TB Elimination
Treatment of Drug-Resistant Tuberculosis

Introduction

Drug-resistant tuberculosis (TB) is TB disease caused by *Mycobacterium tuberculosis* (*M.tb.*) organisms that are resistant to at least one first-line anti-TB drug. Multidrug-resistant TB (MDR TB) is caused by an organism that is resistant to at least isoniazid (INH) and rifampin (RIF), the two most potent TB drugs. 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 diagnosed by drug-susceptibility testing in the laboratory. However, since these tests can take several weeks, treatment could be started with an empirical treatment regimen based on expert advice, depending on the probability that the person has drug-resistant TB disease. When 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) should always be used in the treatment of drug-resistant TB to ensure adherence.

Special Considerations

People infected with HIV

Although the treatment of drug-resistant TB in persons with HIV infection is similar to patients without HIV (see Table 1) (http://www.cdc.gov/tb/publications/guidelines/TB_HIV_Drugs/Table1.htm), 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 Managing Drug Interactions in the Treatment of HIV-Related Tuberculosis (http://www.cdc.gov/tb/publications/guidelines/TB_HIV_Drugs/default.htm) for the most recent recommendations.

Children

In cases of suspected drug-resistant TB in a child, specimens for microbiological evaluation should be obtained. For pulmonary disease, if the child is too young to provide adequate sputum specimens, nasogastric lavage or bronchoscopy should be considered. For pleural disease, thoracentesis with pleural biopsy may be considered. For extrapulmonary disease, needle aspiration or biopsy of the affected tissue can provide a microbiological diagnosis. In addition to microscopy, culture, and drug susceptibility tests, some of the newer molecular methods may be able to detect *M.tb.* DNA as well as DNA mutations associated with drug resistance. Initial treatment for children with suspected drug-resistant TB disease (e.g., after exposure to a person with drug-resistant TB) should be guided by the source-case susceptibility results until the drug susceptibility results for the child's isolate are available. If an isolate from the child under treatment is not available, drug susceptibilities can be inferred by the drug susceptibility pattern of isolates from the adult source case. 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 with close clinical monitoring, until their susceptibility pattern is known and then the regimen should be adjusted accordingly. As in adults, treating and curing drug-resistant TB is complicated; all children with suspected or

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confirmed drug-resistant TB should be managed in consultation with an expert. For more information on TB in Children, please visit the TB in Children Web page (http://www.cdc.gov/tb/topic/populations/TBinChildren/default.htm).

Pregnant Women

Case management for pregnant women who have drug-resistant TB requires consultation with an expert because most second-line anti-TB drugs have unknown effects on the fetus. In most cases, pyrazinamide (PZA) is not recommended as part of the treatment regimen for pregnant women. Counseling concerning risks to the fetus should be provided. To learn more about TB and pregnancy, please visit the Tuberculosis and Pregnancy (http://www.cdc.gov/tb/publications/factsheets/specpop/pregnancy.htm) Web page.

Close Contacts of Drug-Resistant TB Patients

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

Contacts of MDR TB. For persons with known or suspected LTBI resulting from contact with a source case who had TB disease resistant to both INH and RIF, alternative regimens should be considered. Alternative regimens should include two drugs to which the TB strain is susceptible. 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

1. American Thoracic Society, Centers for Disease Control and Prevention, and Infectious Diseases Society of America. Treatment of tuberculosis. *MMWR* 2003; 52 (No. RR-11). http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5211a1.htm

2. 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). http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4906a1.htm

3. 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). http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5231a4.htm

4. 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). http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5302a6.htm

5. Francis J. Curry National Tuberculosis Center and California Department of Public Health, 2008: Drug-Resistant Tuberculosis: A Survival Guide for Clinicians, 2nd ed. (http://www.currytbcenter.ucsf.edu/drtb/)

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http://www.cdc.gov/tb