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TUBERCULOSIS AND IT'S TREATMENT

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ABSTRACT

Tuberculosis (TB) remains a global health concern, affecting millions worldwide. This comprehensivereview aims to provide an update on the current understanding of TB diagnosis, treatment, and management strategies. We discuss the epidemiology, pathogenesis, and clinical manifestations of TB, as well as recent advances in diagnostic techniques, including molecular tests and imaging modalities.

The review focuses on current treatment regimens, including first-line and second-line therapies, and exploresemerging treatment strategies, such as host-directed therapies and vaccine development. We also examine thechallenges posed by drug-resistant TB, co-infections (e.g., HIV), and comorbidities.

Furthermore, we highlight novel research directions, including nanotechnology-based drug delivery systems and immunotherapies. Our review underscores the need for continued research, improved healthcare infrastructure, and enhanced global collaboration to combat this ancient yet persistent disease.

INTRODUCTION

- Tuberculosis is an infectious disease that has more than 1 million cases per year in India. It is caused by bacteria Mycobacterium tuberculosis. Generally, it affects the A pulmonary portion ofthe human body, but it can also affect other parts if it remains untreated. In 1990, the World HealthOrganisation (WHO) concluded on the GlobalBurden of disease that TB is the seventh most fatal disease in the world1
- In 2001, the WHO estimated that 32% of the world population has been suffering from TB. Every year, nearly 8 million people suffer from TB and 2 million atients die because of impropertreatment.Tuberculosis is a potentially serious infectious disease that mainly affects our lungs. Bacteria that causes tuberculosis are spread from one person to another through tiny droplets released into the air via coughs and sneezes2

HISTORY OF TB

- "Just sleep and eat nutritious foods" was advice given to TB patients in the 1800s infected with Mycobacterium tuberculosis, an airborne disease that usually affects the pulmonary region leading tosevere coughing, fever and chest pains 3 German microbiologist
- Robert Koch reported that Mycobacterium tuberculosis cause TB in humans in 18824 This revolutionary finding along with the later invention of tuberculin in 18903-5 With the starting of AIDS,
- TB is transmitted from person to person through airborne droplets when an individual with active TBdisease coughs, sneezes, or speaks. However, not everyone infected with M. tuberculosis becomes ill. Most individuals with a healthy immune response are able to control the infection, leading to a latent TB state in which the bacteria remain dormant.
- This latent infection can later progress to active TB disease, particularly in individuals with weakenedimmune systems, such as those with HIV, diabetes, or malnutrition.

WHO Global Tuberculosis Report (2017). concluded 4,90,000 cases of multidrug resistant (MDR) TB, with only 50% survival in patients who received recommended WHO treatment regimens. The report explains theneed for new therapies and access for elaborating TB treatment delivery and management conclusion. Many challenges remain in developing optimal tuberculosis treatmert regimens. Combined attempts by stakeholders,advocates and researchers are promoting further development of shorter courses, more potent, safer and better tolerated treatment regimens. Only three novel drugs are in an advanced phase of evolution for MDR TB andnine are being analysed in phase 1 and 2 trials. Rather than new drugs, a bunch of immune based therapy andhost directed therapies are under expansion aimed to wipe off Mycobacterium tuberculosis infection, reducing the duration of treatment, preventing permanent lung damage and avoiding the development of new drug resistance.

The International Union against TB is one of the most ancient uniors dealing with health issues related to TB. It was first registered in 1902 and started its publication Tuberculosis in French, German and English. Its mainaim to provide care to an innumerable number of TB patients in poorer countries through the National Tuberculosis Program (NTP). This program is aimed at providing the skill to the person responsible for the task at the Basic

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LITERATURE OF SURVEY

1. Mehraj J. et al., 2016 confirmed that there is a need to focus on extrapulmonary TB among femalepopulations to document the epidemiology in South Asia, and examine the risk factors, diagnosticmodalities, treatment strategies, and outcomes to carry out preventive and controls40.
2. Cataldi A.A. et al., 2017 illustrated that there is a number of drugs that can cure TB but his The article focuses on azole compounds and All azole compounds tested in his study showed inhibitory activity against MDR M. tuberculosis clinical isolates bacterias41.
3. Wakamatsu K. et al., 2018 concluded in his article that Prognostic factors in patients with miliarytuberculosis that in patients with miliary tuberculosis, old age, ARDS(Acute Respiratory Distress Syndrome) and consciousness disturbance were factors associated with poor prognosis42-45.
4. Aziza R. et al., 2015 ascertained that it raised the harmful impact of smoking on the clinical and radiological presentation of tuberculosis, and late bacteriological negativity, therefore we need tointegrate smoking control into the national TB control program to completely obsolete TB39.
5. Mehraj J. et al., 2016 confirmed that there is a need to focus on extrapulmonary TB among femalepopulations to document the epidemiology in South Asia, and examine the risk factors, diagnosticmodalities, treatment strategies, and outcomes to carry out preventive and controls40.
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AIM: To the aim of this review is to provide a comprehensive analysis of tuberculosis (TB),focusing on its epidemiology, pathogenesis, diagnostic methods, and treatment strategies.

OBJECTIVE

1. To summarize the epidemiology and pathogenesis of tuberculosis.
2. To evaluate the effectiveness of current diagnostic methods (traditional and molecular).
3. To review first-line and second-line treatment regimens for tuberculosis.
4. To discuss emerging treatment strategies, including host-directed therapies and vaccine development.
5. To examine the challenges posed by drug-resistant tuberculosis, co-infections (e.g., HIV), and comorbidities.
6. To identify novel research directions in tuberculosis treatment, including nanotechnology and immunotherapies.
7. To highlight the need for improved healthcare infrastructure and global collaboration in combating tuberculosis.

PATHOPHYSIOLOGY

Pathogenesis of Tuberculosis

Tuberculosis (TB) pathogenesis involves the complex interaction between Mycobacterium tuberculosis(Mtb) and the human immune system. The process is multifaceted, starting from the moment the bacterium enters the body, leading to either latent or active disease. Understanding the stages of TB pathogenesis is essential for developing better treatments and vaccines. Below is a detailed breakdown ofTB pathogenesis:

Inhalation: TB spreads primarily through airborne droplets. When a person with active pulmonary TBcoughs, sneezes, or talks, tiny droplets containing M. tuberculosis are released into the air. These droplets can be inhaled by others, leading to infection.

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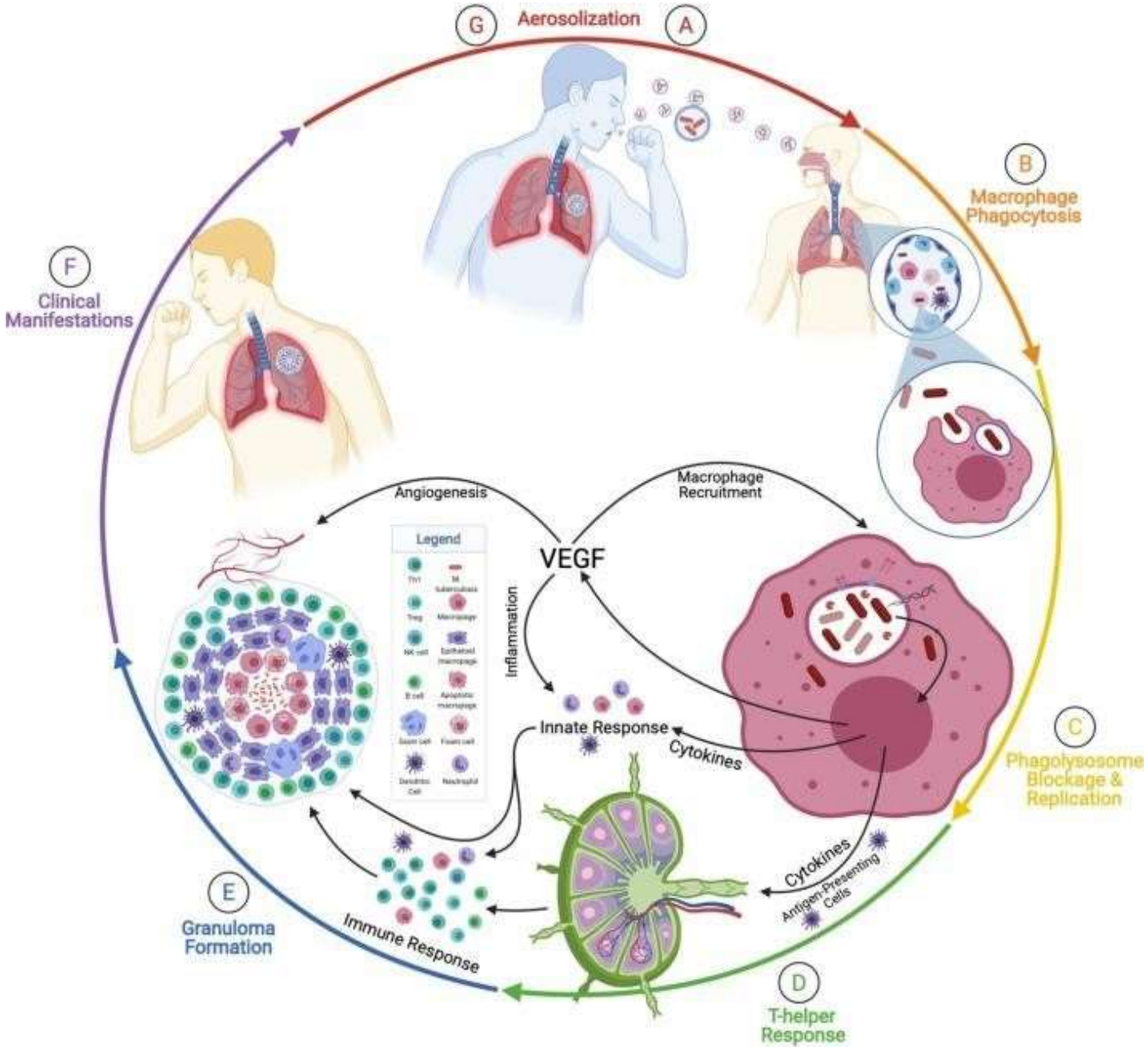

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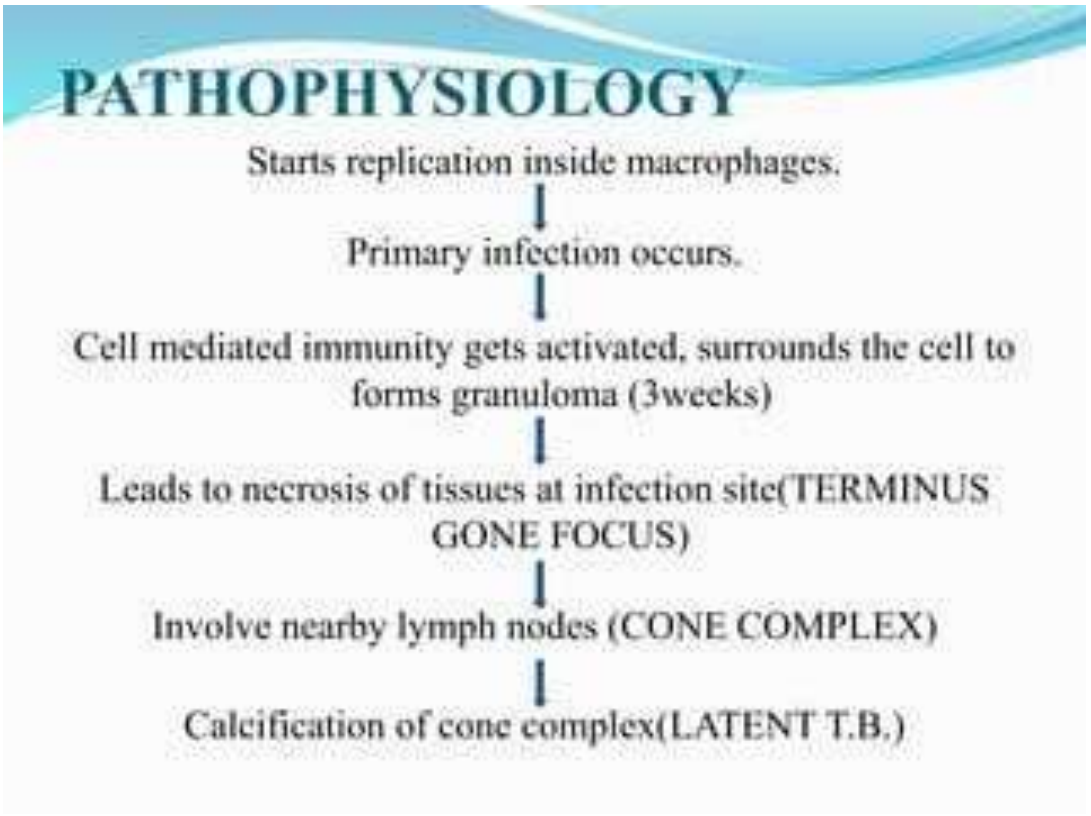

Diagnosis of Tuberculosis

Effective diagnosis of tuberculosis (TB) is crucial for timely treatment and controlling the spread ofthe disease. The diagnostic process varies based on the type of TB (pulmonary or extrapulmonary), the patient's immune status, and the resources available. Advances in diagnostic tools have improveddetection rates, but challenges remain, particularly in resource-limited settings. Below is a review of key TB diagnostic methods, their advantages, limitations, and emerging technologies.

1. Clinical Symptoms and Patient History

Symptom Assessment: The initial diagnosis of TB is often based on clinical symptoms, particularlyin high-burden areas. Common symptoms of pulmonary TB include Persistent cough lasting more than two weeksHemoptysis (coughing up blood) Chest pain Unexplained weight lossNight sweats and fever

2. Molecular Diagnostic Tools

GeneXpert MTB/RIF: A rapid molecular test that detects M. tuberculosis DNA and rifampicin resistance in less than two hours using PCR (polymerase chain reaction) technology. It is particularlyuseful in diagnosing TB in people living with HIV and in detecting multidrug-resistant TB (MDR- TB).

Advantages: High sensitivity and specificity, rapid diagnosis, can detect drug resistance.
Limitations: Expensive, requires electricity and maintenance, and may not be widely available in allregions.
tests that detect specific gene mutations associated with resistance to first- and second-line TB drugs,particularly rifampicin and isoniazid.

Advantages: Can detect drug-resistant TB quickly, enabling appropriate treatment initiation.Limitations: Requires specialized laboratory facilities and trained personnel.

3. Immunological Tests

Tuberculin Skin Test (TST) or Mantoux Test: This test involves injecting purified protein derivative (PPD) into the skin and measuring the immune response (induration) after 48–72 hours. A positive result indicates TB exposure but cannot distinguish between latent and active TB.
Advantages: Widely available and inexpensive.

Limitations: False positives may occur due to prior BCG vaccination or exposure to non-tuberculous mycobacteria. It cannot differentiate between latent and active TB

Mantoux Text: A healthcare provider injects a small amount of tuberculin, a substance derived from deadTB bacteria, into your forearm. A small blister appears at the injection site, which disappears within 20 minutes. A small lump may form over the next few days, and you'll need to return to your healthcare provider to have it assessed. The size of the lump indicates whether you have a latent TB infection.

4. Extrapulmonary TB Diagnosis

Biopsy and Histopathology: For diagnosing TB in non-pulmonary sites (e.g., lymph nodes, pleura), a biopsy of the affected tissue followed by histopathological examination can reveal the presence of caseating granulomas, a hallmark of TB.
Advantages: Direct visualization of TB-related pathology.

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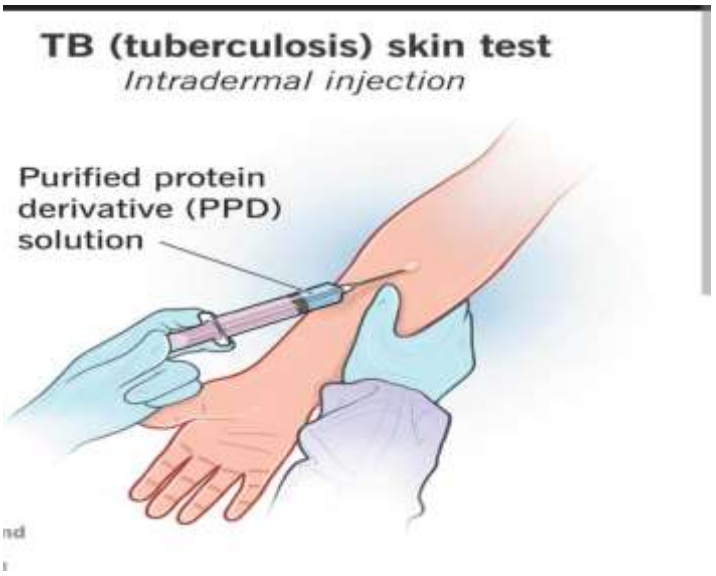
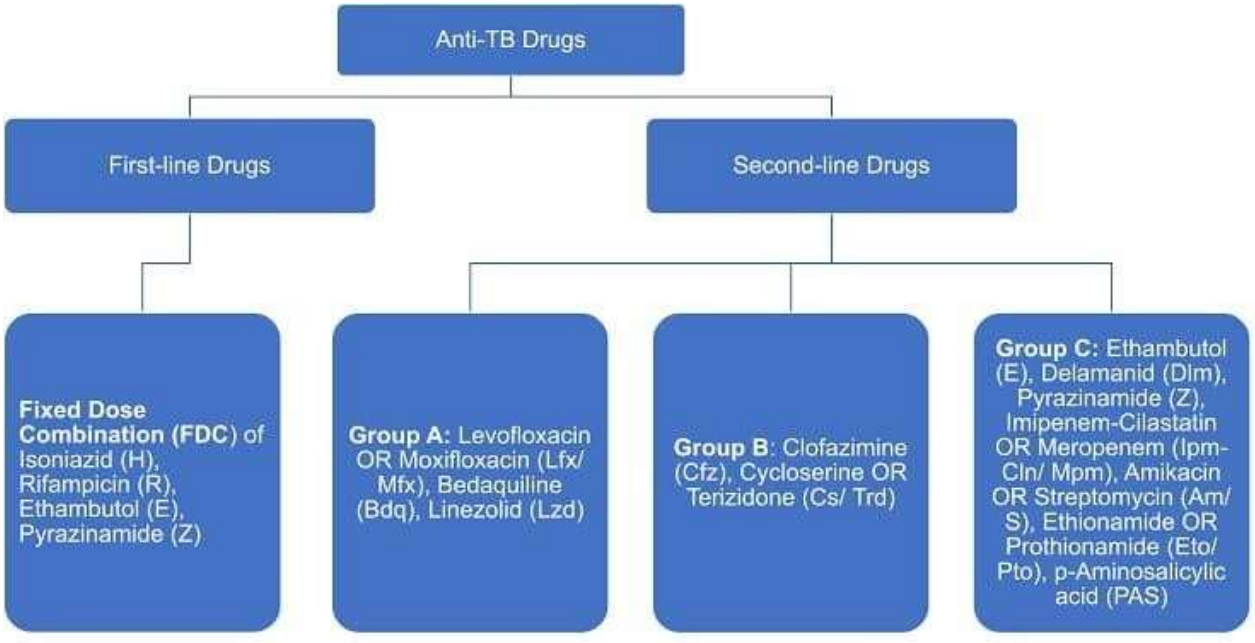
Limitations: Invasive procedures may be required to obtain samples



Classification of TB



TUBERCULOSIS INFECTION CONTROL15

Administrative controls

- Assign responsibility for TB infection control.Conduct TB risk assessment.
- Develop and institute a written TB infection control plan.
- Ensure proper cleaning and sterilization or disinfection of potentially contaminated equipment.Train and educate health-care workers.
- Test and evaluate health-care workers for TB infection and disease.Apply epidemiology based prevention principles.

Environmental controls

- Reduce the concentration of infectious droplet nuclei through the following technologies:Ventilation technologies, including natural ventilation.
- Mechanical ventilation.
- High-efficiency particulate air filtration (HEPA). Ultraviolet germicidal irradiation (UVGI)

Respiratory protection control

- Implement respiratory protection program.
- Train health care workers on respiratory system

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protection.

- Educate patients on respiratory hygiene and the importance of covering their cough.Wear mask for protection

Challenges

- HIV Co-infection: Diagnosing TB in people with HIV is particularly challenging due to atypical clinical presentations and lower bacterial loads in sputum, which reduce the sensitivityof smear microscopy.
- Extrapulmonary TB: Diagnosing TB in organs other than the lungs often requires more invasiveprocedures and advanced imaging techniques, which are not always available in resource-poorsettings.
- Resource Limitations: Many high-burden countries lack access to advanced molecular diagnostics and rely on slower, less sensitive methods like smear microscopy, leading to delays in diagnosis and treatment.

CONCLUSIONS

The treatment of tuberculosis, particularly drug-resistant forms, remains a major global health challenge. While the standard 6-month regimen for drug-sensitive TB is highly effective, the increasing prevalence of MDR-TB and XDR-TB calls for new drugs and shorter, less toxic regimens. Improving treatment adherence, monitoring for drug resistance, and ensuring equitable access to new treatments and diagnostics are essential to achieving global TB control. Advances in drug development, patient-centered treatment strategies, and vaccine research hold promise for future TB management.

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