline and repeat as needed audiometry and renal function tests	Ultrasound and warm compresses to injection site might reduce pain. Maximum dose for patients ≥60 years is 1.0 g.

EMB=ethambutol; INH=isoniazid; PZA=pyrazinamide; RFB=rifabutin; RIF=rifampin; SM=streptomycin.
NNRTIs=nonnucleoside reverse transcriptase inhibitors; PI=protease inhibitor.
IM=intramuscular; IV=intravenous; PO=by mouth.

*All intermittent dosing should be administered with directly observed therapy.
†The concurrent use of RFB is contraindicated with ritonavir, saquinavir (Inverase™), and delavirdine. Information regarding the use of rifabutin with saquinavir (Fortovase™), amprenavir, efavirenz, and nevirapine is limited.
§Not applicable. If nelfinavir, indinavir, or amprenavir is administered with RFB, blood concentrations of these protease inhibitors decrease. Thus, when RFB is used concurrently with any of these three drugs, the daily dose of RFB is reduced from 300mg to 150mg (the twice-weekly dose of RFB is unchanged, however).
¶NA=not applicable. If efavirenz is administered with RFB, blood concentrations of RFB decrease. Thus, when RFB is used concurrently with efavirenz, the dose of RFB for both daily and twice weekly administration should be increased from 300mg to 450mg.

particularly high among HIV-infected contacts of persons with infectious pulmonary or laryngeal TB, these persons must be evaluated for TB as soon as possible after learning of exposure to a patient with infectious TB.

The Mantoux-method TST, with 5 TU of purified protein derivative, is used to diagnose *M. tuberculosis* infection. A TST reaction size of greater than or equal to 5 mm of induration is considered positive (i.e., indicative of *M. tuberculosis* infection) in persons who are infected with HIV. Whenever *M. tuberculosis* infection is suspected in a patient, an evaluation to rule out active TB and assess the need for preventive therapy should be conducted. All TST-positive persons coinfected with HIV should complete a full recommended course of preventive therapy unless such therapy is contraindicated.

HIV-infected persons who have had recent contact with an infectious TB patient should receive TB preventive treatment, regardless of their age, results of TSTs, or history of previous TB preventive treatment

HIV-infected persons with a history of prior untreated or inadequately treated, healed TB should receive TB preventive treatment, regardless of their age or results of TSTs.

Several TB preventive therapy regimens are currently recommended and these are shown in Table 3.

Virginia Cases of HIV-related TB Disease

Over the past five years, about 6% of all persons diagnosed with TB disease in Virginia were coinfected with HIV. However, in 1998, less that two-thirds (64%) of all Virginians diagnosed with TB disease were tested for HIV. Current guidelines from the American Thoracic Society and the Centers for Disease Control and Prevention state that all persons with TB infection or disease should be tested for HIV.

Do you have questions about TB or HIV-related TB disease? For information, please call the Division of Tuberculosis Control at the Virginia Department of Health: (804)786-6251.

Table 3. TB preventive therapy regimens for adults with HIV infection

Drug	Interval and Duration	Comments	Indications	Contraindications
INH	Daily for 9 months	INH can be administered concurrently with NRTIs, protease inhibitors, or NNRTIs.	HIV-infected persons who are candidates for TB preventive therapy.	History of an INH-induced reaction, including hepatic, skin, or other allergic reactions, or neuropathy.
INH	2 times/week for 9 months		DOPT must be used when twice-weekly dosing is used.	Known exposure to person who has INH-resistant TB.
				Chronic severe liver disease.
RIF and PZA*	Daily for 2 months	Protease inhibitors or NNRTIs should not be administered concurrently with RIF; in this situation, an alternative is the use of RFB† and PZA.	HIV-infected persons who are candidates for TB preventive therapy.	History of a rifamycin-induced reaction, including hepatic, skin, or other allergic reactions, or thrombocytopenia.
RFB and PZA*	Daily for 2 months	If RFB is administered, patient should be monitored carefully for potential RFB drug toxicity and potential decreased antiretroviral drug activity.	HIV-infected persons known to be contacts of patient who has INH-resistant, rifamycin-susceptible TB.	Pregnancy.
				Chronic severe hyperuricemia.
		Dose adjustments, alternative therapies, or other precautions might be needed when rifamycins are used (e.g., patients using hormonal contraceptives must be advised to use barrier methods, and patients using methadone require dose adjustments).		Chronic severe liver disease.

INH=isoniazid; PZA=pyrazinamide; RFB=rifabutin; RIF=rifampin.
DOPT=directly observed preventive therapy; NNRTI=nonnucleoside reverse transcriptase inhibitor; NRTI=nucleoside reverse transcriptase inhibitor.

***For patients with intolerance to PZA, some experts recommend the use of rifamycin (RIF or RFB) alone for preventive treatment. Most experts agree that available data support the recommendation that this treatment can be administered for as short a duration as 4 months, although some experts would treat for 6 months.**
†The concurrent use of RFB is contraindicated with ritonavir, hard-gel saquinavir (Invirase™), and delavirdine. The information regarding the use of RFB with soft-gel saquinavir (Fortovase™), amprenavir, efavirenz, and nevirapine is limited.

Central Virginia Rabies Conference

For Physicians and Veterinarians

6:00 pm to 9:10 pm

March 30, "The Place" at Innsbrook Corporate Center, Glen Allen

March 31, Hotel Roanoke, Roanoke

Topics

Epidemiology of Animal and Human Rabies in the U.S.

Rabies Trends and Control Procedures in Virginia

Principles of Pre- and Post Exposure Prophylaxis

Is It Rabies? - the Virginia Case

Speakers

Charles Rupprecht, VMD, MS, PhD, Chief, Rabies Section, Centers for Disease Control and Prevention

Thomas Kerkering, MD, Professor of Medicine, Medical College of Virginia

Suzanne Jenkins, VMD, MPH, Assistant State Epidemiologist, Office of Epidemiology, Virginia Department of Health

Robert Stroube, MD, MPH, Director, Office of Epidemiology, Virginia Department of Health

Pre-Registration Required, (804) 786-6262 (Glen Allen location) or (540) 381-7100, ext. 156 (Roanoke location)

Seating is limited. Category I CME Credits available.

A similar conference for Public Health, Animal Control and Other Interested Professionals will be held during the afternoons of the same dates. Pre-Registration Required. Call (804) 786-6262 or (540) 381-7100, ext. 156 for more information.

Presented by the Office of Epidemiology, Virginia Department of Health, with support from Chiron Corporation, Merial Limited and the Virginia Veterinary Medical Association.

Cases of Selected Notifiable Diseases Reported in Virginia*

Disease	Total Cases Reported, January 1999						Total Cases Reported Statewide, January		
		Regions							
	State	NW	N	SW	C	E	This Year	Last Year	5 Yr Avg
AIDS	52	2	6	1	28	15	52	36	66
Campylobacteriosis	20	4	4	6	2	4	20	17	14
E. coli O157:H7	2	2	0	0	0	0	2	0	1
Giardiasis	16	5	4	0	5	2	16	19	9
Gonorrhea	1037	55	75	62	261	584	1037	548	854
Hepatitis A	3	1	1	0	1	0	3	10	9
B, acute	2	0	1	0	1	0	2	3	4
C/NANB, acute	0	0	0	0	0	0	0	1	1
HIV Infection	40	2	10	1	15	12	40	41	52
Lead in Children†	39	1	8	7	15	8	39	20	20
Legionellosis	1	1	0	0	0	0	1	2	1
Lyme Disease	0	0	0	0	0	0	0	1	0
Measles	0	0	0	0	0	0	0	0	0
Meningococcal Infection	1	0	1	0	0	0	1	4	3
Mumps	0	0	0	0	0	0	0	0	0
Pertussis	1	1	0	0	0	0	1	0	1
Rabies in Animals	20	2	4	3	4	7	20	34	23
Rocky Mountain Spotted Fever	0	0	0	0	0	0	0	0	0
Rubella	0	0	0	0	0	0	0	0	0
Salmonellosis	33	5	4	12	6	6	33	41	43
Shigellosis	2	0	2	0	0	0	2	8	14
Syphilis, Early§	30	0	2	12	8	8	30	62	78
Tuberculosis	9	2	0	0	1	6	9	7	17

Localities Reporting Animal Rabies This Month: Accomack 1 raccoon; Amelia 1 raccoon; Appomattox 1 raccoon; Fairfax 2 raccoons, 1 skunk; Hampton 1 raccoon; Hanover 1 groundhog, 1 raccoon; Isle of Wight 1 raccoon; Loudoun 1 raccoon; Lynchburg 1 cat; Middlesex 1 raccoon; Newport News 1 raccoon; Page 2 raccoons; Pulaski 1 cow; Suffolk 1 raccoon; Sussex 1 raccoon; Virginia Beach 1 raccoon.

Occupational Illnesses: Asbestosis 47; Carpal Tunnel Syndrome 45; De Quervain's Syndrome 4; Hearing Loss 28; Lead Exposure 9; Pneumoconiosis 14.

*Data for 1999 are provisional. †Elevated blood lead levels ≥10µg/dL.

§Includes primary, secondary, and early latent.

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