

## New Guidelines Issued for the Treatment of Drug-Resistant Tuberculosis

In November 2019, the American Thoracic Society (ATS), the European Respiratory Society (ERS), the Infectious Diseases Society of America (IDSA) and the U.S. Centers for Disease Control and Prevention (CDC) issued new guidelines for the treatment of drug-resistant tuberculosis (DR-TB).

The guidelines were published in the November 15, 2019 issue of the American Journal of Respiratory Critical Care Medicine (https://www.atsjournals.org/doi/pdf/10.1164/rccm.201909-1874ST).

DR-TB is a global health issue. According to the World Health Organization (WHO), there were 484,000 new TB patients globally in 2018 who were resistant to one or more anti-TB drugs. Of that number, 78% had multi drug-resistant (MDR) TB, where the patient is resistant to isoniazid (INH) and rifampin (RIF). Three countries accounted for 50% of drug-resistant TB cases in 2018 - India (27%), China (14%) and the Russian Federation (9%).

Of the 9,025 new TB cases in the U.S. in 2018, 703 (or 7.7%) were resistant to one or more anti-TB drugs. Of that number, 605 (6.7%) were resistant to INH alone, 97 (1%) had MDR TB and one patient had XDR TB, defined as resistant to INH, RIF, any fluoroquinolone and at least one of three injectable second-line drugs (i.e., amikacin, kanamycin, or capreomycin).

DR-TB can develop when a patient with TB disease is not treated with the recommended anti-TB drug regimen and/or does not complete the full course of therapy. Patients with DR-TB disease can transmit the DR-TB bacteria to others.

The best way to prevent drug resistance is to use the recommended anti-TB drug regimen and to provide treatment via directly observed therapy (DOT) to ensure treatment completion.

Patients with MDR and especially XDR TB are often very ill, may need to be hospitalized for an extended period early-on during treatment and can require treatment for two years or more. The cost of treating XDR and MDR TB is therefore very high.

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In the U.S., it is estimated that it costs \$544,000 to treat one case of XDR and \$175,000 to treat a case of MDR. For comparison, the typical cost to treat drug-susceptible TB is \$19,000.

The new guidelines list six good practices for clinicians to follow for patients suspected of, or being evaluated for, drug-resistant TB:

- 1. Consult with a TB expert when there is suspicion or confirmation of a case of DR-TB. This guidance is consistent with the new requirement in the current five-year (2020-2024) cooperative agreement between the CDC and U.S. TB programs that clinicians managing a suspected or confirmed case of MDR or XDR TB must consult with the assigned CDC-funded TB Center of Excellence (COE). The COE responsible for Pennsylvania is the Global TB Institute (GTBI) at Rutgers (1-800-482-3627). TB Clinicians in Pennsylvania can also consult with the state TB consultants for adult or pediatric TB by contacting the TB Program at 717-787-6267.
- 2. Molecular drug-susceptibility tests to detect mutations associated with drug resistance should be done promptly.
- 3. The TB treatment regimen should include only those drugs to which the patient's *M. tuberculosis* isolate is known or highly likely to be drugsusceptible.
- 4. The patient's response to treatment should be monitored clinically, radiographically, and bacteriologically. Patients with pulmonary TB should have cultures obtained at least monthly. If cultures remain positive after 3 months of treatment, drug susceptibility tests should be repeated.
- 5. Patients should be educated and asked about adverse effects at each visit.
- 6. **Patient-centered case management** helps patients understand their diagnoses, understand and participate in their treatment, and discuss potential barriers to treatment.

If you have a suspected or confirmed case of DR-TB, notify the TB Program promptly by calling 717-787-6267 and speaking with the TB program manager.

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