IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 5, Issue 1, November 2025
Impact Factor: 7.67

A Review on Tuberculosis

Kadam Omkar P and Sonawane Kajol B
Sahakar Maharshi Kisanrao Varal Patil College of Pharmacy, Nighoj
Assistant Professor, Sahakar Maharshi Kisanrao Varal Patil College of Pharmacy, Nighoj

Tuberculosis: Drug Resistance Strains and Current Treatment Challenge

Abstract: *Tuberculosis (TB), caused by Mycobacterium tuberculosis, remains a major global health concern, especially with the rise of drug-resistant strains. Multidrug-resistant (MDR-TB) and extensively drug- resistant (XDR-TB) forms have significantly complicated control efforts and treatment outcomes. These resistant strains arise primarily due to inadequate or incomplete treatment regimens and poor adherence to prescribed therapies. The limited efficacy of current drugs against resistant forms, coupled with lengthy treatment durations and toxic side effects, presents significant challenges to healthcare systems. Moreover, the emergence of totally drug-resistant (TDR-TB) cases highlights the urgent need for novel therapeutics and improved diagnostic tools. This review explores the mechanisms behind drug resistance in TB, outlines the limitations of current treatment protocols, and discusses recent advances and challenges in developing more effective therapies.*

Keywords: Tuberculosis, MDR-TB, XDR-TB, Drug resistance, Treatment challenges, Mycobacterium tuberculosis, Antibiotic resistance, Novel therapies

I. INTRODUCTION

Tuberculosis (TB) is an infectious disease primarily affecting the lungs, caused by the bacterium Mycobacterium tuberculosis. Despite significant advancements in diagnostic methods and therapeutic strategies, TB remains one of the top ten causes of death worldwide, particularly in low- and middle- income countries. The global fight against TB has been further complicated by the emergence and spread of drug-resistant strains, including multidrug-resistant TB (MDR-TB) and extensively drug- resistant TB (XDR-TB). These forms do not respond to the most effective first-line anti-TB drugs, such as isoniazid and rifampicin, making treatment more complex, prolonged, and expensive.[1]

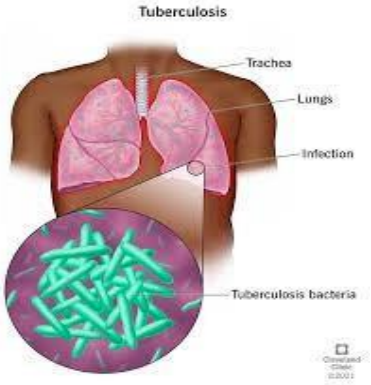

Fig 1. Tuberculosis

Drug resistance in TB often develops due to poor patient adherence, inadequate treatment regimens, and the misuse of antibiotics. This resistance poses a major threat to public health, as it leads to higher mortality rates, increased transmission, and greater financial burdens on healthcare systems. In recent years, there has been growing concern about totally drug-resistant TB (TDR-TB), a form of the disease that appears impervious to all available anti-TB medications.[2]

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 5, Issue 1, November 2025 Impact Factor: 7.67

Addressing these challenges requires a multifaceted approach that includes the development of new antibiotics, improved diagnostics, better patient monitoring, and global cooperation in TB control efforts. This paper examines the mechanisms behind drug resistance in M. tuberculosis, evaluates current treatment limitations, and explores potential strategies to overcome these challenges.

The Complex Genetics of TB Drug Resistance:

- Mycobacterium tuberculosis develops drug resistance mainly through spontaneous chromosomal mutations, not through horizontal gene transfer.
- These mutations typically occur under selective pressure from improper or incomplete antibiotic treatment.[3]
- Isoniazid resistance is most commonly associated with mutations in the katG gene or the inhA
- promoter region.
- Rifampicin resistance results from mutations in the rpoB gene, particularly in the rifampicin resistance-determining region (RRDR).
- Multidrug-resistant TB (MDR-TB) is defined by resistance to both isoniazid and rifampicin.
- Extensively drug-resistant TB (XDR-TB) includes additional resistance to fluoroquinolones (via gyrA and gyrB mutations) and second-line injectable drugs (via rrs, eis, or tlyA mutations).
- Mutations can vary by region due to differences in drug use, treatment practices, and local TB strains.
- Some mutations have a fitness cost, meaning they may reduce bacterial growth or transmission capacity, while others may have little to no impact on fitness.
- Heteroresistance can occur, where different bacterial populations in the same patient have varying levels of resistance, complicating diagnosis and treatment.
- Whole-genome sequencing (WGS) is increasingly used to detect resistance mutations quickly and improve treatment decisions.
- Understanding genetic mechanisms of resistance is crucial for developing new diagnostics and next-generation anti-TB drugs.[4]

Diagnosis of TB Drug Resistance: From Culture to Whole-Genome Sequencing

- Early detection of drug-resistant TB is essential for timely and effective treatment, as well as to limit transmission.
- Traditional diagnostic methods relied on phenotypic drug susceptibility testing (DST)
- performed on culture-based systems, which are slow, often taking weeks to yield results.
- Culture-based DST involves growing M. tuberculosis in the presence of anti-TB drugs and observing growth patterns to determine resistance.
- These methods, although accurate, are time-consuming, labor-intensive, and require
- biosafety level 3 (BSL-3) laboratories.[5]
- To speed up diagnosis, molecular techniques have been developed to detect genetic mutations associated with drug resistance.
- Line Probe Assays (LPAs) are DNA strip-based tests that detect specific resistance mutations, mainly for rifampicin and isoniazid, within 1–2 days.
- The GeneXpert MTB/RIF system is a rapid, automated PCR-based test that simultaneously detects M. tuberculosis and rifampicin resistance in under 2 hours.

• Limitations of molecular tests include:

- Inability to detect rare or novel resistance mutations
- Limited coverage of second-line drug resistance
- Dependence on known mutation databases

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 5, Issue 1, November 2025 Impact Factor: 7.67

- Whole-genome sequencing (WGS) has emerged as a powerful tool that provides
- comprehensive genetic profiles of M. tuberculosis strains.[6]
- WGS can identify both known and novel mutations linked to resistance across all first- and second-line drugs.
- It enables strain typing, epidemiological tracking, and detection of mixed infections or
- heteroresistance.
- WGS is increasingly used in reference laboratories and national TB programs in high- burden countries.

Challenges of WGS include:

- High cost and technical infrastructure
- Need for skilled personnel and bioinformatics capacity
- Longer turnaround time compared to rapid molecular tests

Despite limitations, WGS is expected to play a central role in the future of TB diagnostics, surveillance, and treatment personalization.

History of Tuberculosis (TB)

- Ancient origins: Evidence of TB dates back over 9,000 years, with signs of spinal TB (Pott's disease) found in prehistoric human remains and Egyptian mummies.
- Classical descriptions: Ancient Greek physicians like Hippocrates described a disease called "phthisis," which resembled modern-day pulmonary TB.
- Middle Ages: TB was widespread in Europe, often referred to as the "king's evil" or "consumption," and believed to be hereditary rather than infectious.
- 18th and 19th centuries: TB became a major public health crisis in Europe and North America, especially in crowded urban settings during the Industrial Revolution.[7]
- The disease was romanticized in literature and art, often associated with sensitivity and creativity due to its lingering, wasting symptoms.
- In 1882, German physician Robert Koch identified the causative agent, Mycobacterium tuberculosis, marking a turning point in understanding and controlling the disease.
- Early 20th century: Sanatoriums became common for isolating and treating TB patients with rest, fresh air, and nutrition.
- The BCG vaccine (Bacillus Calmette–Guérin), developed in the 1920s, provided some protection against severe forms of TB, especially in children.
- Streptomycin, discovered in 1943, became the first effective antibiotic against TB, followed by other key drugs like isoniazid and rifampicin in the 1950s and 60s.
- Widespread use of antibiotics led to a dramatic decline in TB rates in many high-income countries during the mid-20th century.[8]
- However, in the 1980s and 1990s, TB re-emerged globally due to factors such as HIV/AIDS, drug resistance, poverty, and weakened public health systems.
- The emergence of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) in recent decades has reignited global concern.
- Today, TB remains one of the world's top infectious killers, particularly affecting low- and middle-income countries, despite being preventable and curable.

Tuberculosis (TB) Symptoms

1. Pulmonary Tuberculosis (TB) – Symptoms related to the lungs

Pulmonary TB is the most common form of TB, accounting for the majority of cases. It primarily affects the lungs and is the main source of transmission.

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 5, Issue 1, November 2025 Impact Factor: 7.67

- Persistent Cough: One of the earliest and most common symptoms. The cough often starts as dry and becomes productive over time, lasting for more than three weeks.
- Coughing up Blood (Hemoptysis): In some patients, the cough may produce blood-streaked sputum or frank blood due to damage to lung tissue or erosion of blood vessels.
- Chest Pain: A dull or sharp pain may occur, especially when breathing deeply, coughing, or exerting effort. This is usually due to inflammation of the pleura (the membrane surrounding the lungs).[9]
- Fever: Patients often experience low-grade fevers, especially in the late afternoon or evening. This fever may be intermittent or persistent.
- Night Sweats: One of the hallmark signs of TB. Patients often wake up with soaked clothing and bedsheets, even in cool environments.
- Unexplained Weight Loss: Significant weight loss occurs due to increased metabolic demands of the infection and reduced appetite.
- Fatigue and Weakness: The body's immune response to TB drains energy, leading to a constant feeling of tiredness and reduced physical stamina.
- Loss of Appetite: Common during TB infection, contributing to weight loss and malnutrition.
- Shortness of Breath: In advanced cases, where lung tissue is extensively damaged, patients may feel breathless even with mild exertion.

2. Extrapulmonary Tuberculosis (TB) – Symptoms outside the lungs

Extrapulmonary TB occurs when the infection spreads beyond the lungs. While less common than pulmonary TB, it is particularly prevalent among immunocompromised individuals (e.g., people with HIV/AIDS).[10]

• Lymph Node TB (Tuberculous Lymphadenitis):

o Painless swelling of lymph nodes, most often in the neck.
o Nodes may become tender, soft, or drain pus if they rupture.
o Common among children and people with HIV.

• Spinal TB (Pott's Disease):

o Chronic back pain, often in the lower thoracic or lumbar region.
o Spinal deformities or hunching in advanced cases.
o Neurological symptoms like numbness or paralysis may occur if the spinal cord is compressed.

• TB Meningitis:

o Affects the membranes around the brain and spinal cord.
o Symptoms include severe headache, neck stiffness, vomiting, sensitivity to light, confusion, and seizures.
o Potentially life-threatening and requires immediate medical attention.

• Genitourinary TB (Kidneys, Bladder, Reproductive Organs):

o Blood in the urine (hematuria), frequent urination, and pain while urinating.
o In men: may involve the epididymis or prostate; in women: may cause infertility if fallopian tubes are affected.[11]

• Bone and Joint TB:

o Swelling and pain in affected joints (commonly the hip and knee).
o Joint stiffness and limited mobility.
o Slow progression often leads to joint destruction if untreated.

• Abdominal TB:

o Involves the intestines, peritoneum, or abdominal lymph nodes.
o Symptoms may include abdominal pain, bloating, weight loss, fever, and sometimes obstruction of the bowel.

When to Seek Medical Attention

Early identification and treatment of TB are critical to prevent complications and transmission. Individuals experiencing a persistent cough (especially if lasting more than 2–3 weeks), unexplained weight loss, night sweats, and fatigue—particularly in high TB prevalence regions—should seek medical evaluation.

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 5, Issue 1, November 2025 Impact Factor: 7.67

Heteroresistance — Another Complicating Factor in Tuberculosis Treatment

Heteroresistance refers to the coexistence of both drug-susceptible and drug-resistant populations of Mycobacterium tuberculosis within the same infected individual. This phenomenon adds a significant layer of complexity to TB diagnosis, treatment, and control efforts.[12]

- Mechanism: During infection, spontaneous mutations can give rise to subpopulations of M. tuberculosis that possess resistance-conferring genetic changes. These resistant bacteria exist alongside susceptible ones, creating a mixed bacterial population within the host.
- Diagnostic Challenges: Conventional drug susceptibility tests (DST), especially culture-based or molecular assays, may fail to detect heteroresistance if the resistant subpopulation is small. This can lead to false-negative results, where resistance goes unnoticed, causing inappropriate treatment.
- Treatment Implications: If heteroresistant strains are not identified and treatment is based on drug susceptibility results reflecting only the susceptible bacteria, patients may receive ineffective therapy. This can result in treatment failure, ongoing transmission of resistant strains, and the eventual dominance of resistant populations.
- Clinical Impact: Heteroresistance has been observed with resistance to key anti-TB drugs such as rifampicin and isoniazid. Its presence can contribute to the development of multidrug- resistant TB (MDR-TB) and complicate treatment regimens, leading to longer therapy duration and poorer outcomes.[13]
- Detection Advances: Recent improvements in diagnostics, including whole-genome sequencing (WGS) and deep sequencing techniques, have enhanced the ability to identify heteroresistant populations by detecting minority variants within bacterial samples.
- Epidemiological Importance: Understanding heteroresistance is crucial for accurate surveillance of drug-resistant TB, as it can influence estimates of resistance prevalence and transmission dynamics.
- Future Directions: Addressing heteroresistance requires the development of more sensitive diagnostic tools and personalized treatment approaches that consider the presence of mixed bacterial populations. This will help in optimizing therapy and reducing the spread of resistant TB strains.[14]

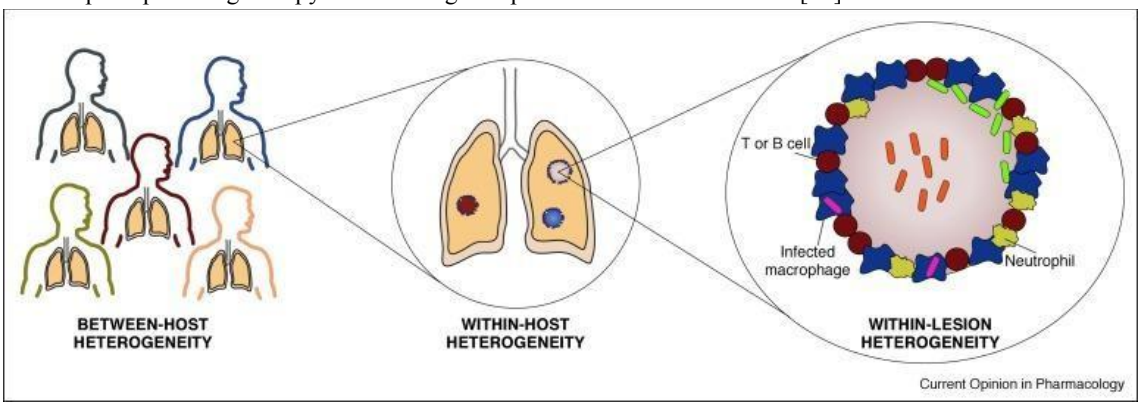

Fig 2. Heteroresistance

Public Health Consequences of Simplified Diagnosis and Treatment for a Complex Disease

Tuberculosis is a complex infectious disease with variable clinical presentations, diverse drug resistance patterns, and significant public health implications. While simplifying diagnosis and treatment protocols can improve access and adherence, it also carries risks that impact public health outcomes.[15]

• Benefits of Simplification:

Simplified diagnostic methods and treatment regimens are designed to improve accessibility, especially in resource-limited settings. Rapid tests like GeneXpert and standardized treatment protocols facilitate earlier detection and initiation of therapy, reducing delays and improving patient compliance.

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 5, Issue 1, November 2025 Impact Factor: 7.67

• Risk of Misdiagnosis and Underdiagnosis:
Simplified diagnostic tools may lack the sensitivity or specificity to detect drug resistance comprehensively. For example, rapid molecular tests might miss rare or emerging resistance mutations or fail to identify extrapulmonary TB cases. This can lead to underdiagnosis of resistant TB forms and inappropriate treatment.

• Inadequate Treatment of Drug-Resistant Strains:
Standardized treatment regimens may not be sufficiently tailored to the complexity of drug resistance in certain patients. Without detailed drug susceptibility testing, patients harboring resistant strains may receive ineffective drugs, increasing the risk of treatment failure and further resistance development.[16]

• Increased Transmission of Resistant TB:
Failure to accurately diagnose and effectively treat drug-resistant TB strains can lead to ongoing transmission within communities, exacerbating public health challenges.

• Development of Further Resistance:
Simplified treatment regimens that do not account for individual resistance profiles can contribute to the emergence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB, complicating future control efforts.

• Impact on Surveillance and Data Quality:
Reliance on simplified diagnostics may limit the collection of detailed epidemiological data on resistance patterns, hindering public health monitoring and the design of targeted interventions.

• Equity and Access Considerations: While simplification improves access for many, it risks creating gaps where vulnerable populations with complex resistance profiles may be underserved or mismanaged.

• Need for Balance:
Public health strategies must balance the advantages of simplified approaches—such as wider reach and faster treatment initiation—with the need for accurate, comprehensive diagnosis and personalized treatment where necessary.

• Role of Capacity Building:
Strengthening laboratory infrastructure, training healthcare workers, and integrating advanced diagnostics like whole-genome sequencing in reference centers can help mitigate the risks associated with simplification.[17]

How Do We Minimise Future Resistance Emergence in Tuberculosis?

The emergence of drug-resistant TB — including multidrug-resistant (MDR), extensively drug- resistant (XDR), and even totally drug-resistant (TDR) strains — poses a critical threat to global TB control. Preventing further resistance requires a multifaceted approach that addresses clinical practices, public health systems, patient behavior, and research innovation.

1. Ensure Accurate and Early Diagnosis

• Use of rapid molecular diagnostics (e.g., GeneXpert MTB/RIF, line probe assays) to detect drug resistance early.
• Expand access to drug susceptibility testing (DST) to tailor treatment based on individual resistance profiles.
• Scale up whole-genome sequencing (WGS) in reference labs for comprehensive resistance detection and surveillance.

2. Promote Proper and Complete Treatment

• Ensure full adherence to TB treatment regimens, even after symptoms improve, to prevent the survival of partially resistant bacteria.[18]
• Provide directly observed therapy (DOT) or digital adherence technologies to support patients during the lengthy treatment process.
• Avoid monotherapy or incomplete drug regimens, which increase the risk of selecting resistant strains.

3. Strengthen Health Systems and Access to Quality Care

• Ensure a consistent supply of high-quality anti-TB drugs through regulated procurement systems.
• Avoid substandard or counterfeit medications, which can lead to subtherapeutic dosing and resistance.
• Train healthcare providers on current TB treatment protocols, resistance risks, and individualized care strategies.

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 5, Issue 1, November 2025 Impact Factor: 7.67

4. Improve Infection Control Measures

• Enhance airborne infection control in healthcare facilities, prisons, shelters, and other high- risk settings.
• Early isolation of infectious TB patients can reduce transmission of resistant strains in the community and hospitals.
• Promote use of protective equipment and environmental controls like proper ventilation and UV lights where feasible.[19]

5. Expand Preventive Strategies

• Wider use of TB preventive therapy (TPT) in high-risk populations (e.g., people with HIV, household contacts).
• Improve BCG vaccination coverage in endemic regions, especially in children.
• Support ongoing research into more effective TB vaccines that can prevent both infection and disease progression.

6. Invest in Research and Development

• Accelerate the development of new TB drugs that are effective against resistant strains, with novel mechanisms of action.
• Promote shorter, more tolerable treatment regimens to improve patient compliance and reduce resistance pressure.
• Support research into host-directed therapies and diagnostic tools that can detect resistance faster and more accurately.[20]

7. Strengthen Surveillance and Global Coordination

• Implement national and global surveillance systems to monitor resistance trends and treatment outcomes.
• Share data across borders, particularly for tracking resistant TB in migratory or high-travel populations.
• Collaborate internationally through organizations like WHO and The Global Fund to coordinate funding, training, and supply chains.

8. Address Social Determinants of Health

• Tackle poverty, malnutrition, overcrowding, and stigma, which increase the risk of treatment interruption and transmission.
• Empower patients through education, community support, and integration of TB care into general health services.

Epidemiology of Tuberculosis (TB)

Tuberculosis (TB) remains one of the leading infectious causes of illness and death globally, despite being a preventable and curable disease. The epidemiology of TB reflects complex interactions between biological, social, economic, and environmental factors. Understanding the distribution and determinants of TB is crucial for effective control and elimination efforts.

Global Burden

• According to recent WHO estimates, over 10 million people develop TB each year, with more than 1.3 million deaths among HIV-negative individuals and an additional over 200,000 deaths among those living with HIV.[21]
• TB is among the top 13 causes of death worldwide and remains the leading cause of death from a single infectious agent, surpassing HIV/AIDS.
• Despite being curable, many TB cases go undiagnosed or are diagnosed late, particularly in resource-limited settings.

High-Burden Regions

• The majority of TB cases occur in low- and middle-income countries, with the highest incidence rates in:
o South-East Asia (particularly India, Indonesia, and Bangladesh)
o Sub-Saharan Africa, where TB and HIV co-infection is highly prevalent
o Western Pacific regions such as China and the Philippines

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 5, Issue 1, November 2025 Impact Factor: 7.67

• Eight countries accounted for over two-thirds of global TB cases in 2023, including India, China, Indonesia, the Philippines, Pakistan, Nigeria, Bangladesh, and the Democratic Republic of the Congo.[22]

Drug-Resistant TB

• Approximately 3–4% of new TB cases and 15–20% of previously treated cases are estimated to have multidrug-resistant TB (MDR-TB).
• Drug-resistant TB is a major public health threat, especially in areas with weak health systems and inconsistent drug supply.
• Detection of drug-resistant TB remains a challenge, with many cases undiagnosed or improperly managed.

HIV Co-Infection

• HIV significantly increases the risk of developing active TB due to immunosuppression.
• In regions with high HIV prevalence, such as Southern Africa, TB is often the most common opportunistic infection and cause of death among people living with HIV.
• Integrated TB/HIV care programs have become a cornerstone of public health strategies in these areas.

Age and Gender Distribution

• TB can affect people of all ages, but adults in their most productive years (15–49 years) bear the highest burden.
• Men are generally more affected than women, though women may face greater barriers to diagnosis and treatment in some societies.
• Children under 5 are at increased risk of severe forms like TB meningitis and miliary TB.

Risk Factors for TB Infection and Disease

• HIV infection
• Malnutrition
• Diabetes mellitus
• Tobacco smoking
• Alcohol abuse
• Close contact with active TB cases
• Living in overcrowded or poorly ventilated settings
• Occupational exposure (e.g., healthcare workers, miners)

Impact of COVID-19

• The COVID-19 pandemic disrupted TB services globally, leading to a decline in case detection and an increase in deaths due to delayed diagnosis and treatment.
• Many countries reported setbacks in TB control targets as health systems shifted resources to the pandemic response.[1]

Control and Elimination Efforts

• The WHO's End TB Strategy aims to reduce TB deaths by 90% and cases by 80% by 2030 (compared to 2015 levels).
• Efforts focus on early diagnosis, universal drug susceptibility testing, shorter and more effective treatment regimens, preventive therapy, and research into new vaccines.

Types of Tuberculosis (TB)

Tuberculosis can be classified in several ways depending on where the disease occurs, whether it is active or latent, and the presence or absence of drug resistance. Understanding these types is essential for proper diagnosis, treatment, and public health management.

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 5, Issue 1, November 2025 Impact Factor: 7.67

1. Based on Site of Infection

a. Pulmonary TB

• The most common form, accounting for the majority of TB cases.
• Affects the lungs and is the main source of transmission through airborne droplets.
• Symptoms include persistent cough, chest pain, coughing up blood, fever, night sweats, and weight loss.

b. Extrapulmonary TB

• Occurs outside the lungs, affecting other organs or systems.
• More common in immunocompromised individuals (e.g., those with HIV).

• Types of extrapulmonary TB include:

o Lymph Node TB: Swollen, often painless lymph nodes (usually in the neck).[2]
o Spinal TB (Pott's disease): Involves vertebrae; causes back pain and potential spinal deformities.
o TB Meningitis: Affects the brain and spinal cord; presents with headache, fever, neck stiffness, and neurological signs.
o Pleural TB: Infection of the pleural space; causes chest pain and difficulty breathing.
o Genitourinary TB: Involves kidneys, bladder, or reproductive organs; may cause urinary symptoms or infertility.
o Abdominal TB: Affects intestines or peritoneum; presents with abdominal pain, fever, and weight loss.
o Bone and Joint TB: Affects joints and bones other than the spine.

c. Miliary TB

• A rare and severe form of TB where the bacteria spread through the bloodstream to multiple organs.
• Named for the millet seed–like appearance of lesions on imaging.
• Can be life-threatening without prompt treatment.[3]

2. Based on Disease Activity

a. Latent TB Infection (LTBI)

• The person is infected with M. tuberculosis, but the bacteria are inactive.
• No symptoms and not contagious.
• Can remain dormant for years or a lifetime.
• May reactivate under conditions like immunosuppression (e.g., HIV, diabetes, chemotherapy).
• Treated with preventive therapy to avoid progression to active disease.

b. Active TB Disease

• The bacteria are actively multiplying and causing symptoms.
• Can be pulmonary or extrapulmonary.
• Highly infectious in pulmonary form.
• Requires full course of anti-TB treatment to cure and prevent spread.

3. Based on Drug Resistance Profile

a. Drug-Susceptible TB

• Responds to standard first-line TB drugs (e.g., isoniazid, rifampicin, ethambutol, pyrazinamide).
• Most TB cases fall into this category.
• Treatment usually lasts 6 months.[5]

b. Multidrug-Resistant TB (MDR-TB)

• Resistant to at least isoniazid and rifampicin, the two most powerful first-line drugs.
• Requires second-line drugs and longer treatment (often 18–24 months).

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 5, Issue 1, November 2025 Impact Factor: 7.67

• Treatment is more complex and toxic.

c. Extensively Drug-Resistant TB (XDR-TB)
• Resistant to isoniazid and rifampicin (i.e., MDR-TB), plus any fluoroquinolone and at least one second-line injectable drug (e.g., amikacin).
• Very difficult to treat and associated with poor outcomes.

d. Pre-XDR TB (as per newer WHO definition)
• MDR-TB that is also resistant to either a fluoroquinolone or a second-line injectable, but not both.
• Indicates progression towards XDR-TB.

e. Totally Drug-Resistant TB (TDR-TB) (not officially recognized by WHO)
• Refers to strains resistant to all available TB drugs.
• Rare but extremely concerning from a public health perspective.[7]

Transmission and Risk Factors of Tuberculosis (TB)
Understanding how TB spreads and the factors that increase a person's risk of infection or disease progression is essential for designing effective control strategies.

1. Transmission of TB
Tuberculosis is a highly contagious airborne disease caused by the bacterium Mycobacterium tuberculosis. It spreads from person to person under specific conditions.

Mode of Transmission
• TB is transmitted through the air when a person with active pulmonary TB coughs, sneezes, speaks, laughs, or sings.
• Tiny droplets containing TB bacteria are expelled and can remain suspended in the air for hours, especially in poorly ventilated indoor environments.
• Inhalation of these droplets by another person can lead to infection, particularly after prolonged or repeated exposure.

Non-Transmissible Forms
• Extrapulmonary TB (affecting organs other than the lungs) is generally not contagious.
• Latent TB infection (where the bacteria are inactive) does not spread to others.[11]

2. Risk Factors for TB Infection and Disease
Several factors increase a person's susceptibility to TB infection or raise the risk of latent TB progressing to active disease.
A. Biological and Health-Related Risk Factors
• HIV/AIDS: The most significant risk factor due to weakened immunity.
• Diabetes mellitus: Triples the risk of developing active TB.
• Malnutrition: Compromises immune function and increases vulnerability.
• Young children and the elderly: Have weaker immune systems.[13]
• Immunosuppressive therapy: Such as chemotherapy, corticosteroids, or organ transplantation.

B. Environmental and Social Risk Factors
• Close contact with an active TB case, especially within households or crowded settings.
• Living in overcrowded or poorly ventilated environments (e.g., prisons, refugee camps, slums).
• Poverty: Associated with poor nutrition, housing, and limited access to healthcare.
• Lack of access to TB diagnosis and treatment, leading to delayed care and continued transmission.

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 5, Issue 1, November 2025 Impact Factor: 7.67

• Substance abuse: Alcoholism and drug use weaken immunity and reduce treatment adherence.

C. Occupational Risk Factors

• Healthcare workers, especially in high-TB-burden regions, due to frequent exposure to infectious patients.[17]
• Miners and industrial workers, particularly in settings with silica dust exposure (linked to silicosis, a TB risk factor).

D. Behavioral Risk Factors

• Smoking tobacco increases the risk of TB infection and disease progression.
• Poor treatment adherence in patients with TB can lead to persistent infection, transmission, and drug resistance.

3. Special High-Risk Populations

• People living with HIV/AIDS
• Prisoners and those in correctional facilities
• Migrant workers, refugees, and internally displaced persons
• Homeless populations
• Residents of long-term care facilities

Pathophysiology of Tuberculosis (TB)

The pathophysiology of tuberculosis describes the biological mechanisms through which Mycobacterium tuberculosis (M. tuberculosis) infects the body, evades the immune system, and causes disease. TB primarily affects the lungs (pulmonary TB) but can involve almost any organ (extrapulmonary TB).[21]

1. Entry and Initial Infection

• Transmission begins when a person inhales aerosolized droplets containing M. tuberculosis
bacilli expelled by someone with active pulmonary TB.
• The bacilli reach the alveoli (small air sacs) in the lungs, where they are engulfed by alveolar macrophages, the immune cells responsible for destroying pathogens.

2. Intracellular Survival and Immune Evasion

• Instead of being destroyed, M. tuberculosis can survive and replicate inside macrophages by:
o Inhibiting phagosome-lysosome fusion, which normally kills bacteria.
o Producing lipid-rich cell walls that resist destruction.
• This allows the bacteria to persist undetected by the host immune system for weeks.

3. Immune Response and Granuloma Formation

• The body eventually mounts a cell-mediated immune response:[23]
o T lymphocytes (especially CD4+ T-cells) recognize infected macrophages and release cytokines like interferon-gamma (IFN-γ) to activate them.
o Activated macrophages release enzymes and reactive oxygen species to try to contain the infection.
• This leads to the formation of a granuloma — a structured collection of immune cells that walls off the infection.
o In the center, infected macrophages (sometimes forming multinucleated giant cells) are surrounded by T-cells, fibroblasts, and epithelial cells.
o Granulomas aim to contain the infection but do not eliminate the bacteria.

4. Latent TB Infection (LTBI)

• In many cases, the immune system contains the infection, leading to latent TB, where:
o The bacteria remain alive but dormant within granulomas.
o The person shows no symptoms and is not contagious.
o Latent TB can reactivate later if the immune system weakens.

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 5, Issue 1, November 2025 Impact Factor: 7.67

5. Reactivation and Active Disease

• Reactivation occurs when immunity declines (e.g., due to HIV, diabetes, malnutrition, or aging).
• Granulomas break down, releasing active bacilli.
• This leads to tissue destruction, caseation necrosis (cheese-like tissue), and cavitation (hollow spaces in the lungs).
• In active pulmonary TB, patients develop symptoms such as:[22]
o Persistent cough, fever, weight loss, and hemoptysis.
• The bacilli are now transmissible to others via coughing or sneezing.

6. Disseminated or Extrapulmonary TB

• In some cases, especially in immunocompromised individuals, the bacteria spread through the bloodstream or lymphatic system to other organs.
• This can cause:
o Miliary TB: Widespread infection with small nodular lesions in multiple organs.
o TB meningitis, spinal TB, renal TB, or peritoneal TB, depending on the site.

7. Tissue Damage and Healing

• TB causes chronic inflammation, resulting in:
o Fibrosis (scarring)
o Calcification of granulomas
o Lung cavitation and structural damage
• Healing may involve fibrotic scars or calcified nodules visible on chest X-rays, known as Ghon complexes.

Clinical Features of Tuberculosis (TB)

The clinical presentation of tuberculosis varies depending on the site of infection, the immune status of the individual, and whether the disease is active or latent. While pulmonary TB is the most common and contagious form, extrapulmonary TB can affect almost any organ in the body.

1. General (Systemic) Symptoms

These occur in both pulmonary and extrapulmonary TB:
• Fever – often low-grade and worse in the evening
• Night sweats – drenching, especially at night
• Unexplained weight loss – common and progressive
• Fatigue and weakness – due to chronic inflammation
• Loss of appetite – often leads to malnutrition[12]

2. Pulmonary TB (Lungs)

Most common form; responsible for disease transmission.
Typical symptoms:
• Persistent cough (lasting more than 2–3 weeks)
• Cough with sputum – may be clear, yellowish, or blood-stained
• Hemoptysis – coughing up blood or blood-tinged sputum
• Chest pain – may worsen with deep breaths or coughing
• Shortness of breath – in advanced or extensive disease
Physical examination may reveal:
• Decreased breath sounds
• Rales (crackles)

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 5, Issue 1, November 2025 Impact Factor: 7.67

• Signs of lung consolidation or cavitation

3. Extrapulmonary TB (Outside the Lungs)
Accounts for ~15–20% of TB cases in immunocompetent people and up to 50% in HIV-infected individuals.

a. Lymph Node TB (Tuberculous Lymphadenitis):
• Painless swelling of lymph nodes, especially in the neck (cervical nodes)
• Nodes may become matted or drain pus in advanced cases[15]

b. TB Meningitis:
• Headache, fever, vomiting
• Neck stiffness, altered mental status, or coma in severe cases
• Risk of seizures or cranial nerve palsies

c. Skeletal TB (e.g., spinal TB or Pott's disease):
• Back pain, stiffness, or deformity
• Neurological deficits if spinal cord is compressed
• Joint swelling or pain in other skeletal TB cases

d. Genitourinary TB:
• Flank pain, frequent urination
• Blood in urine (hematuria)
• Possible infertility in both men and women[12]

e. Abdominal TB:
• Abdominal pain, distension
• Changes in bowel habits (e.g., constipation or diarrhea)
• Weight loss, fever
• Can mimic cancers or Crohn's disease

f. Miliary TB:
• Disseminated TB involving multiple organs
• Non-specific symptoms: high fever, weakness, weight loss
• Chest X-ray shows "millet seed"–like infiltrates
• Life-threatening if not treated promptly

4. Latent TB Infection (LTBI):
• No symptoms or physical findings
• Not contagious
• Detected through positive tuberculin skin test (TST) or interferon-gamma release assay (IGRA)
• Carries a lifetime risk (~5–10%) of progressing to active TB, especially if immunity drops

5. TB in Immunocompromised Individuals (e.g., HIV Patients):
• More likely to have atypical or extrapulmonary presentations
• Symptoms may be milder or non-specific[11]
• Rapid progression from latent to active TB is common
• Higher mortality rates without early diagnosis and treatment

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 5, Issue 1, November 2025 Impact Factor: 7.67

Treatment of Tuberculosis (TB)

Tuberculosis is a curable disease when diagnosed early and treated with the correct combination of anti- tubercular drugs. Treatment varies depending on the type of TB (drug-sensitive or drug-resistant), the site of infection, and the patient's clinical condition.

1. Treatment of Drug-Sensitive TB Standard First-Line Regimen

For new cases of pulmonary or extrapulmonary TB that are not drug-resistant:

• Intensive Phase (2 months):
o H = Isoniazid
o R = Rifampicin
o Z = Pyrazinamide
o E = Ethambutol[19]
o This phase aims to kill most bacilli and prevent resistance.
• Continuation Phase (4 months):
o H = Isoniazid
o R = Rifampicin
o Continued to eliminate remaining bacteria and prevent relapse.

Total Duration:

• 6 months for most drug-sensitive TB cases.
• 9–12 months for certain extrapulmonary TB types (e.g., TB meningitis, bone and joint TB).

Directly Observed Treatment, Short-Course (DOTS):

• A WHO-recommended strategy where a healthcare worker supervises drug intake.
• Improves adherence and reduces resistance risk.

2. Treatment of Latent TB Infection (LTBI)

• Used to prevent progression to active TB in high-risk individuals (e.g., HIV+, close contacts).
• Options include:
o Isoniazid daily for 6–9 months
o Rifampicin daily for 4 months
o Isoniazid + rifapentine weekly for 3 months (3HP regimen)[21]

3. Treatment of Drug-Resistant TB

Drug-resistant TB requires second-line drugs and longer, more complex regimens.

a. Multidrug-Resistant TB (MDR-TB)

• Defined as resistance to at least isoniazid and rifampicin.
• Treatment duration: 9 to 20 months (depending on drug combinations and patient response).
• WHO-recommended regimens may include:
o Bedaquiline (newer drug, improves outcomes)
o Linezolid
o Levofloxacin or Moxifloxacin (fluoroquinolones)
o Clofazimine, Cycloserine, or Delamanid

b. Extensively Drug-Resistant TB (XDR-TB)

• Resistant to isoniazid, rifampicin, a fluoroquinolone, and at least one second-line injectable.
• Requires individualized regimens based on drug susceptibility testing (DST).[23]
• Treatment can extend up to 24 months or more.
• Combination therapy with newer drugs like pretomanid, bedaquiline, and linezolid (BPaL regimen) may be used.

4. Monitoring and Support During Treatment

• Regular follow-ups to assess response and manage side effects.

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 5, Issue 1, November 2025 Impact Factor: 7.67

• Sputum testing (smear/culture) during and after treatment to confirm cure.
• Monitor for adverse drug reactions, such as:
o Hepatotoxicity (isoniazid, rifampicin, pyrazinamide)
o Optic neuritis (ethambutol)
o Peripheral neuropathy (isoniazid, linezolid)
• Provide nutritional and psychosocial support for better outcomes.
• Educate patients about adherence and the importance of completing the full course.

5. TB Treatment in Special Populations

a. HIV Co-infection

• TB and HIV are treated concurrently.
• Antiretroviral therapy (ART) should start within 2–8 weeks of TB treatment initiation.

b. Pregnancy

• First-line drugs (except streptomycin) are generally safe.
• Pyridoxine (vitamin B6) is recommended with isoniazid.[17]

c. Children

• Use weight-based dosing and child-friendly formulations.
• Often present with paucibacillary disease, making diagnosis and treatment more challenging.

6. New and Emerging Treatments

• Shorter regimens (e.g., 4-month treatment with rifapentine + moxifloxacin) are under study or used in select patients.
• All-oral regimens for MDR/XDR-TB are replacing older regimens that included painful injectable drugs.
• Ongoing research focuses on developing more effective, shorter, and safer treatments.[18]

II. CONCLUSION

Tuberculosis remains one of the most persistent public health threats worldwide, particularly due to the growing emergence of drug-resistant strains. While the disease is preventable and curable, challenges such as delayed diagnosis, treatment non-adherence, and limited access to advanced diagnostics and drugs continue to hinder global control efforts. The evolution of multidrug-resistant (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) has made treatment more complex, costly, and less effective. Traditional treatment regimens, once highly successful, are now being replaced by longer, more toxic, and less predictable second-line therapies. Although new drugs like bedaquiline, delamanid, and pretomanid offer hope, their availability is limited in many high-burden countries.

REFERENCES

[1]. World Health Organization. Global Tuberculosis Report 2024. Geneva: WHO.
[2]. World Health Organization. "1.3 Drug-resistant TB." In Global Tuberculosis Report 2024. (World Health Organization)
[3]. World Health Organization. Anti-tuberculosis drug resistance in the world: fourth global report. Geneva: WHO. (wkc.who.int)
[4]. World Health Organization. "Guidelines for surveillance of drug resistance in tuberculosis – 5th edition." Geneva: WHO. (tdr.who.int)
[5]. Centers for Disease Control and Prevention (CDC). "Drug-resistant TB Fact Sheet." Mar 2025. (CDC)
[6]. International Union Against Tuberculosis and Lung Disease & WHO. Drug-resistant tuberculosis: review of the worldwide situation and the WHO/IUATLD Global Surveillance Project. 1995. (PubMed)
[7]. World Health Organization / IUATLD. Anti-tuberculosis drug resistance in the world: third global report / 1999–2002. Geneva: WHO. (iris.who.int)
[8]. Coll F, McNerney R, Preston MD, et al. Rapid determination of anti-tuberculosis drug resistance from whole-genome sequences. Genome Medicine. 2015;7:51.

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 5, Issue 1, November 2025
Impact Factor: 7.67

[9]. Cohen KA, Manson AL, Desjardins CA, et al. Deciphering drug resistance in Mycobacterium tuberculosis using whole-genome sequencing: progress, promise, and challenges. Genome Medicine. 2019;11:45.

[10]. Hazra D, Lam C, Chawla K, Sintchenko V, Dhyani VS, Venkatesh BT. Impact of Whole-Genome Sequencing of Mycobacterium tuberculosis on Treatment Outcomes for MDR-TB/XDR-TB: A Systematic Review. Pharmaceutics. 2023;15(12):2782.

[11]. Akhmedullin R, Algazyeva G, Rakisheva A, et al. Treatment outcomes for drug-resistant tuberculosis: a retrospective longitudinal study. BMC Infectious Diseases. 2025;25:1125.

[12]. Hu X, Wu Z, Lei J, et al. Prevalence of bedaquiline resistance in patients with drug-resistant tuberculosis: a systematic review and meta-analysis. BMC Infectious Diseases. 2025;25:689.

[13]. Kanjoori AH, Hosseinian-Far A, Hasheminezhad R, Mansouri K, Mohammadi M. Global prevalence of drug-resistant tuberculosis: a systematic review and meta-analysis. Infectious Diseases of Poverty. 2023;12:57.

[14]. Nellums LB, Rustage K, Hargreaves S, et al. Multidrug-resistant tuberculosis treatment adherence in migrants: a systematic review and meta-analysis. BMC Medicine. 2018;16:27.

[15]. "25 years of surveillance of drug-resistant tuberculosis: achievements, challenges, and way forward." Lancet Infectious Diseases. Dean AS, Tosas Auguet O, Glaziou P, Zignol M, Ismail N, Kasaeva T, et al. (World Health Organization)

[16]. Ogunlade B, Tadesse LF, Li H, et al. Rapid, antibiotic incubation-free determination of tuberculosis drug resistance using machine learning and Raman spectroscopy. Preprint arXiv. 2023. (arXiv)

[17]. Shastry P, Muthulur SC, Kumarasami N, et al. Advancing Chronic Tuberculosis Diagnostics Using Vision-Language Models: A Multimodal Framework for Precision Analysis. Preprint arXiv. 2025. (arXiv)

[18]. Wu E, Ellington C, Lengerich B, Xing EP. Patient-Specific Models of Treatment Effects Explain Heterogeneity in Tuberculosis. Preprint arXiv. 2024. (arXiv)

[19]. Lu Z, Li Y, Tang F, et al. DeepGB-TB: A Risk-Balanced Cross-Attention Gradient-Boosted Convolutional Network for Rapid, Interpretable Tuberculosis Screening. Preprint arXiv. 2025. (arXiv)

[20]. Bahadur A, et al. (or similar) — you can search for "heteroresistance in TB" in journals like

[21]. Journal of Clinical Microbiology to get case studies and molecular data.

[22]. Zhang X, Lam C, Martinez E, Sim E, Crighton T, Marais BJ, Sintchenko V. Genomic markers of drug resistance in Mycobacterium tuberculosis populations with minority variants. Journal of Clinical Microbiology. 2023;61(10):e00485-23.

[23]. WHO. "Other patterns of drug resistance" section, in Global Tuberculosis Report 2024. (World Health Organization)

[24]. WHO. Global Task Force on TB Impact Measurement: Background document on estimating incidence of drug-resistant TB. Geneva: WHO; 2022. (cited in WHO documents)

[25]. WHO. "Guidance for the surveillance of drug resistance in tuberculosis." Geneva: WHO; latest edition.

[26]. CDC / Global HIV & TB Program. Updates on programme interventions, diagnostics, and drug-resistant TB strategies (various technical briefs).