# ADVANCEMENTS IN TUBERCULOSIS PREVENTION AND TREATMENT: A COMPREHENSIVE REVIEW

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**ABSTRACT:**

Tuberculosis (TB) is an infectious disease usually caused by Mycobacterium tuberculosis (MTB) bacteria. Tuberculosis mostly affects the lungs, but it can also affect other body parts. Tuberculosis is spread from one person to another one by the air when people who suffering from active TB in their lungs speak, sneeze, cough, or spit. People who having latent TB do not spread the disease person to person. Chances of active infection occurs more in people who having HIV/AIDS and in those who smoke. Active TB can be diagnosed by chest X-rays, as well as culture of body fluids and microscopic examination. Diagnosis of latent TB can be done by using the tuberculin skin test (TST) or blood tests. Prevention of TB includes early detection, screening those at high risk, treatment of critical cases, and vaccination of infected people with the bacillus Calmette-Guérin (BCG) vaccine. Treatment for TB include the uses of multiple antibiotics therapy over a long period of time. This review article aims to understand the TB's epidemiology causes, signs and symptoms, risk factors, pathogenesis, diagnosis, prevention, treatment.

**KEYWORDS:** Tuberculosis, prevention, treatment, advancements, vaccines, drug resistance.

## 1. INTRODUCTION-

TB is caused by bacteria (Mycobacterium tuberculosis) and it most often affects the lungs. TB is spread through the air when people with lung TB cough, sneeze or spit. A person needs to inhale only a few germs to become infected. Every year, 10 million people fall ill with tuberculosis (TB). Despite being a preventable and curable disease, 1.5 million people die from TB each year – making it the world's top infectious killer. [1] TB is the leading cause of death of people with HIV and also a major contributor to antimicrobial resistance. Most of the people who fall ill with TB live in low- and middle-income countries, but TB is present all over the world. About half of all people with TB can be found in 8 countries: Bangladesh, China, India, Indonesia, Nigeria, Pakistan, Philippines and South Africa. About a quarter of the global population is estimated to have been infected with TB bacteria, but most people will not go on to develop TB disease and some will clear the infection. [2] Those who are infected but not (yet) ill with the disease cannot transmit it. People infected with TB bacteria have a 5–10% lifetime risk of falling ill with TB. Those with compromised immune systems, such as people living with HIV, malnutrition or diabetes, or people who use tobacco, have a higher risk of falling ill. Tuberculosis (TB) has plagued humanity since antiquity, with evidence of the disease dating back to 17,000 years ago. [3] While the exact origin of human TB remains under debate, recent

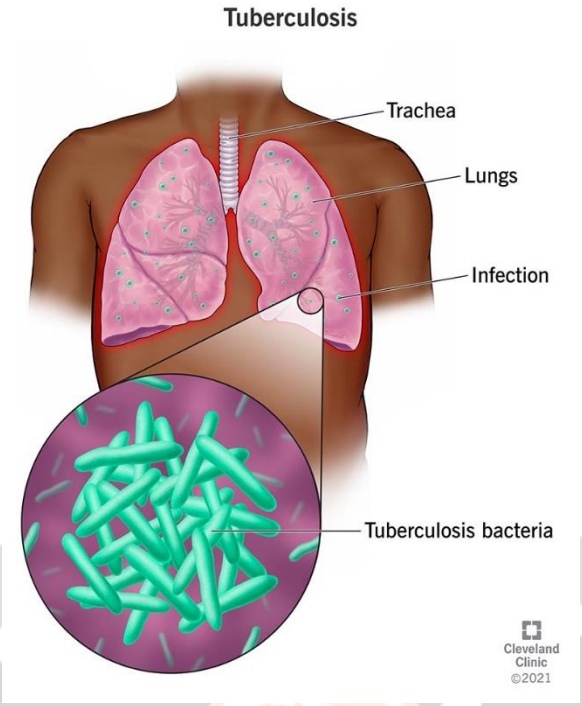


**Fig 1. Infected lungs with tuberculosis bacteria** [4]

genetic studies suggest an even earlier divergence from a common ancestor. This review explores advancements in preventing and treating this persistent public health threat, acknowledging its historical presence alongside the folklore surrounding it, such as the association with vampires. We discuss progress in understanding drug resistance, faster diagnostics, and novel treatment strategies. Additionally, the importance of public health interventions for effective TB control is highlighted. [5]

**EPIDEMIOLOGY-**

TB is contagious and airborne disease. It is a disease of poverty that thrives where social and economic determinants of ill health prevail, and it affects mostly young adults in their most productive years; 95% of TB deaths are in the developing world. About one third of the world's population is estimated to be latently infected with TB bacteria. Only a small proportion of those infected will become sick with TB, but people with weakened immune systems have a greater risk of falling ill from TB. In particular, a person living with HIV is over 15 times more likely to develop active TB. We know from historical data that, left untreated, smear-positive TB has a 10-year case fatality variously reported between 53 and 86%, with a weighted mean of 70%, compared with ~3% of HIV-uninfected treated patients with TB expected to die due to TB. [6,7]

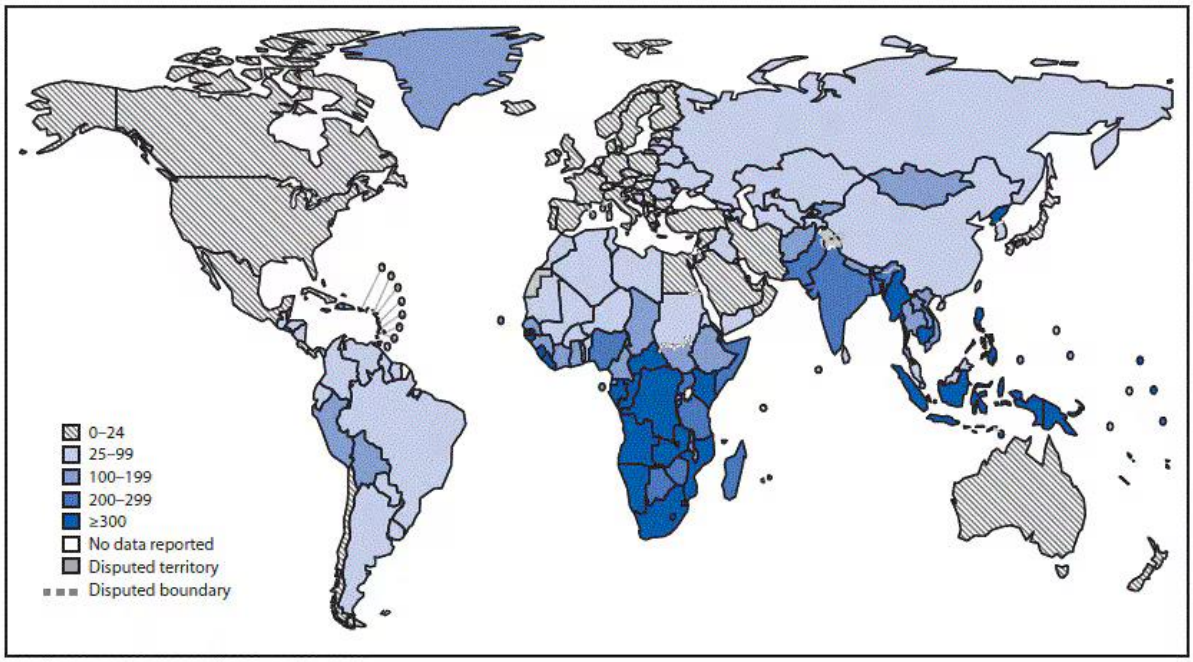


**Fig 2. Annual tuberculosis incidence (per 100,000 population), worldwide, 2017** [8]

The WHO regions of South-East Asia and Africa accounted for nearly 70% of overall global TB. Although total case numbers were higher in South-East Asia, overall incidence was similar in both regions (226 per 100,000 [South-East Asia], 237 [Africa]) (Table). Most high-incidence countries in 2017 were located in these two regions (Figure 1); however, the proportion of TB cases among persons with HIV infection in Africa (27%) was higher than that in South-East Asia (3%). [8]

**CAUSES-**

Tuberculosis is caused by a bacterium called Mycobacterium tuberculosis. People with active TB disease in the lungs or voice box can spread the disease. They release tiny droplets that carry the bacteria through the air. This can happen when they're speaking, singing, laughing, coughing or sneezing. A person can get an infection after inhaling the droplets. Tuberculosis bacteria spread through the air, just like a cold or the flu. You can get TB only if you come into contact with people who have it. If you breathe in these germs, you can get the disease. This is why people who have active tuberculosis in their lungs or throat are more likely to infect others. You usually can't spread TB if you have it in other areas of your body. TB is not easy to catch. You're most likely to get it from co-workers, friends, or family members with whom you spend lots of time indoors. [9,10]

Tuberculosis germs don't thrive on surfaces. You can't get it from:

- Shaking hands
- Kissing
- Sharing food or drink
- Sharing bed sheets, towels, or toothbrushes
- Toilet seats

**SIGNS AND SYMPTOMS-**

When tuberculosis (TB) germs survive and multiply in the lungs, it is called a TB infection. A TB infection may be in one of three stages. Symptoms are different in each stage.

**Primary TB infection.** The first stage is called the primary infection. Immune system cells find and capture the germs. The immune system may completely destroy the germs. But some captured germs may still survive and multiply. Most people don't have symptoms during a primary infection. Some people may get flu-like symptoms, such as:

- Low fever.
- Tiredness.
- Cough.

**Latent TB infection.** Primary infection is usually followed by the stage called latent TB infection. Immune system cells build a wall around lung tissue with TB germs. The germs can't do any more harm if the immune system keeps them under control. But the germs survive. There are no symptoms during latent TB infection. [11]

**Active TB disease.** Active TB disease happens when the immune system can't control an infection. Germs cause disease throughout the lungs or other parts of the body. Active TB disease may happen right after primary infection. But it usually happens after months or years of latent TB infection. Symptoms of active TB disease in the lungs usually begin gradually and worsen over a few weeks. They may include:

- Cough.
- Coughing up blood or mucus.
- Chest pain.
- Pain with breathing or coughing.
- Fever.
- Chills.
- Night sweats.
- Weight loss.
- Not wanting to eat.
- Tiredness.
- Not feeling well in general.

**Active TB disease outside the lungs.** TB infection can spread from the lungs to other parts of the body. This is called extrapulmonary tuberculosis. Symptoms vary depending on what part of the body is infected. Common symptoms may include: [12]

- Fever.
- Chills.
- Night sweats.
- Weight loss.
- Not wanting to eat.
- Tiredness.
- Not feeling well in general.
- Pain near the site of infection.

Active TB disease in the voice box is outside the lungs, but it has symptoms more like disease in the lungs. Common sites of active TB disease outside the lungs include:

- Kidneys.
- Liver.
- Fluid surrounding the brain and spinal cord.
- Heart muscles.
- Genitals.
- Lymph nodes.
- Bones and joints.
- Skin.
- Walls of blood vessels.
- Voice box, also called larynx.

**Active TB disease in children.** Symptoms of active TB disease in children vary. Typically, symptoms by age may include the following: [13]

- **Teenagers.** Symptoms are similar to adult symptoms.
- **1- to 12-year-olds.** Younger children may have a fever that won't go away and weight loss.
- **Infants.** The baby doesn't grow or gain weight as expected. Also, a baby may have symptoms from swelling in the fluid around the brain or spinal cord, including:
    - Being sluggish or not active.
    - Unusually fussy.
    - Vomiting.
    - Poor feeding.
    - Bulging soft spot on the head.

**RISK FACTORS-**

Anyone can get tuberculosis, but certain factors increase the risk of getting an infection. Other factors increase the risk of an infection becoming active TB disease. The Centers for Disease Control and Prevention recommends a TB test for people who have an increased risk of TB infection or active TB disease. Talk to your health care provider if you have one or more of the following risk factors. [14]

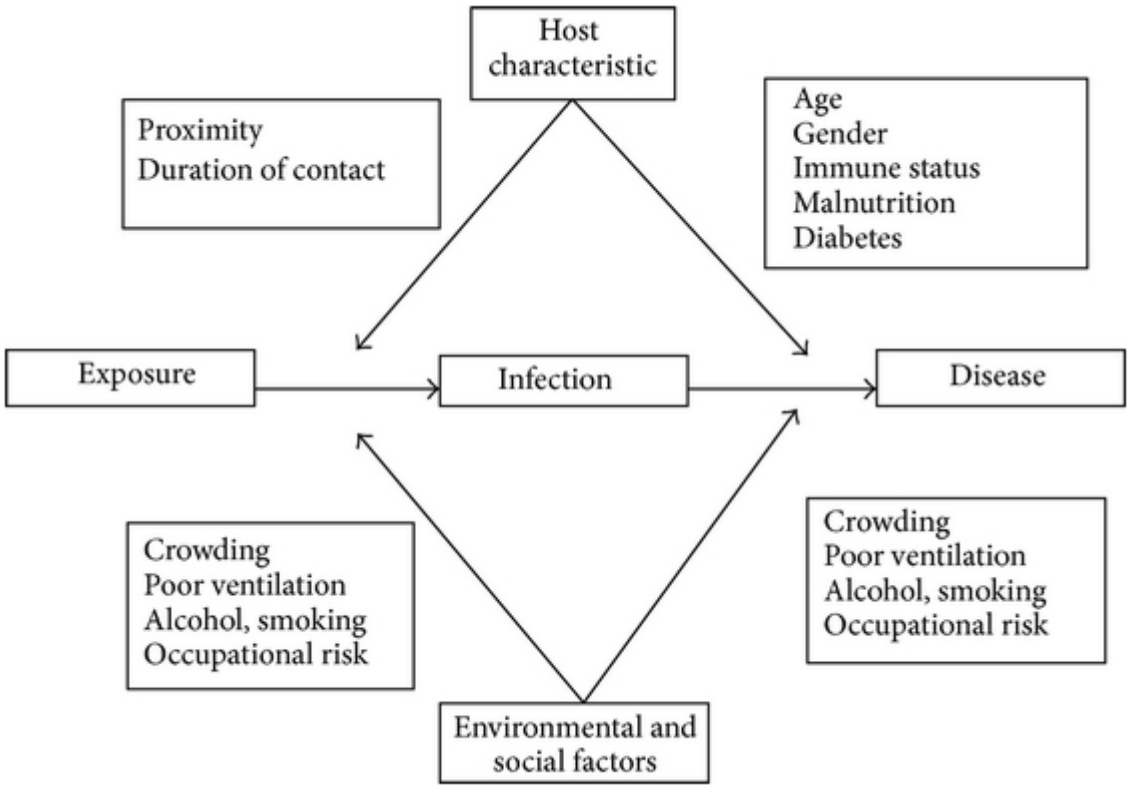


**Fig 3. Risk factors for Tuberculosis infection and disease.** [15]

Risk of TB infection- Certain living or working conditions make it easier for the disease to pass from one person to another. These conditions increase the risk of getting a TB infection:

- Living with someone with active TB disease.
- Living or traveling in a country where TB is common, including several countries in Latin America, Africa, Asia and the Pacific Islands.
- Living or working in places where people live close together, such as prisons, nursing homes and shelters for homeless people.
- Living in a community identified as being at high risk of tuberculosis.

- Working in health care and treating people with a high risk of TB.

Risk of active TB disease- A weakened immune system increases the risk of a TB infection becoming active TB disease. Conditions or treatments that weaken the immune system include: [16]

- HIV/AIDS.
- Diabetes.
- Severe kidney disease.
- Cancers of the head, neck and blood.
- Malnutrition or low body weight.
- Cancer treatment, such as chemotherapy.
- Drugs to prevent rejection of transplanted organs.
- Long-term use of prescription steroids.
- Use of unlawful injected drugs.
- Misuse of alcohol.
- Smoking and using other tobacco products.

**PATHOGENESIS-**

Transmission of TB is by inhalation of infectious droplet nuclei containing viable bacilli (aerosol spread). Mycobacteria-laden droplet nuclei are formed when a patient with active pulmonary TB coughs and can remain suspended in the air for several hours. Sneezing or singing may also expel bacilli. Factors influencing the chance of transmission include the bacillary load of the source case (sputum smear-positive or lung cavities on chest radiograph), as well as the proximity and duration of exposure. Transmission is dramatically and rapidly reduced with effective treatment. In general, the risk of infection among household contacts of TB patients is ~30 %. [17]

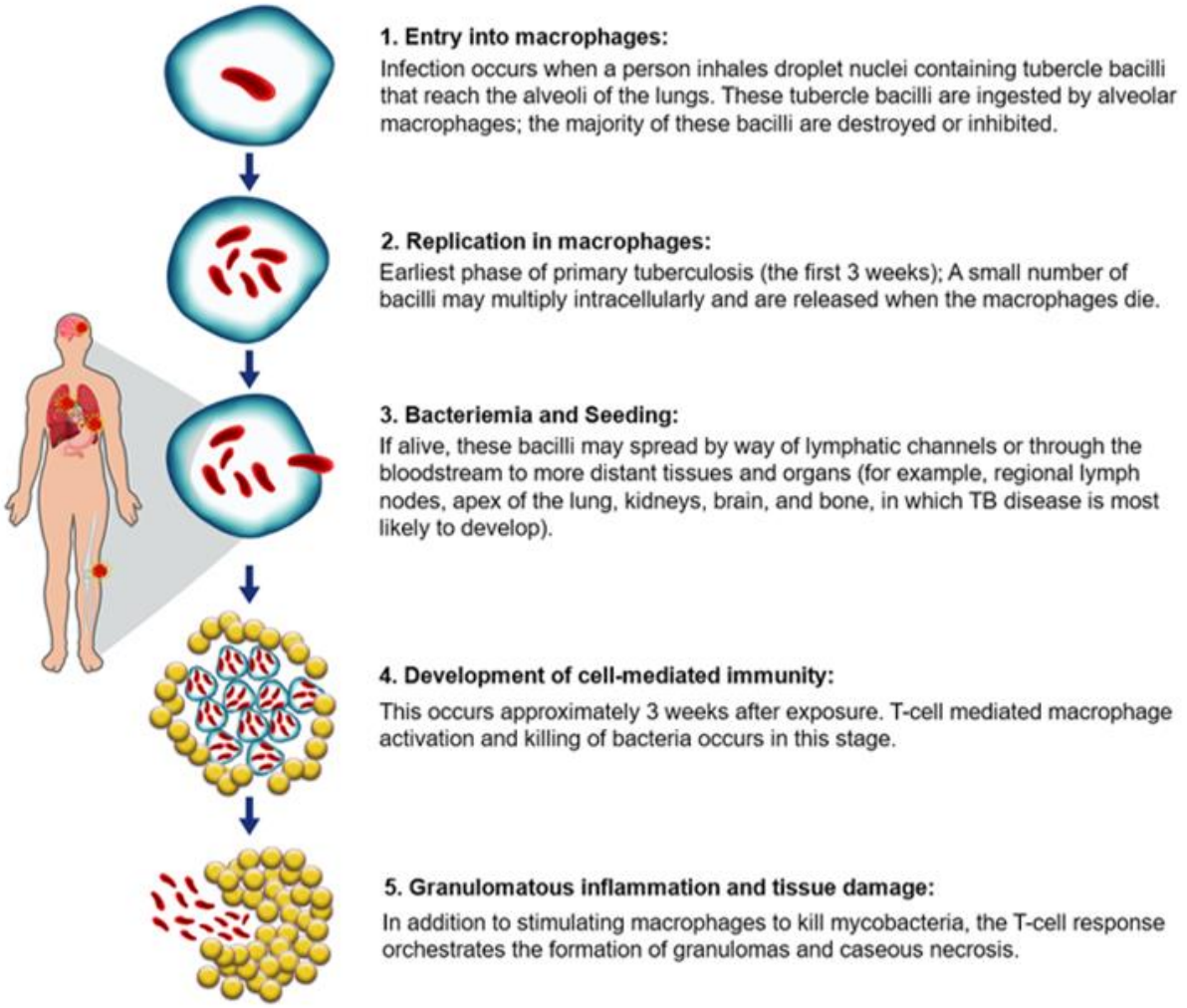


**Fig 4. Pathogenesis of TB.** [19]

**DIAGNOSIS-** [20,21]

To look for tuberculosis, your doctor may start with a physical exam that includes listening to your lungs and looking for swollen lymph nodes.

**Tuberculosis testing**- There are two common tests for tuberculosis:

- **Tuberculosis skin testing.** This is also known as the Mantoux tuberculin skin test. A technician injects a small amount of fluid into the skin of your lower arm. After 2-3 days, they'll check for swelling in your arm. You might get this test more than once.
- **Tuberculosis blood testing.** These tests, also called interferon-gamma release assays (IGRAs), measure the response when TB proteins are mixed with a small amount of your blood.

**Tuberculosis test results**- If your skin test results are positive, you most likely have TB bacteria. But you could also get a false positive. If you've gotten a tuberculosis vaccine called Bacillus Calmette-Guerin (BCG), the test could say you have TB when you really don't. You can also get a false negative, saying that you don't have TB when you really do, if your infection is very new. Skin and blood tests can't show whether your infection is latent or active. To figure that out, your doctor can do:

- **A chest X-ray or CT scan** to look for changes in your lungs.
- **Acid-fast bacillus (AFB) tests** for TB bacteria in your sputum, the mucus that comes up when you cough.

**PREVENTION-** [22,23]

If you test positive for latent TB infection, you may need to take drugs to prevent active TB disease. If you have active TB disease, you'll need to take steps to prevent other people from getting an infection. You will take drugs for four, six or nine months. Take all of the drugs as directed during the entire time. During the first 2 to 3 weeks, you will be able to pass TB bacteria to others. Protect others with these steps:

- Stay home. Don't go to work or school.
- Isolate at home. Spend as little time as possible among members of your household. Sleep in a separate room.
- Ventilate the room. Tuberculosis germs spread more easily in small, closed spaces. If it's not too cold outdoors, open the windows. Use a fan to blow air out. If you have more than one window, use one fan to blow air out and another to blow air in.
- Wear face masks. Wear a mask when you have to be around other people. Ask other members of the household to wear masks to protect themselves.
- Cover your mouth. Use a tissue to cover your mouth anytime you sneeze or cough. Put the dirty tissue in a bag, seal it and throw it away.

**Vaccinations-**

In countries where tuberculosis is common, infants often are vaccinated with the bacille Calmette-Guerin (BCG) vaccine. This protects infants and toddlers who are more likely to have active TB disease in the fluid surrounding the brain and spinal cord. The vaccine may not protect against disease in the lungs, which is more likely in the United States. Dozens of new TB vaccines are in various stages of development and testing.

**TREATMENT-** [24,25]

TB disease is curable. It is treated by standard 6-month course of 4 antibiotics. Common drugs include rifampicin and isoniazid. In some cases, the TB bacteria does not respond to the standard drugs. In this case, the patient has drug-resistant TB. Treatment for drug-resistant TB is longer and more complex. The course of TB drugs is provided to the patient with information, supervision and support by a health worker or trained volunteer. Without such support, treatment adherence can be difficult. If the treatment is not properly completed, the disease can become drug-resistant and can spread. In the case of TB infection (where the patient is infected with TB bacteria but not ill), TB preventive treatment can be given to stop the onset of disease. This treatment uses the same drugs for a shorter time. Recent treatment options have shortened the duration to treatment to only 1 or 3 months, as compared to 6 months in the past.

Drug Therapy:

- First-Line Drugs: The most commonly used antibiotics for treating TB are isoniazid (INH), rifampin (RIF), ethambutol (EMB), and pyrazinamide (PZA). These drugs are typically used in combination to effectively target the tuberculosis bacteria.
- Drug Combinations: TB treatment usually involves a combination of several antibiotics to reduce the risk of developing drug-resistant strains and improve efficacy.
- Directly Observed Therapy (DOT): In many settings, TB treatment is administered through directly observed therapy, where a healthcare worker or trained individual ensures that the patient takes their medications as prescribed. This helps to improve treatment adherence and reduce the risk of treatment failure or relapse.

Antituberculosis drugs. [26]

| Drug | Mean daily dosage |
|---|---|
| Isoniazid | 5 mg/kg |

| | |
|---|---|
| **Rifampicin** | 10 mg/kg |
| **Ethambutol** | 15–25 mg/kg |
| **Pyrazinamide** | 30–40 mg/kg |
| **Streptomycin** | 15–20 mg/kg |
| **Amikacin** | 15–20 mg/kg |
| **Kanamycin** | 15–20 mg/kg |
| **Capreomycin** | 15–20 mg/kg |
| **Ofloxacin** | 800 mg |
| **Ciprofloxacin** | 1000 mg |
| **Gatifloxacin** | 400 mg |
| **Moxifloxacin** | 400 mg |
| **Levofloxacin** | 1000 mg |
| **Ethionamide** | 15–20 mg/kg |
| **Prothionamide** | 15–20 mg/kg |
| **Cycloserine** | 500–1000 mg |
| **Para-aminosalicylic acid** | 150 mg/kg |
| **Linezolid** | 600 mg |
| **Clofazimine** | 200–300 mg |
| **Amoxicillin/clavulanate** | 875/125 mg BID or<br>500/125 mg TID |
| **Clarithromycin** | 1000 mg |
| **Terizidone** | 600–900 mg |
| **Thiacetazone** | 150 mg |
| **Thioridazine** | 75 mg |
| **Bedaquiline** | 400 mg (for 2 wk)<br>200 mg TIW (for 22 wk) |
| **Delamanid** | 200 mg |

**CONCLUSION-**

In conclusion, tuberculosis (TB) remains a significant global health challenge despite centuries of efforts to control and eradicate it. This comprehensive review has highlighted various aspects of TB, including its historical significance, epidemiology, pathogenesis, diagnosis, and treatment. Throughout history, TB has left an indelible mark on human populations, affecting individuals across continents and cultures. In recent decades, concerted efforts have been made to combat TB through improved diagnostics, treatment regimens, and prevention strategies. The development of rapid molecular diagnostic tests, such as GeneXpert MTB/RIF, has revolutionized TB diagnosis, enabling prompt identification of cases and initiation of treatment. Innovations in TB treatment, including the development of new drugs and treatment regimens, offer hope for improved outcomes and reduced treatment duration. However, sustained investment in TB research and development is needed to accelerate progress towards the goal of TB elimination.

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