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Guest Editors: Logan Bailey and Lindsey Hansen, Pharm.D. Candidates 2025; Wesley Lindsey, Pharm.D.



Key Inforbits

- What is tuberculosis?
- The importance of early diagnosis
- Current TB treatment options
- Preventing the spread of TB
- New developments in TB treatment
- Global efforts to end TB



Understanding Tuberculosis: A Brief Overview

Tuberculosis (TB) is an infectious disease caused by the bacterium *Mycobacterium tuberculosis*.¹ While it primarily affects the lungs, it can spread to other parts of the body if left untreated. TB occurs in two phases: latent and active. In the latent phase, the immune system keeps the infection under control, and the individual experiences no symptoms. People with latent TB cannot transmit the disease to others, and the only indication of infection is typically a positive TB skin or blood test. In contrast, active pulmonary TB presents with symptoms such as a persistent cough, hemoptysis (coughing up blood), purulent sputum, fever, night sweats, and unintentional weight loss. This form of TB is highly contagious and spreads through aerosolized droplets when an infected person coughs, sneezes, or speaks. Tuberculosis is the infectious disease that causes the most deaths worldwide- as a comparison, the World Health Organization (WHO) estimates 1.25 million TB deaths versus 0.63 million deaths from the Human Immunodeficiency virus (HIV).²

The Importance of Early Diagnosis

Early diagnosis of TB includes detection of individuals without symptoms in the latent stage of TB as well as detection of TB in its preliminary stages of infection by the nonspecific symptoms it creates such as persistent cough, fever, night sweats, and unintentional weight loss.³ Early detection of TB is vital as it prevents the transmission of the disease to others and prevents more severe symptomatology that occurs when TB remains untreated such as extensive pulmonary destruction, respiratory failure, sepsis, and a two-fold increase in lung cancer risk.⁴ Around 75% of patients who experience a reactivation of TB experienced multiple missed opportunities for detection of the disease.⁵ Frequent causes of these missed detection opportunities included chronic respiratory symptoms, outpatient or emergency department settings, weekend visits, patient age, presentation during flu season, and prior fluoroquinolone use.

Current Treatment Options for Tuberculosis

The primary goals of tuberculosis treatment are to eradicate the infection, prevent transmission to others, reduce the risk of recurrence, and minimize drug resistance.⁶ There are two main approaches to the treatment of active TB.

The first is the traditional six-month regimen, commonly known as RIPE therapy, which includes rifampin, isoniazid, pyrazinamide, and ethambutol.

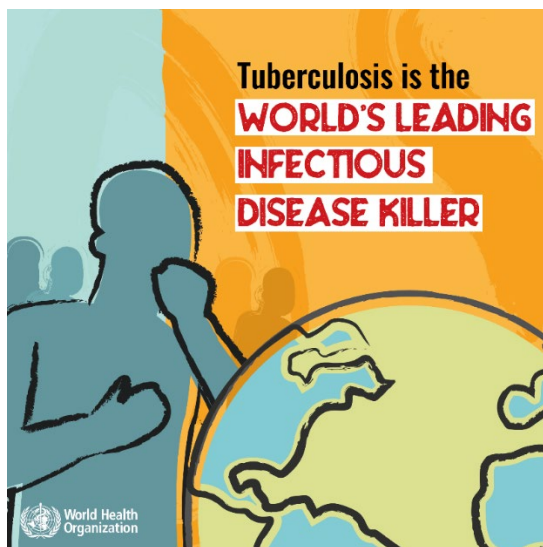
The alternative is a four-month regimen consisting of isoniazid, rifapentine, moxifloxacin, and pyrazinamide for patients who meet specific eligibility criteria.

Both regimens consist of an intensive phase and a continuation phase. The intensive phase typically lasts two months and aims to reduce the likelihood of developing resistance.⁶ The duration and medication selection for the continuation phase depend on the patient's clinical course.

Most patients show clinical improvement within 2–3 weeks of starting effective treatment.⁷ If symptoms do not improve, further evaluation is necessary to assess potential drug resistance, non-adherence, or other treatment-related issues. In the traditional regimen, if susceptibility testing confirms that the TB strain is sensitive to isoniazid and rifampin at the transition to the continuation phase, ethambutol can be discontinued.⁶ In the alternative regimen, the continuation phase proceeds without pyrazinamide.

The treatment of latent TB involves shorter and more manageable regimens compared to active TB treatment.⁸ There are three primary recommended regimens: isoniazid and rifapentine taken once weekly for three months, rifampin taken daily for four months, and a combination of isoniazid and rifampin taken daily for three months.⁸ Additionally, an alternative regimen of isoniazid for six or nine months, administered daily or twice weekly, is also an option. However, this extended treatment duration is generally less preferred due to lower therapy completion rates.

Drug-Resistant TB: Challenges and Solutions



There are three primary types of drug resistance in TB.⁹ Mono-resistant TB refers to strains resistant to a single anti-TB drug. Polyresistant TB is resistant to more than one drug but does not include simultaneous resistance to both isoniazid and rifampin. Multidrug-resistant TB (MDR-TB) is characterized by resistance to both isoniazid and rifampin, with or without additional resistance to other drugs. Treating drug-resistant TB requires careful consideration of factors such as disease severity, susceptibility testing, cross-resistance, and prior use of antituberculosis medications.

One of the key goals of antibiotic treatment in tuberculosis is preventing the emergence and spread of antibiotic resistance.¹⁰ Ensuring patient adherence to therapy is crucial, as incomplete treatment can lead to further drug resistance. Additionally, selecting appropriate antibiotic regimens helps achieve complete eradication of the infection, minimize adverse effects, and reduce resistance levels.

The Role of Nutrition in TB

Unexplained weight loss is a common symptom of tuberculosis, highlighting the important role nutrition plays in the recovery process. TB infection can lead to reduced appetite, impaired nutrient absorption, micronutrient deficiencies, and metabolic alterations.¹¹ However, malnutrition is not just a consequence of TB, it is also a risk factor for developing the disease. Studies indicate that individuals with higher body mass indexes (BMIs) have a lower risk of TB infection compared to those with lower BMIs.¹²

Proper nutritional intake can enhance recovery.¹¹ Patients who receive adequate nutrition experience faster bacterial clearance, earlier radiographic improvements, and greater weight gain compared to those with poor nutritional intake.

Global Trends in TB

In 2023, there was an estimated worldwide gap between the number of people diagnosed and officially reported as TB cases of 2.7 million, although the gap has narrowed since 2020.² The WHO identifies thirty nations with a high TB case burden, with Lesotho (664 cases per 100,000), the Philippines (640 per 100,000), and Myanmar (558 cases per 100,000) with the highest estimated incidence rates.²

The UN set a goal of mobilizing at least \$22 billion USD by 2027, but the reality is that funding for TB has been decreasing since 2019- total funding in 2023 for the low to middle income countries with 99% of the TB case burden was \$5.7 billion, significantly short (26%) of the 2027 goal. This gap is largely due to a significant drop in monies promised by the BRICS group of nations (Brazil, Russia, India, China, South Africa), particularly Russia. The UN Global fund contributes more than half of international monies for TB treatment, with the US government providing half of the Global Fund's money. Research on new methods to identify and prevent TB continue globally, with new point-of-care tests being developed by groups from Japan, the US, South Korea, Sweden, and China.²

Emerging Therapies

Several new medications have been developed and approved since the 2010s for treatment of tuberculosis including bedaquiline, a diarylquinolone that blocks the proton pump of ATP synthase; delamanid, a nitroimidazole that inhibits synthesis of a specific cell wall lipid prevalent

Preventing the Spread: The CDC's TB Prevention Suggestions

- Ensure that any case of TB, active or latent, gets treated. Even latent TB can spread.
- Ensure that all TB medicines are taken as directed. Treatment adherence is key to eradication.
- Patients with TB need to cover all coughs with a tissue that is then put into a closed bag and discarded.
- Ensure that patients are quarantined from others until they are given clearance by their medical provider.
- Air out rooms to the outside of the building. TB germs spread in enclosed spaces with stagnant air.

Centers for Disease Control: "Preventing Tuberculosis"
www.cdc.gov/tb/prevention/index.html

in *M. tuberculosis*, and several other medications that are currently in phase 2 trials including multiple oxazolidinones.¹³

The endTB trial, a collaboration between Partners in Health, Médecins Sans Frontières, and Interactive Research and Development, published an article in the *New England Journal of Medicine* on in January 2025 with phase 3 trial results for new all-oral treatment regimens targeting strains of rifampin-resistant, fluoroquinolone-susceptible tuberculosis.¹⁵ Patients in Georgia, India, Kazakhstan, Lesotho, Pakistan, Peru, and South Africa with rifampin-resistant TB were randomized to receive various combinations of new and repurposed antibiotics. Combinations of bedaquiline, linezolid, pyrazinamide, and either moxifloxacin, clofazimine/levofloxacin, or delamanid/linezolid/levofloxacin were found to be noninferior compared to the standard of care produced favorable outcomes in more than 85% of trial participants after 72 weeks of treatment.¹⁴

Frequently Asked Questions about TB

Q: Wait, is TB still a major threat in the United States?

A: Yes, and the incidence rate has been growing steadily since the COVID-19 pandemic. In 2023, there were 9,633 reported cases, an increase of 15.6% compared to 2022 and 8.3% compared to 2019.¹⁵

Q: Isn't that what made the child sick in The Velveteen Rabbit?

A: No, that was scarlet fever.¹⁶ Tuberculosis is what Nicole Kidman's character had in *Moulin Rouge!*¹⁷

Q: Are children particularly susceptible?

A: Yes. Children under 5 years old are at high risk of tuberculosis infection, progressing to disseminated forms of the disease.¹⁸

Q: If someone is infected, are they mandated to quarantine for a particular amount of time?

A: Yes. 42 U.S.C. 264(b and d) "...the apprehension and examination of any individual reasonably believed to be infected with a communicable disease in a qualifying stage..." and "any such individual is found to be infected, he may be detained for such time and in such manner as may be reasonably necessary."¹⁹ 42 U.S.C. 271 specifies that anyone breaking a mandated quarantine is subject to a fine of not more than \$1000, imprisonment, or both.²⁰

Q: Are there any medications that make you more susceptible to tuberculosis?

A: Immunosuppressive therapies such as TNF- α antagonists, high dose systemic corticosteroids (≥ 15 mg of prednisone/day), or immunosuppressive drug therapies given following organ transplantation.²¹

In Summary

Tuberculosis is still a major threat to the safety of the world's population and still occurs within the United States. Existing treatments are effective and new therapies are emerging to counter the growing incidence of drug-resistant tuberculosis; the problem is getting these treatments to the populations in greatest need, then monitoring and follow up as the length of treatment can be contribute to nonadherence.

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The last “dose” ...

“In the end, we must remember that the war against TB will not be won at meetings in Moscow, Delhi or New York. It will be won in communities. It will not be won with declarations. It will be won by nurses, doctors, community health workers and others at the frontlines. Our job is to give them the resources they need to find every last person with TB, to diagnose them, to treat them, and to cure them. That’s the measure of success”.

– Dr. Tedros Adhanom Ghebreyesus, WHO Director-General²²

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