Tuberculosis, Multidrug-Resistant, in Adults

What We Know

› Tuberculosis (TB) is a chronic infection caused by Mycobacterium tuberculosis, which spreads by aerosolized droplets that are released when an infected person talks or coughs. (1,9) (For more information, see Quick Lesson About ... Tuberculosis in Adults and Quick Lesson About ... Tuberculosis in Children and Adolescents)
   • Approximately one-third of the world’s population is infected with M. tuberculosis, and about 10% of infected individuals will develop active TB during their lifetime. (1,5)
   • In the United States, the incidence of TB has declined by 3.8% each year since 2000. Although it is estimated that rates of new cases and deaths due to TB are declining throughout the world, the emergence and spread of resistance to anti-TB drugs may reverse this trend. (5)
› Drug-resistant TB is a global problem that is associated with increased morbidity, mortality, and healthcare costs. (4,6,9,12)
   • Multidrug-resistant TB (MDR-TB) is defined as a strain of TB with documented resistance to both isoniazid and rifampin, which are the two most powerful anti-TB drugs currently available. (3,4,6,7,12)
     - The World Health Organization (WHO) estimates that 480,000 cases of MDR-TB occurred in 2014. (12)
     - Globally in 2014, MDR-TB accounted for 3.3% of newly diagnosed cases of TB and 20% of previously treated TB cases; major variation in prevalence by geographic region was reported. (12)
     - The highest rates of MDR-TB were found in India, China, and the Russian Federation. (12)
   • Extensively drug-resistant TB (XDR-TB) is defined as a strain of TB with documented resistance to all first-line agents, an injectable agent (e.g., streptomycin, kanamycin, amikacin, capreomycin), and to a fluoroquinolone (e.g., moxifloxacin, gatifloxacin, levofloxacin, ofloxacin, ciprofloxacin). (3,6,12)
     - Nearly 10% of cases of MDR-TB are XDR-TB; at least one case of XDR-TB was reported by 105 countries in 2014. (12)
› Drug resistance can be classified as primary or acquired. (6)
   • Primary drug resistance refers to the development of resistant TB in a person with no history of TB treatment, implying that the patient was infected with a drug-resistant strain of TB
   • Acquired drug resistance refers to the development of resistant TB in a person with a history of TB treatment. In these cases, it is assumed that drug resistance was acquired during treatment for TB, although infection or reinfection with a resistant strain of TB is possible
› Risk factors for drug-resistant TB include factors related to treatment and factors related to the specific patient. (5,6)
   • Poor adherence to treatment, incorrectly prescribed treatment regimens, and inadequate drug supplies contribute to the development of drug-resistant strains of TB. (1)
• A history of TB, recent contact with a person who has drug-resistant TB, and HIV infection are risk factors for infection with or reactivation of a drug-resistant TB strain\(^1\)

–HIV infection is associated with a substantially elevated risk for developing active TB, which may contribute to the spread of resistant strains of TB\(^2\)

–Researchers in a recent prospective study of 1,278 patients with MDR-TB in 8 countries found a significant association between previous treatment with a second-line anti-TB drug and the development of resistance to these drugs\(^3\)

Diagnosis of drug-resistant TB requires microbiologic confirmation of resistance\(^6\)-\(^10\)

• Diagnosis is complicated by the need for pure cultures of \textit{M. tuberculosis} and the bacterium’s slow replication rate. In addition, the equipment and supplies needed for drug susceptibility testing are often unavailable in settings with limited resources\(^2\)-\(^10\)

–Drug-resistance testing is accomplished by incorporation of anti-TB drugs in culture media; results for these tests can take several weeks, which often causes a delay in diagnosis

- Microscopic-observation drug susceptibility and thin layer agar assays appear to be inexpensive, rapid alternatives to conventional drug-resistance testing methods\(^10\)

–Use of molecular methods to identify bacterial genetic mutations that are responsible for drug resistance is becoming more common in industrialized countries\(^2\)-\(^10\)

It is not known whether strains of MDR-TB and XDR-TB are more transmittable or more virulent than drug-susceptible strains of TB\(^5\)

• Management of MDR-TB and XDR-TB is more complicated and difficult than management of TB strains that are not resistant because treatment must involve the use of second-line drugs that are less effective and more toxic, which reduces the chance of a cure\(^6\)-\(^10\)

–According to the WHO, all first-line drugs (e.g., isoniazid, rifampicin, pyrazinamide, ethambutol) to which the TB strain that has been identified as being responsible for the infection is still susceptible should be used, including a fluoroquinolone (e.g., moxifloxacin, gatifloxacin, levofloxacin, ofloxacin, ciprofloxacin) whenever possible; a daily injectable agent (e.g., streptomycin, kanamycin, amikacin, capreomycin) until sputum culture has been negative for 6 consecutive months; and other second-line agents (e.g., ethionamide, prothionamide, cycloserine, para-aminosalicylic acid, thiacetazone) to increase the total number of drugs to which the TB strain is susceptible to a total of four or five\(^6\)

- In 2014, 50% of patients with MDR-TB were successfully treated\(^12\)

- In 2014, ~ 190,000 persons died of MDR-TB\(^12\)

–Patients should receive directly observed therapy (DOT) for at least 20 months\(^13\)

- DOT is prescribed to improve adherence to treatment; however, the authors of a meta-analysis concluded that DOT was not significantly better than self-administered therapy in preventing microbiologic failure, relapse, or acquired drug resistance\(^11\)

–Researchers are working to identify new drugs with efficacy against MDR-TB. In 2012, the U.S. FDA approved the new drug bedaquiline (Sirturo) for treatment of adults with MDR-TB when other treatment options are not available. WHO has issued interim guidelines regarding the use of bedaquiline\(^13\)

- Researchers of a study on MDR-TB and the combined used of delamanid and bedaquiline report that a small number of patients responded positively to the treatment; in some cases, however, some patients developed adverse events (e.g., poor drug tolerability); the recommendation is that more specialized experience combining these two drugs may address the issue of MDR-TB\(^8\)

• Pulmonary resection may be indicated in patients with MDR-TB who have localized TB involvement such as cavitary lesions or disease in a single lobe of the lung\(^14\)

What We Can Do

› Learn about MDR-TB so you can accurately assess your patients’ personal characteristics and health education needs; share this knowledge with your colleagues

› Follow facility infection control protocols for airborne precautions and for mandatory reporting of infectious disease to the local public health department so it can begin contact investigation and screening of other contacts

› For the most effective treatment, request referral to an infectious disease expert in the field of MDR-TB if one is not already part of the treatment team
› Assess patient history and evaluate risk factors for MDR-TB
› As appropriate, administer purified protein derivative (PPD) skin tests and interpret results
› Administer the prescribed regimen for anti-TB medications, and educate patients about dosage, potential side effects, and potential drug interactions
› Emphasize the importance of strict adherence to the prescribed medication regimen(1)
› Request testing for HIV infection for your patients with MDR-TB and XDR-TB, and emphasize the importance of receiving testing for HIV infection
› Request referral to a social worker, if appropriate, for identification of local resources for support groups, in-home resources, and financial, medical, or legal resources
› Educate that more information can be obtained at the American Lung Association at http://www.lung.org/
**References**


**Coding Matrix**

*References are rated using the following codes, listed in order of strength:

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