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A REVIEW ON TUBERCULOSIS: CURRENT CHALLENGES AND RECENT ADVANCES IN TREATMENT

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ABSTRACT

Tuberculosis (TB) is a chronic infectious disease caused by *Mycobacterium tuberculosis* and remains one of the leading causes of morbidity and mortality worldwide. Despite the availability of effective chemotherapy, tuberculosis continues to pose a major public health challenge due to delayed diagnosis, poor treatment adherence, HIV co-infection, and the increasing prevalence of multidrug-resistant (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB). According to the World Health Organization (WHO), approximately 10.8 million people developed tuberculosis globally in 2023, resulting in nearly 1.25 million deaths. Early diagnosis using rapid molecular diagnostic techniques such as GeneXpert MTB/RIF, along with appropriate chemotherapy, has significantly improved treatment outcomes. The standard treatment regimen for drug-susceptible tuberculosis consists of a six-month multidrug therapy, while newer drugs including bedaquiline, delamanid, and pretomanid have revolutionized the management of drug-resistant tuberculosis. Recent advances in host-directed therapy, nanotechnology-based drug delivery systems, artificial intelligence-assisted diagnosis, and novel vaccine candidates have shown promising results in improving disease control and patient outcomes. This review summarizes the epidemiology, etiology, pathophysiology, clinical manifestations, diagnosis, conventional treatment, drug-resistant tuberculosis, recent therapeutic advances, patient counseling, and future perspectives in tuberculosis management. Continuous research, early detection, effective treatment strategies, and global public health initiatives are essential to achieve the WHO End TB Strategy and reduce the worldwide burden of tuberculosis.

KEYWORDS: Tuberculosis; Mycobacterium tuberculosis; Multidrug-resistant tuberculosis (MDR-TB); Extensively drug-resistant tuberculosis (XDR-TB); GeneXpert; Bedaquiline; Delamanid; Pretomanid; Anti-tubercular therapy; Host-directed therapy; Nanotechnology; Tuberculosis vaccine; WHO End TB Strategy.

INTRODUCTION

Tuberculosis (TB) is a chronic infectious disease caused by *Mycobacterium tuberculosis* and remains one of the leading causes of morbidity and mortality worldwide despite the availability of effective chemotherapy. It primarily affects the lungs (pulmonary tuberculosis) but may also involve extrapulmonary sites such as lymph nodes, bones, kidneys, meninges, and the gastrointestinal tract. The disease is transmitted through airborne droplet nuclei expelled when an infected individual coughs, sneezes, or speaks.[1,2] Tuberculosis continues to be a major public health challenge, particularly in low- and middle-income countries where poverty, malnutrition, overcrowding, and limited access to healthcare contribute to disease transmission. The World Health Organization (WHO) estimated that approximately 10.8 million people developed tuberculosis globally in 2023, with 1.25 million deaths attributed to the disease.[1] India

contributes the highest number of TB cases worldwide.[3] The emergence of multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) has further complicated disease management. Drug resistance develops because of poor treatment adherence, inappropriate drug regimens, interrupted drug supply, and delayed diagnosis. Patients co-infected with Human Immunodeficiency Virus (HIV) are at a significantly higher risk of developing active tuberculosis.[4] Recent advances in molecular diagnostics, novel anti-tubercular drugs such as bedaquiline, delamanid, and pretomanid, shorter all-oral treatment regimens, host-directed therapies, and vaccine development have significantly improved TB management.[5] These innovations support the WHO End TB Strategy aimed at reducing TB incidence and mortality worldwide.[1,5]

Epidemiology

Tuberculosis (TB) remains one of the leading infectious diseases worldwide and continues to pose a significant public health challenge. According to the World Health Organization (WHO) Global Tuberculosis Report 2024, an estimated 10.8 million people developed TB globally in 2023, including 6.0 million men, 3.6 million women, and 1.3 million children.[1] Approximately 1.25 million deaths were attributed to TB among HIV-negative individuals, while an additional 161,000 deaths occurred among people living with HIV.[1] The burden of TB is unevenly distributed across the globe. The highest number of cases occurs in the South-East Asia, African, and Western Pacific Regions, accounting for the majority of reported cases.[1] India contributes nearly 26% of the global TB burden, making it the country with the highest number of TB cases.[2] The incidence of tuberculosis is strongly associated with socioeconomic determinants such as poverty, overcrowding, malnutrition, HIV infection, diabetes mellitus, tobacco smoking, alcohol abuse, and limited access to healthcare services.[6] These factors increase susceptibility to infection and contribute to disease transmission within communities.

Etiology and Risk Factors

Tuberculosis is caused by *Mycobacterium tuberculosis*, a slow-growing, aerobic, acid-fast bacillus belonging to the *Mycobacterium tuberculosis* complex.[7] The organism possesses a lipid-rich cell wall containing mycolic acids, which provide resistance to many disinfectants and enable survival within host macrophages.[7,8]

Characteristics of Mycobacterium tuberculosis

- Acid-fast bacillus
- Obligate aerobe
- Non-motile
- Non-spore-forming
- Slow-growing (generation time 18–24 hours)
- Intracellular pathogen
- High lipid content due to mycolic acids[7,8]

Risk Factors

Several factors increase the risk of developing active tuberculosis following infection:

- HIV infection
- Diabetes mellitus
- Malnutrition
- Tobacco smoking
- Alcohol abuse
- Chronic kidney disease
- Immunosuppressive therapy
- Silicosis
- Overcrowded living conditions
- Poverty
- Extremes of age[6,9]

Individuals with weakened immune systems are more likely to progress from latent tuberculosis infection to active disease.[9]

Pathophysiology

Tuberculosis begins when *Mycobacterium tuberculosis* is inhaled into the lungs through infectious droplet nuclei released by individuals with active pulmonary tuberculosis.[7] The bacilli reach the alveoli, where they are phagocytosed by alveolar macrophages. However, *M. tuberculosis* has evolved mechanisms that allow it to survive and multiply within macrophages by inhibiting phagosome–lysosome fusion.[10]

The infected macrophages release cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-12 (IL-12), which recruit additional immune cells, including T lymphocytes. Activated $CD4^+$ T cells produce interferon-gamma (IFN-γ), enhancing the bactericidal activity of macrophages and promoting granuloma formation.[10,11]

Granulomas consist of macrophages, epithelioid cells, Langhans giant cells, lymphocytes, and fibroblasts. They serve to contain the infection and prevent bacterial dissemination. In immunocompetent individuals, the infection may remain dormant as **latent tuberculosis infection (LTBI)**. However, in immunocompromised individuals, the granuloma may break down, allowing bacilli to proliferate and cause active tuberculosis with caseous necrosis and cavitary lung lesions.[11,12]

Inhalation of *M. tuberculosis*
↓
Deposition in alveoli
↓
Phagocytosis by alveolar macrophages
↓
Intracellular survival of bacilli
↓
Activation of cell-mediated immunity
↓
Granuloma formation
↓

Latent tuberculosis infection
↓
Immune suppression
↓
Active tuberculosis disease

Figure 1: Pathogenesis of Tuberculosis.

Clinical Manifestations

The clinical presentation of tuberculosis depends on the site of infection and the patient's immune status.[12]

➢ **Pulmonary Tuberculosis**

Pulmonary TB is the most common form and presents with:

- Persistent cough lasting more than two weeks
- Fever
- Night sweats
- Weight loss
- Loss of appetite
- Fatigue
- Chest pain
- Hemoptysis (blood-stained sputum).[12,13]

➢ **Extrapulmonary Tuberculosis**

Extrapulmonary TB may involve several organs, including:

- Lymph nodes
- Pleura
- Bones and joints
- Kidneys
- Gastrointestinal tract
- Meninges
- Genitourinary system
- Pericardium[13]

Diagnosis

Early diagnosis is essential for reducing disease transmission and improving treatment outcomes.[1]

➢ **Laboratory Diagnosis**

1. Sputum Smear Microscopy

Ziehl–Neelsen staining is used to detect acid-fast bacilli (AFB) in sputum samples. Although inexpensive, its sensitivity is lower than molecular diagnostic methods.[14]

2. Culture

Culture on Löwenstein–Jensen medium or liquid culture systems remains the **gold standard** for confirming tuberculosis and performing drug susceptibility testing.[14]

3. GeneXpert MTB/RIF Assay

The GeneXpert assay rapidly detects *Mycobacterium tuberculosis* DNA and rifampicin resistance within approximately two hours. It is recommended by WHO as an initial diagnostic test for many patients with suspected TB.[1,15]

4. Line Probe Assay (LPA)

Line probe assays identify genetic mutations associated with resistance to rifampicin and isoniazid, facilitating early diagnosis of multidrug-resistant tuberculosis.[15]

5. Chest Radiography

Chest X-ray assists in identifying pulmonary lesions such as infiltrates, cavitations, fibrosis, and pleural effusion but is not diagnostic on its own.[12]

6. Tuberculin Skin Test (Mantoux Test)

The Mantoux test is primarily used to detect latent tuberculosis infection and has limited specificity in BCG-vaccinated populations.[16]

7. Interferon-Gamma Release Assays (IGRAs)

IGRAs measure T-cell responses to *M. tuberculosis*-specific antigens and are useful for diagnosing latent TB infection, especially in BCG-vaccinated individuals.[16]

Treatment of Tuberculosis

The primary goals of tuberculosis (TB) treatment are to eliminate *Mycobacterium tuberculosis*, prevent the development of drug resistance, reduce disease transmission, and minimize relapse after treatment completion (17). The World Health Organization (WHO) recommends standardized multidrug therapy because monotherapy rapidly leads to the emergence of resistant strains.[1,17]

Treatment of Drug-Susceptible Tuberculosis

Drug-susceptible pulmonary tuberculosis is treated with a **6-month regimen** consisting of an intensive phase followed by a continuation phase.[17]

➢ **Intensive Phase (First 2 Months)**

- Isoniazid (H)
- Rifampicin (R)
- Pyrazinamide (Z)
- Ethambutol (E)

➢ **Continuation Phase (Next 4 Months)**

- Isoniazid (H)
- Rifampicin (R)

This regimen is commonly abbreviated as 2HRZE/4HR and is recommended for most newly diagnosed patients with drug-susceptible TB.[17,18]

Table 1: First-Line Anti-Tubercular Drugs.

Sr.No	Drug	Mechanism of Action	Major Adverse Effects
1.	Isoniazid	Inhibits mycolic acid synthesis	Hepatotoxicity, peripheral neuropathy
2.	Rifampicin	Inhibits DNA-dependent RNA polymerase	Hepatotoxicity, orange discoloration of body fluids
3.	Pyrazinamide	Active against intracellular bacilli	Hepatotoxicity, hyperuricemia
4.	Ethambutol	Inhibits arabinogalactan synthesis	Optic neuritis

Directly Observed Treatment Short-course (DOTS)
The DOTS strategy, recommended by the WHO, ensures that patients receive supervised treatment to improve adherence and reduce treatment failure (1).

The five components of DOTS include
- Government commitment
- Early diagnosis using sputum microscopy or rapid molecular tests
- Standardized short-course chemotherapy
- Direct observation of treatment
- Reliable drug supply and recording systems[17]

DOTS has significantly improved treatment success rates in high-burden countries, including India.[3]

Drug-Resistant Tuberculosis
Drug-resistant tuberculosis has become a major obstacle to global TB control.

➢ **Multidrug-Resistant Tuberculosis (MDR-TB)**
MDR-TB is defined as tuberculosis caused by strains resistant to at least:
- Isoniazid
- Rifampicin[19]

Common causes include
- Poor treatment adherence
- Inappropriate drug regimens
- Irregular drug supply
- Previous incomplete treatment **(19)**

➢ **Extensively Drug-Resistant Tuberculosis (XDR-TB)**
XDR-TB is a more severe form of MDR-TB with additional resistance to important second-line drugs, making treatment more difficult and reducing treatment success rates (19,20).

Patients with MDR/XDR-TB require prolonged treatment using second-line agents and close monitoring for adverse drug reactions (20).

Recent Advances in Tuberculosis Treatment
Significant progress has been achieved in TB management during the past decade.

➢ **Bedaquiline**
Bedaquiline was the first new anti-tuberculosis drug approved in more than 40 years.

Mechanism of Action
- Inhibits mycobacterial ATP synthase.
- Causes depletion of cellular energy leading to bacterial death.[21]

Advantages
- Effective against MDR-TB.
- Improves treatment success.
- Enables shorter all-oral treatment regimens.

➢ **Delamanid**
Delamanid inhibits mycolic acid synthesis in *Mycobacterium tuberculosis*.
It is mainly indicated for MDR-TB patients who cannot receive standard therapy.[22]

➢ **Pretomanid**
Pretomanid is a nitroimidazole antimicrobial approved for use in combination with bedaquiline and linezolid in selected patients with highly drug-resistant TB.[23]

Advantages include
- Improved bactericidal activity.
- Shorter treatment duration in eligible patients.
- Better outcomes in extensively drug-resistant tuberculosis.

Shorter All-Oral Regimens
Recent WHO guidelines recommend shorter all-oral regimens for eligible MDR-TB patients, reducing the need for injectable drugs and improving treatment adherence.[20]

Benefits include
- Reduced treatment duration.
- Better patient compliance.
- Lower risk of injectable-related adverse effects.
- Improved quality of life.

Host-Directed Therapy (HDT)
Host-directed therapy (HDT) is an emerging strategy that enhances the host immune response rather than directly targeting *Mycobacterium tuberculosis*. HDT aims to improve bacterial clearance, reduce lung damage, shorten treatment duration, and improve treatment outcomes.[24]

Several agents under investigation include
- Vitamin D supplementation
- Metformin
- Statins

- Corticosteroids (in selected forms of TB)
- Immunomodulatory agents

These therapies may be used as adjuncts to standard anti-tubercular treatment, although further clinical studies are needed to establish their routine use.[24,25]

Vaccine Development

The Bacillus Calmette–Guérin (BCG) vaccine is currently the only licensed vaccine for tuberculosis. It provides protection against severe forms of TB, particularly tuberculous meningitis and miliary tuberculosis in children, but offers variable protection against pulmonary tuberculosis in adults.[26]

Several vaccine candidates are currently under clinical evaluation, including

- M72/AS01E
- VPM1002
- MTBVAC

These candidates aim to provide stronger and longer-lasting protection than BCG and support the WHO End TB Strategy.[27]

Nanotechnology in Tuberculosis Treatment

Nanotechnology has emerged as a promising approach to improve anti-tubercular drug delivery[28]

Potential advantages include:

- Targeted drug delivery to infected macrophages
- Improved drug bioavailability
- Sustained drug release
- Reduced dosing frequency
- Lower systemic toxicity
- Improved patient adherence

Nanocarriers such as liposomes, polymeric nanoparticles, solid lipid nanoparticles, and nanoemulsions are being investigated for TB therapy.[28]

Patient Counseling

Patient education is essential for successful tuberculosis management and prevention of disease transmission.[29]

Key counseling points include

- Complete the entire course of anti-tubercular therapy.
- Do not discontinue medication without medical advice.
- Take medicines regularly at the prescribed time.
- Report adverse drug reactions immediately.
- Maintain adequate nutrition and hydration.
- Avoid smoking and alcohol consumption.
- Practice cough etiquette and wear a mask when appropriate.
- Attend all scheduled follow-up visits.
- Encourage household contacts to undergo TB screening when advised.

Proper counseling improves medication adherence and reduces the risk of relapse and drug resistance.[29]

Future Perspectives

Future tuberculosis research focuses on:

- ✓ Development of shorter treatment regimens
- ✓ Discovery of novel anti-TB drugs
- ✓ Artificial intelligence-assisted diagnosis
- ✓ Precision medicine approaches
- ✓ Host-directed therapies
- ✓ Improved rapid molecular diagnostics
- ✓ Development of more effective vaccines

Advances in genomics, bioinformatics, and nanotechnology are expected to transform TB diagnosis and treatment over the coming years.[30]

CONCLUSION

Tuberculosis remains a major global public health challenge despite significant advances in diagnosis and treatment. The emergence of multidrug-resistant and extensively drug-resistant tuberculosis, HIV co-infection, delayed diagnosis, poor treatment adherence, and socioeconomic factors continue to hinder global TB control. Recent innovations, including rapid molecular diagnostic techniques, all-oral treatment regimens, novel anti-tubercular drugs such as bedaquiline, delamanid, and pretomanid, host-directed therapies, nanotechnology-based drug delivery systems, and new vaccine candidates, have substantially improved tuberculosis management. Continued research, early diagnosis, patient education, strengthened healthcare systems, and global collaboration are essential to achieve the WHO End TB Strategy and reduce the worldwide burden of tuberculosis.

REFERENCES

1. World Health Organization. Global Tuberculosis Report 2024. Geneva: World Health Organization, 2024.
2. Brunton LL, Hilal-Dandan R, Knollmann BC, editors. Goodman & Gilman's The Pharmacological Basis of Therapeutics. 14th ed. New York: McGraw-Hill Education, 2023.
3. Government of India. Ministry of Health and Family Welfare. India TB Report 2024. New Delhi: Central TB Division, 2024.
4. Jameson JL, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J, editors. Harrison's Principles of Internal Medicine. 22nd ed. New York: McGraw-Hill Education, 2024.
5. Nahid P, Mase SR, Migliori GB, et al. Treatment of drug-susceptible tuberculosis: updated clinical recommendations. Clin Infect Dis., 2023.
6. Lönnroth K, Jaramillo E, Williams BG, Dye C, Raviglione M. Drivers of tuberculosis epidemics: the role of risk factors and social determinants. Soc Sci Med., 2009; 68(12): 2240–2246.
7. Murray PR, Rosenthal KS, Pfaller MA. Medical Microbiology. 10th ed. Philadelphia: Elsevier, 2023.

8. Jawetz E, Melnick JL, Adelberg EA. Medical Microbiology. 29th ed. New York: McGraw-Hill Education, 2024.
9. Centers for Disease Control and Prevention. Tuberculosis (TB): Risk Factors. Atlanta: CDC.
10. Flynn JL, Chan J. Immunology of tuberculosis. Annu Rev Immunol, 2001; 19: 93–129.
11. Ramakrishnan L. Revisiting the role of the granuloma in tuberculosis. Nat Rev Immunol, 2012; 12(5): 352–366.
12. Jameson JL, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J, editors. Harrison's Principles of Internal Medicine. 22nd ed. New York: McGraw-Hill Education, 2024.
13. Golden MP, Vikram HR. Extrapulmonary tuberculosis: an overview. Am Fam Physician, 2005; 72(9): 1761–1768.
14. Forbes BA, Sahm DF, Weissfeld AS. Bailey & Scott's Diagnostic Microbiology. 15th ed. St. Louis: Elsevier, 2022.
15. World Health Organization. WHO consolidated guidelines on tuberculosis: Module 3 – Diagnosis. Geneva: World Health Organization, 2023.
16. Lewinsohn DM, Leonard MK, LoBue PA, et al. Official clinical practice guidelines: Diagnosis of tuberculosis in adults and children. Clin Infect Dis., 2017; 64(2): e1–e33.
17. Kaufmann SHE, Dorhoi A, Hotchkiss RS, Bartenschlager R. Host-directed therapies for bacterial and viral infections. Nat Rev Drug Discov, 2018; 17(1): 35–56.
18. Wallis RS, Hafner R. Advancing host-directed therapy for tuberculosis. Nat Rev Immunol, 2015;15(4):255–263.
19. World Health Organization. BCG vaccines: WHO position paper. Wkly Epidemiol Rec., 2018; 93(8): 73–96.
20. Tait DR, Hatherill M, Van Der Meeren O, et al. Final analysis of a trial of the M72/AS01E tuberculosis vaccine. N Engl J Med., 2019; 381(25): 2429–2439.
21. Pandey R, Khuller GK. Nanotechnology-based drug delivery system(s) for the management of tuberculosis. Drug Discov Today, 2006; 11(17–18): 857–863.
22. World Health Organization. Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis. Geneva: World Health Organization, 2014.
23. World Health Organization. End TB Strategy. Geneva: World Health Organization, 2015.
24. World Health Organization. WHO operational handbook on tuberculosis. Module 4: Treatment – Drug-susceptible tuberculosis treatment. Geneva: World Health Organization, 2022.
25. Nahid P, Mase SR, Migliori GB, et al. Treatment of drug-susceptible tuberculosis. Clin Infect Dis. 2023.
26. World Health Organization. Global Tuberculosis Report 2024. Geneva: World Health Organization, 2024.
27. World Health Organization. WHO operational handbook on tuberculosis. Module 4: Treatment – Drug-resistant tuberculosis treatment. Geneva: World Health Organization, 2022.
28. Andries K, Verhasselt P, Guillemont J, et al. A diarylquinoline drug active on ATP synthase of Mycobacterium tuberculosis. Science, 2005; 307(5707): 223–227.
29. Gler MT, Skripconoka V, Sanchez-Garavito E, et al. Delamanid for multidrug-resistant pulmonary tuberculosis. N Engl J Med., 2012; 366(23): 2151–2160.
30. Conradie F, Diacon AH, Ngubane N, et al. Treatment of highly drug-resistant pulmonary tuberculosis with bedaquiline, pretomanid and linezolid. N Engl J Med., 2020; 382(10): 893–902.