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Review Article

A REVIEW ON LATENT TUBERCULOSIS: PATHOGENESIS AND REACTIVATION

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Tuberculosis (TB) is a chronic infectious disease caused by MycoBacterium tuberculosis and remains one of the leading causes of death from a single infectious agent worldwide . It primarily affects the lungs (pulmonary TB) but can also involve almost any organ (extra-pulmonary TB). The disease burden is disproportionately high in low- and middle-income countries, where poverty, overcrowding, co-infection with HIV, and limited healthcare access perpetuate transmission . Despite effective anti-TB drugs and the availability of the BCG vaccine, challenges such as drug-resistant strains, long treatment duration, poor adherence, and weak public-health infrastructure impede global compromised. This review summarizes the epidemiology, pathogenesis, diagnostic approaches, current treatment regimens, and emerging therapies, and highlights priorities for future research and policy to achieve TB elimination targets.

Keywords: Pulmonary TB, Extra-pulmonary TB, BCG vaccine, BCG vaccine, drug-resistant tuberculosis ,DOTS.

INTRODUCTION

Tuberculosis has afflicted humanity for centuries and continues to impose a heavy toll on global health despite being preventable and curable. The causative agent, Mycobacterium tuberculosis, spreads through airborne droplets from individuals with active pulmonary TB, leading to both latent infection and active disease when the host immune system is compromised. TB is a major killer among people living with HIV and is strongly associated with poverty, malnutrition, diabetes mellitus, and other social determinants of health. Recent estimates indicate millions of new TB cases and over a million deaths annually[1], underscoring the need for sustained investment in diagnostics, treatment, and prevention. This review aims to provide a comprehensive update on TB, focusing on its burden, biology, diagnosis, treatment, challenges, and future directions.[2-3]

Early historical descriptions of TB date back to ancient civilizations, but the identification of M. tuberculosis by Robert Koch in 1882 [4] marked a turning point in understanding the disease. Landmark developments in the mid-20th century, including the discovery of streptomycin and isoniazid [5], transformed TB from a frequently fatal illness into a treatable disease. The introduction of multidrug regimens and directly observed treatment, short-course (DOTS), helped reduce mortality and improve cure rates in many settings.

In recent decades, the global TB landscape has

been reshaped by the emergence of drug-resistant TB (especially multidrug-resistant and extensively drug-resistant TB), the HIV/TB epidemic, and the recognition of latent TB infection as a major reservoir for reactivation disease. New molecular diagnostics, such as Xpert MTB/RIF and line-probe assays, have improved detection of TB and rifampicin resistance [6], although access remains uneven across regions. Parallel advances in pathogenesis and immunology have clarified the role of granuloma formation, host immune responses, and bacterial persistence in latency and reactivation.[7] Several reviews also emphasize the need for shorter, safer, and more effective regimens and the development of novel vaccines to complement existing strategiaperture.

This review follows a narrative-review design, synthesizing key evidence from recent systematic reviews, guidelines, and original research articles on TB. The primary sources include peer-reviewed publications indexed in databases such as PubMed and sites of the World Health Organization (WHO), as well as comprehensive textbooks and clinical-review articles on infectious diseases and pharmacotherapy. Searches were conducted using MeSH terms and keywords such as "tuberculosis," "latent TB infection," "drug-resistant tuberculosis," "diagnosis," "treatment," and "control programs," with emphasis on publications from the last 10–15 years to ensure currency. Papers were selected based on relevance, methodological rigor, and concordance with major guidelines (e.g., WHO and national TB programs). Data were extracted on epidemiology, pathogenesis, diagnosis, treatment regimens, resistance patterns, and emerging therapeutic strategies, then synthesized into thematic sections.

Epidemiology and burden

TB is the world's leading cause of death from a single infectious agent, with millions of incident cases and over a million deaths reported annually, including a substantial proportion among people living with HIV [1]. The disease burden is highest in low- and middle-income countries of Asia and Africa, though migration and HIV contribute to TB in high-income regions [2,3]. A large proportion of the global population is estimated to harbor latent TB infection, representing a reservoir for future active disease if immunity wanes. [8,9]

Pathogenesis and clinical forms

Following inhalation, M. tuberculosis is phagocyte by alveolar macrophages but evades killing, leading to formation of granulomas that may wall off the bacilli (latent phase) or become necrotic and cavitate (active disease).

Pulmonary TB is the most common form, typically presenting with chronic cough,

hemoptysis, fever, night sweats, weight loss, and radiological abnormalities. Extra-pulmonary TB—in lymph nodes, pleura, central nervous system, bones, kidneys, and other sites can occur via hematogenous or lymphatic spread and may show atypical or subtle clinical features, complicating diagnosis. [10]

Diagnosis

Sputum smear microscopy remains a rapid, low-cost initial test but has limited sensitivity, especially in children and based co-infected patients. Mycobacterial culture is the gold standard for TB confirmation but is slow (weeks), prompting broader use of liquid-culture and molecular assays such as Xpert MTB/RIF and line-probe tests for rapid detection and rifampicin resistance screening.[6,11] Interferon-gamma release assays and tuberculin skin tests are used to detect latent TB infection, albeit with limitations in specificity and interpretation in BCG-vaccinated populations [8].

Treatment and drug-resistance

Standard first-line treatment for drug-sensitive pulmonary TB consists of a 6-month regimen of isoniazid, rifampicin, pyrazinamide, and ethambutol during an intensive phase, followed by continuation with isoniazid and rifampicin. [12] Treatment of latent TB infection typically uses isoniazid alone, rifampicin-based regimens, or combination therapy for shorter durations [12]. Drug-resistant TB—especially multi-drug-resistant (MDR-TB) and extensively drug-resistant (XDR-TB)—requires prolonged regimens with second-line drugs (e.g., fluoroquinolones, injectables, bedaquiline, delamanid), which are more toxic, costly, and logistically demanding.[13] Newer regimens including shorter all-oral MDR-TB regimens have shown improved tolerability and adherence, supporting WHO-recommended policy shifts. [14]

Vaccines and prevention

The Bacillus Calmette - Guérin (BCG) vaccine reduces the risk of severe forms of TB in children (e.g., miliary TB and tuberculous meningitis) but provides variable protection against adult pulmonary TB.[15] Intensive research is ongoing into next-generation vaccines (e.g., viral-vector and sub-unit vaccines) aimed at preventing infection, reactivation, or transmission, many of which are under clinical evaluation

Discussion

The global TB response has made significant progress, yet the disease remains a formidable public-health challenge due to persistent gaps in prevention, diagnosis, and treatment coverage. High rates of drug-resistant TB and the co-epidemic with HIV underscore the need for integrated, patient-centered care models that ensure early detection, adherence support, and access to newer drugs and diagnostics.

Despite advances, diagnostic limitations persist, especially for extra-pulmonary and pediatric TB, and smear-negative pulmonary TB, leading to delayed or missed diagnoses. The long duration of treatment and cumulative toxicity of second-line drugs continue to affect adherence and outcomes in drug-resistant cases, even as newer regimens offer shorter, oral, and safer alternatives.

Social and economic factors—poverty, malnutrition, overcrowded living conditions, stigma, and fragmented health systems—amplify TB transmission and hinder effective control. Addressing these determinants requires multi-sectoral collaboration beyond the health sector, including social protection, housing, employment, and education initiatives. At the same time, investment in research on novel drugs, shorter regimens, biomarkers of cure, and improved vaccines is essential to move toward TB elimination and reduce relapse and mortality. [16]

CONCLUSION

Tuberculosis remains a major global infectious disease with profound health, social, and economic impacts. Current control strategies based on early diagnosis, standardized treatment, and preventive therapy have reduced mortality, but persistent challenges—drug resistance, HIV co-infection, diagnostic delays, and weak health systems—limit progress. Strengthening primary-care platforms, expanding access to rapid molecular diagnostics and newer anti-TB drugs, and advancing vaccine development are critical to achieving global TB elimination targets. Sustained political commitment, adequate funding, and multi sectoral engagement will be indispensable for transforming TB from a persistent epidemic into a controlled and preventable disease in the coming decades.

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Conflict of Interest

The authors declare that they have no conflict of interest