

Treatment of Drug-Resistant Tuberculosis

Introduction

Drug-resistant tuberculosis (TB) is TB disease caused by *M. tuberculosis* organisms that are resistant to at least one first-line anti-TB drug. Multidrug-resistant TB (MDR TB) is resistant to more than one anti-TB drug and at least isoniazid (INH) and rifampin (RIF). Treating and curing drug-resistant TB is complicated. Inappropriate management can have life-threatening results. **Drug-resistant TB should be managed by or in close consultation with an expert in the disease.**

Drug resistance is proven by drug-susceptibility testing. However, since this testing can take weeks, treatment should be started with an empirical treatment regimen based on expert advice as soon as drug-resistant TB disease is suspected. When the testing results are known, the treatment regimen should be adjusted according to the results. Patients should be monitored closely throughout treatment. Directly observed therapy (DOT) always should be used in the treatment of drug-resistant TB to ensure adherence.

Special Considerations

HIV-Infected Persons

Although the treatment of drug-resistant TB in persons with HIV infection is the same as for patients without HIV (see Table 1), management of HIV-related TB requires expertise in the management of both HIV and TB. Providers must monitor the interactions among many of the antiretroviral drugs. RIF should not be used with most antiretroviral drugs. Rifabutin, which has fewer problematic drug interactions, may be used in place of RIF. As new antiretroviral agents and pharmacokinetic data become available, these recommendations are likely to be modified.

Visit http://www.cdc.gov/nchstp/tb/tb_hiv_drugs/toc.htm for the most recent recommendations.

Children

Treatment for children who have TB disease after exposure to a drug-resistant case should be guided by the source-case susceptibility results. When a source is unknown and circumstances suggest an increased risk of drug resistance, children should be treated with a standard four-drug initial-phase regimen until their susceptibility pattern is known. Ethambutol (EMB) can be used safely (15-20 mg/kg per day), in the likelihood of INH resistance. Streptomycin, kanamycin, or amikacin also can be selected as the fourth drug. Long-term use of fluoroquinolones in children has not been approved. However, most experts agree that these drugs should be considered for children with MDR TB. Consultation with a specialist in pediatric TB treatment is recommended.

Pregnant Women

Case management for pregnant women who have drug-resistant TB requires consultation with an expert because most second-line drugs can have harmful effects on the fetus. Pyrazinamide (PZA) should not be used as part of the treatment regimen for pregnant women. Counseling concerning risks to the fetus should be provided.

Close Contacts of Drug-Resistant TB Patients

Contacts of isoniazid-resistant TB. For persons who have been exposed to INH-resistant, RIF-susceptible TB and are known or suspected to have latent TB infection (LTBI), a 4-month regimen of daily RIF is recommended. When RIF cannot be used, rifabutin may be substituted.

Special Considerations, continued

Close Contacts of Drug-Resistant TB Patients

Contacts of MDR TB. For persons with known or suspected LTBI resistant to both INH and RIF, alternative regimens should be considered. Alternative regimens should include two drugs to which the TB strain is susceptible. A potential regimen should include a daily fluoroquinolone. Contacts who are not immunosuppressed may be treated for 6 months or observed without treatment. All persons with suspected MDR LTBI should be monitored for 2 years regardless of the treatment regimen.

For More Information

American Thoracic Society, Centers for Disease Control and Prevention, and Infectious Diseases Society of America. Treatment of tuberculosis. *MMWR* 2003; 52 (No. RR-11).
www.cdc.gov/MMWR/PDF/rr/rr5211.pdf

American Thoracic Society and Centers for Disease Control and Prevention. Targeted tuberculin testing and treatment of latent TB infection. *MMWR* 2000;49 (No. RR- 6).
www.cdc.gov/MMWR/PDF/rr/rr4906.pdf

American Thoracic Society and Centers for Disease Control and Prevention. Update: Adverse event data and revised American Thoracic Society/CDC recommendations against the use of rifampin and pyrazinamide for treatment of latent tuberculosis infection. *MMWR* 2003; 52 (No. 31).
www.cdc.gov/mmwr/preview/mmwrhtml/mm5231a4.htm

Centers for Disease Control and Prevention. Updated guidelines for the use of rifamycins for the treatment of tuberculosis among HIV-infected patients taking protease inhibitors or nonnucleoside reverse transcriptase inhibitors. *MMWR* 2004; 53 (No. 2).
www.cdc.gov/mmwr/preview/mmwrhtml/mm5302a6.htm