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A REVIEW ON ADVANCED MANAGEMENT OF TUBERCULOSIS

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Abstract

Tuberculosis (TB) remains one of the leading infectious diseases globally, posing significant challenges to public health despite the availability of effective treatment. Advanced management of TB integrates modern diagnostic tools, optimized drug regimens, and innovative therapeutic approaches to enhance treatment outcomes and reduce transmission. The use of molecular diagnostics, such as GeneXpert MTB/RIF and whole-genome sequencing, allows for rapid detection of Mycobacterium tuberculosis and drug resistance patterns, enabling early and precise interventions. The development of shorter, more effective multidrug-resistant TB (MDR-TB) treatment regimens, including the use of bedaquiline, delamanid, and pretomanid, has revolutionized management strategies. In addition, patient-centered care models, including digital adherence monitoring and community-based treatment support, improve compliance and reduce relapse rates. Integration of TB-HIV co-management and preventive therapy further contributes to disease control, particularly in high-burden settings. Emerging research in host-directed therapies, vaccines, and artificial intelligence–assisted monitoring provides promising avenues for future TB control. The combination of technological innovation, personalized medicine, and strengthened public health infrastructure represents a transformative approach to TB management. Continued investment in research, diagnostics, and patient care systems is essential to achieve global TB elimination goals and ensure equitable access to advanced management strategies worldwide.

Keywords: Tuberculosis, advanced management, multidrug-resistant TB, molecular diagnostics, bedaquiline, delamanid, patient-centered care, host-directed therapy, digital adherence, TB-HIV co-management.

Introduction

1.Definition:

Tuberculosis is an infectious disease caused by the bacterium Mycobacterium tuberculosis. It most commonly affects the lungs (pulmonary TB), but it can also affect other parts of the body if it remains untreated such as the kidneys, spine, or brain. TB spreads through airborne droplets when an infected person coughs, sneezes, or speaks [1,2].

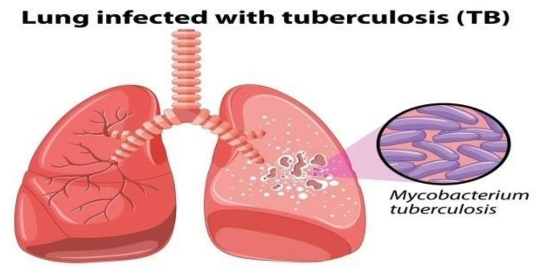

Fig 01: Image of Lung infected with tuberculosis.

2. Historical background of tuberculosis:

Tuberculosis (TB) is one of the oldest known human diseases, with evidence of its presence dating back thousands of years. Skeletal remains from ancient Egypt (around 2400 BCE) show signs of spinal tuberculosis, also known as Pott's disease [3]. Descriptions consistent with TB also appear in the writings of Hippocrates (circa 460-370 BCE), who referred to a disease called "phthisis", meaning "consumption" in Greek, due to the severe weight loss associated with the illness [4].

During the 17th or 19th centuries in Europe, TB reached epidemic proportions and was often called the "white plague" or "consumption" because of its impact on the population and the characteristic pallor of patients [5]. It was romanticized in art and literature, seen as a disease of sensitivity and refinement, even as it devastated communities.

The turning point in understanding TB came in 1882 when German physician Robert Koch discovered the bacterium Mycobacterium tuberculosis, the causative agent of TB. This was a landmark event in medical microbiology and helped shift the perception of TB from a hereditary or environmental condition to an infectious disease [6].

Public health measures and the development of sanatoriums were early efforts to control TB before effective drug treatments. [7]. The mid-20th century saw the introduction of antibiotics such as streptomycin (discovered in 1943), which significantly improved TB treatment outcomes. However, the emergence of drug-resistant strains in recent decades has posed new challenges to global TB control efforts [8,9].

3. Types of TB

Active TB VS Latent TB:

Active TB

Active tuberculosis (TB), also referred to as TB disease, presents with noticeable symptoms and can spread from person to person. The specific symptoms may differ based on whether the infection affects the lungs (pulmonary TB) or other parts of the body (extrapulmonary TB).

Common signs of active TB include:

Unintended weight loss

Reduced appetite

Persistent fever

Episodes of chills

Constant fatigue

Night sweats

If left untreated, active TB can be become severe and potentially life-threatening [10].

Latent TB:

If you have latent TB infection, the TB bacteria are present in your body but remain inactive. As a result, you won't have any symptoms and cannot spread the infections to others. However, the TB blood and skin tests will still show a positive result.

In about 5% to 10% of cases, latent TB can progress to active TB, especially in individuals with weakened immune systems due to certain medications or underlying health conditions [11].

Pulmonary TB:

Pulmonary TB refers to active tuberculosis that affects the lungs and is the form most commonly associated with the disease. It spreads when you inhale air containing TB bacteria released by an infected person through coughing, sneezing, or talking. These germs can linger in the air for several hours.

In addition to the common symptoms of TB, individuals with pulmonary TB may also experience:

A persistent cough that lasts for three weeks or more

Coughing up blood

Producing phlegm while coughing

Chest discomfort or pain

Difficulty breathing or shortness of breath [12].

Extrapulmonary TB

Extrapulmonary TB occurs when tuberculosis affects areas of the body other than the lungs, such as the bones, lymph nodes, or internal organs. The symptoms vary depending on the specific part of the body involved.

TB lymphadentis

TB lymphadentis is the most common form of extrapulmonary tuberculosis, primarily affecting the lymph nodes. It most often involves the cervical lymph nodes in the neck, though lymph nodes in other areas can also be impacted. In some cases, swelling of the lymph nodes may be the only noticeable sign.

However, TB lymphadentis can also lead to;

Fever

Tiredness or fatigue

Unexplained weight loss

Night sweats [13].

Skeletal TB:

It is also known as bone TB, occurs when tuberculosis spreads from the lungs or lymph nodes to the bones. It can affect any bone in the body, including the spine and joints. Although skeletal TB is relatively uncommon, its incidence has been increasing in regions with high rates of HIV and AIDS, as these conditions weaken the immune system. In the early stages, skeletal TB may not cause noticeable symptoms.

However, as the disease progress, it can lead to general symptoms of active TB along with:

- Intense back pain
- Joint stiffness
- Swelling in the affected area
- Formation of abscesses
- Bone deformities.

Miliary TB

Miliary TB is a type of tuberculosis that spreads throughout the body, affecting one or multiple organs. It commonly involves the lungs, bone marrow, and liver but can also reach other areas such as the spinal cord, brain, and heart. This form of TB causes the usual symptoms of active tuberculosis along with additional signs that depend on the organs affected. For instance, if the bone marrow is involved, it may lead to a reduced red blood cell count.

Genitourianry TB

It is the second most common form of extrapulmonary tuberculosis. It can affect any part of the urinary tract or reproductive organs, with the kidneys being the most frequently involved. The infection usually spreads to these areas from the lungs via the blood stream or lymphatic system. Although rare, genitourinary TB can sometimes be transmitted through sexual contact. In some cases, it may cause a tuberculosis ulcer on the penis or within the genital tract.

The symptoms vary depending on the specific area affected may include:

- Swelling of the testicles
- Painful urination
- Reduced or interrupted urine flow
- Pelvic discomfort or pain
- Lower back pain
- Decreased semen volume
- Infertility

Liver TB

Liver TB also known as hepatic TB, occurs when tuberculosis affects the liver and accounts for less than 1% of all TB cases. The infection can reach the liver from the lungs, gastrointestinal tract, lymph nodes, or through the portal vein.

- Common symptoms of liver TB include:
- High fever
- Pain in the upper abdomen
- Enlargement of the liver
- Jaundice [14]

Gastrointestinal TB

Is a form of tuberculosis that affects any part of the digestive tract, from the mouth to the anus. It symptoms often resemble those of other gastrointestinal disorders, such as crohn's disease.

TB meningitis

TB meningitis, also called meningeal tuberculosis, occurs when tuberculosis infects the meninges-the protective membranes covering the brain and spinal cord. The infection usually spreads to the meninges from the lungs or through the bloodstream. Unlike other forms of meningities that appear suddenly, TB meningitis tends to develop slowly over time.

In its early stages, it may cause nonspecific symptoms such as:

- General aches and pains
- Tiredness or fatigue
- Reduced appetite
- Persistent mild headache
- Nausea and vomiting
- Low- grade fever
- As the disease advances, more severe symptoms can develop, including:
- Intense headaches
- Sensitivity to light

Stiffness in the neck.

TB Perinotes

TB peritonitis is a form of tuberculosis that leads to inflammation of the peritoneum, the thin tissue lining the inside of the abdomen and covering most abdominal organs. It occurs in about 3.5% of people with pulmonary TB and up to 58% of those with abdominal TB. The most common signs of TB peritonitis are ascites-an accumulation of fluid in the abdomen that results in swelling, bloating, and tenderness-along with fever.

Other possible symptoms include:

Nausea

Vomiting

Reduced appetite

TB pericarditis

TB pericarditis develops when tuberculosis develops when tuberculosis spreads to the pericardium, the two thin layers if tissue filled with fluid that surround and protect the heart. It can manifest in different forms, such as constructive pericarditis, pericardial effusion, or effusive-constructive pericarditis.

Common symptoms of TB pericarditis include:

Chest discomfort or pain

Fever

Irregular or rapid hearTBeats

Difficulty breathing

Cough

Cutenous TB

It is a rare form of tuberculosis that affects the skin, even in regions where TB is widespread. It can occur in several forms and, in some cases, may spread to other parts of the body.

The primary signs of cutaneous TB are sores or lesions that commonly appear on areas such as the:

- Elbows
- Hands
- Buttocks
- Backs of the knees
- Feet

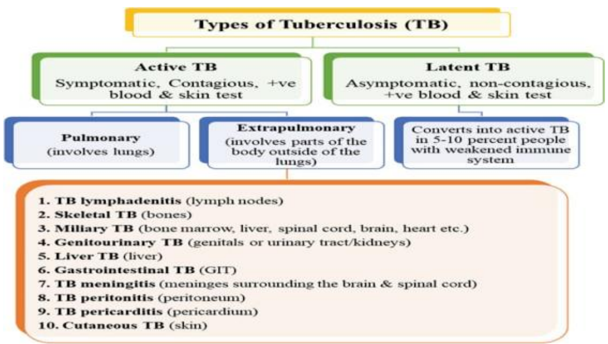

Fig 02: Image of Types of Tuberculosis.

4. Current challenges in TB control:

Despite global progress, TB control continues to be hampered by underfunded health systems, disrupted services, and the growing menace of drug- resistant strains. Large gaps in financing- only about 26% of the US $22 billion needed for TB prevention and care is currently available- have led to shortages in diagnostics, interruptions in medication supply, and weakened surveillance systems. Meanwhile, the rise of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) presents more complex, costly treatment challenges and higher risk of treatment default. Socioeconomic factors like malnutrition, poverty, migration, and climate- related disruptions further intensify vulnerability to the disease and hinder access to timely care and diagnosis [13,14,15]

5. Significance of TB research:

Tuberculosis (TB) research is crucial for achieving global TB elimination targets, as the disease remains one of the leading causes of death from a single infectious agent, causing over 1.2 million deaths annually. Research plays a vital role in developing rapid diagnostics, shorter and safer treatment regimens, and effective vaccines, which are essential to control and eventually eradicate TB. The WHO End TB strategy emphasizes "intensified research and innovation" as a key pillar to accelerate progress. However, global funding remains inadequate, with only US $1 billion invested in TB research in 2022 compared to the required US $5 billion annually, slowing innovation and implementation efforts [15].

Epidemiology

Tuberculosis remains a major global health threat, with an estimated 10.8 million people falling ill in 2023 (95% uncertainty interval: 10.1–11.7 million); among those, around 6.1% were people living with HIV. Of the total, about 55% were men, 33% women and 12% children and young adolescents. In terms of mortality, TB resulted in approximately 1.25 million deaths globally in 2023, which includes about 161,000 deaths among people who also had HIV [16,17].

Over recent years, global TB incidence has shown only modest improvement. Since 2015 incidence has dropped by about 8.3%, far short of the target set under the WHO End TB Strategy (which aims for a 50% reduction by 2025). The mortality reduction over the same period is similarly insufficient: total TB deaths have declined by about 23% between 2015 and 2023, still well below the WHO goal of a 75% cut [16,18].

India contributes substantially to the global burden. In 2023, India accounted for roughly 26% of all TB cases worldwide. Its TB incidence rate fell from ~237 per 100,000 in 2015 to ~195 per 100,000 in 2023 — a 17.7% decline. During the same period, India's TB death rate dropped by about 21.4%, from 28 per 100,000 to 22 per 100,000 [19,20].

Despite progress, key challenges persist: under-diagnosis, particularly among children; drug resistance; disruptions (e.g. due to COVID-19); and insufficient funding. Many countries are off track relative to the 2025 milestones of the End TB Strategy [16,21].

Etiology

Tuberculosis (TB) is an infectious disease caused primarily by Mycobacterium tuberculosis, a slow-growing, aerobic, acid-fast bacillus belonging to the Mycobacterium tuberculosis complex (MTBC). The MTBC also includes M. bovis, M. africanum, M. microti, and M. canettii, but M. tuberculosis is the most common pathogen responsible for human TB [22, 23].

The infection is transmitted mainly through airborne droplets produced when an infected person coughs, sneezes, or speaks. These droplet nuclei, containing the bacilli, can remain suspended in the air and be inhaled by a susceptible host [24]. Once inhaled, the bacilli reach the alveoli of the lungs, where they are phagocytosed by alveolar macrophages. However, M. tuberculosis can survive and multiply within these macrophages by inhibiting phagosome-lysosome fusion, thereby evading the host's immune response [25, 26].

The disease's progression depends on the interaction between the pathogen and the host's immune system. In most immunocompetent individuals, the infection remains latent, meaning the bacteria persist in the body without causing active disease. However, if the immune system becomes compromised, the latent infection can reactivate, leading to active pulmonary or extrapulmonary tuberculosis [27].

Factors such as HIV infection, malnutrition, diabetes mellitus, and smoking increase susceptibility to TB infection and disease progression [28, 29].

Pathophysiology

The pathophysiology of tuberculosis (TB) involves a complex interplay between the host immune system and the bacterium Mycobacterium tuberculosis (MTB). This interaction determines the progression of infection from exposure to either latent infection or active disease [30].

Transmission and Initial Infection

TB is primarily transmitted via inhalation of aerosolized droplets containing MTB, expelled when an infected person coughs, sneezes, or speaks. These droplets can remain suspended in the air for extended periods, facilitating widespread transmission [24].

Upon inhalation, MTB reaches the alveoli, where it is phagocytosed by alveolar macrophages. However, MTB has evolved mechanisms to survive within these macrophages, including inhibition of phagosome-lysosome fusion and modulation of host immune responses [31,32].

Immune Response and Granuloma Formation

In immunocompetent individuals, the innate immune response leads to the formation of granulomas-organized structures composed of macrophages, T lymphocytes, and other immune cells. These granulomas serve to contain the bacteria, preventing their spread. Within the granuloma, MTB can enter a dormant state, leading to latent tuberculosis infection (LTBI) [33, 34].

In some cases, the immune response fails to contain the bacteria, leading to active disease. This progression is influenced by factors such as immune status, comorbidities, and bacterial virulence [35].

Latency and Reactivation

Latent MTB can persist in a non-replicating state within granulomas for years. During this period, the bacteria are metabolically inactive and not transmissible. However, factors like immunosuppression or other stressors can trigger reactivation, leading to active TB disease [36].

Pathogenesis of Active Disease

In active TB, the bacteria replicate and spread, leading to tissue damage and clinical symptoms such as cough, weight loss, and hemoptysis. The immune response contributes to tissue damage through the release of inflammatory cytokines and reactive oxygen species. This inflammation can result in cavitation and necrosis, characteristic of pulmonary TB [37,38].

Understanding the pathophysiology of TB is crucial for developing effective prevention and treatment strategies. While significant progress has been made, challenges remain in managing latent infections and preventing reactivation. Ongoing research into the mechanisms of MTB persistence and host immune evasion continues to inform new therapeutic approaches [39, 40].

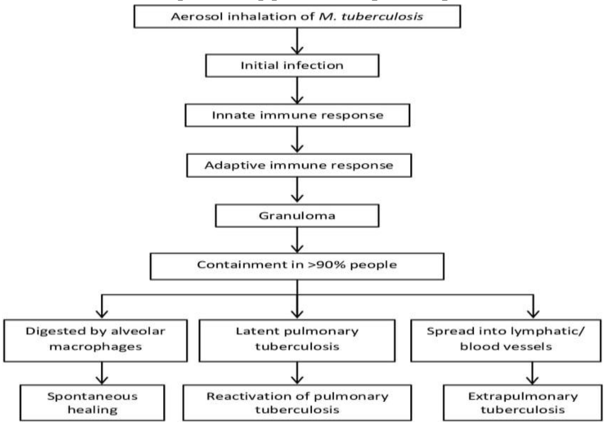

Fig 3: Image of Pathogenesis of Active Disease.

Clinical Manifestations of Tuberculosis

Tuberculosis (TB) presents with a wide range of clinical features depending on the site of infection and the host's immune status. The disease is broadly classified into pulmonary and extrapulmonary TB, with pulmonary TB being the most common and infectious form [41].

1. Pulmonary Tuberculosis

Pulmonary TB primarily affects the lungs and accounts for the majority of TB cases. The main symptoms include

- Persistent cough lasting more than two to three weeks, often producing sputum or, in advanced cases, blood (hemoptysis) [42].
- Fever (especially low-grade and in the evenings) [43].
- Night sweats and unexplained weight loss.
- Fatigue, loss of appetite, and chest pain due to pleural involvement [44].

In severe or untreated cases, progressive lung damage can lead to respiratory distress and cavitary lesions visible on chest radiographs.

2. Extrapulmonary Tuberculosis

Extrapulmonary TB occurs when Mycobacterium tuberculosis spreads beyond the lungs, affecting organs such as the lymph nodes, pleura, bones, kidneys, meninges, and the gastrointestinal tract [46].

- Lymph node TB (scrofula) often presents with painless swelling of the cervical lymph nodes.
- Pleural TB may cause pleuritic chest pain and shortness of breath due to pleural effusion.
- TB meningitis manifests with headache, fever, neck stiffness, and neurological symptoms.
- Skeletal TB (including Pott's disease) can lead to back pain and spinal deformities.
- Genitourinary TB may result in dysuria, hematuria, or infertility [46].

The presentation of extrapulmonary TB varies widely and can mimic other diseases, often leading to diagnostic challenges.

Tuberculosis (TB) remains a global health challenge, but a comprehensive, multi-faceted approach can significantly reduce its burden. Below is an overview of current prevention strategies, supported by recent guidelines and evidence [47,48,49].

Diagnostic Methods for Tuberculosis

1. Microbiological Techniques

- Sputum Smear Microscopy: The Ziehl-Neelsen stain remains a cornerstone for detecting acid-fast bacilli in sputum samples. Fluorescent microscopy has enhanced sensitivity, especially in high-burden settings.
- Culture Methods: Culturing Mycobacterium tuberculosis on solid (Lowenstein-Jensen) or liquid media (MGIT) allows for species identification and drug susceptibility testing. Liquid cultures offer faster results and higher sensitivity.
- Molecular Diagnostics: Nucleic acid amplification tests (NAATs), such as PCR, provide rapid and specific detection of M. tuberculosis. These tests are particularly useful for detecting drug-resistant strains [50].

2. Immunological Tests

- Tuberculin Skin Test (TST): The Mantoux test detects delayed-type hypersensitivity to purified protein derivative (PPD). While useful for screening, it cannot differentiate between latent and active TB or prior BCG vaccination.
- Interferon-Gamma Release Assays (IGRAs): Tests like QuantiFERON-TB Gold measure the release of interferon-gamma from T-cells in response to M. tuberculosis antigens. IGRAs are not affected by BCG vaccination and are more specific than TST [51].

3. Radiological Imaging

- Chest X-ray (CXR): CXR is essential for detecting pulmonary TB, assessing disease extent, and monitoring treatment response. It aids in differentiating TB from other pulmonary conditions [52].

4. Biomarkers and Emerging Technologies

- **Biomarkers:**
  Research into blood-based biomarkers aims to develop non-invasive diagnostic tools for TB. These markers could facilitate early detection and monitoring of treatment efficacy.
- **Artificial Intelligence (AI) in Imaging:**
  AI algorithms are being developed to analyze chest radiographs and CT scans, potentially improving diagnostic accuracy and speed [53].

Pediatric Considerations

Diagnosing TB in children presents unique challenges due to nonspecific symptoms and difficulty in obtaining sputum samples. Clinical evaluation, including history and physical examination, remains pivotal. In some cases, gastric aspirates or stool samples may be used for microbiological testing [54].

Advanced management of tuberculosis

Advanced Pharmacological Treatment of Tuberculosis

Tuberculosis (TB) remains a global health concern, especially with the emergence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) strains of Mycobacterium tuberculosis. Advances in pharmacological therapy have focused on developing novel drugs, optimizing existing regimens, and shortening treatment duration.

1. First-Line Therapy Enhancements

The standard treatment for drug-susceptible TB includes a 6-month regimen of isoniazid, rifampicin, pyrazinamide, and ethambutol (HRZE). Recent studies have evaluated high-dose rifampicin and rifapentine to improve bactericidal activity and potentially shorten treatment to 4 months without compromising efficacy [55,56].

2. Novel and Repurposed Drugs for Drug-Resistant TB

For MDR- and XDR-TB, several newer agents have been introduced:

- **Bedaquiline:**
  A diarylquinoline that inhibits mycobacterial ATP synthase, showing strong activity against resistant TB strains. It significantly improves outcomes when included in MDR-TB regimens [57].
- **Delamanid:**
  A nitroimidazole that inhibits mycolic acid synthesis, improving culture conversion rates in MDR-TB patients.
- **Pretomanid:**
  Another nitroimidazole, often used in combination with bedaquiline and linezolid (the BPaL regimen), has shown high efficacy for highly resistant TB [57].
- **Linezolid:**
  An oxazolidinone effective against MDR-TB, though its toxicity (e.g., neuropathy, myelosuppression) limits long-term use.
- **Clofazimine:**
  Originally used for leprosy, it exhibits antimycobacterial properties and enhances treatment success in resistant TB when added to combination regimens [56].

3. Shorter and All-Oral Regimens

Recent guidelines favor all-oral regimens to replace injectable drugs, reducing adverse effects and improving adherence. The WHO-recommended 6-month BPaLM regimen (bedaquiline, pretomanid, linezolid, and moxifloxacin) is now considered a major advancement for MDR- and XDR-TB treatment [56].

4. Host-Directed Therapies and Adjunctive Approaches

Research on host-directed therapies (HDTs) aims to enhance immune responses and limit lung damage. Agents like metformin, statins, and vitamin D supplementation are under investigation for their immunomodulatory roles [58].

5. Future Directions

Ongoing efforts focus on developing new compounds targeting unique bacterial pathways, such as DprE1 inhibitors (e.g., BTZ-043) and newer nitroimidazoles. Integrating pharmacogenomics and personalized therapy is expected to improve drug selection and minimize resistance [59].

Non pharmacological treatment

Non-pharmacological interventions play a crucial role in the comprehensive management of tuberculosis (TB), particularly in enhancing treatment adherence, addressing psychosocial factors, and reducing stigma. Below is a summary of key non-pharmacological approaches supported by recent evidence:

1. Directly Observed Therapy (DOT) and Supervision

DOT remains a cornerstone of TB treatment strategies. This approach involves healthcare providers observing patients as they take their medications, ensuring adherence and reducing the risk of drug resistance. Community health workers and volunteers often facilitate DOT, integrating it with broader community-based activities to enhance accessibility and support [60].

2. Psychosocial Support and Mental Health Interventions

Psychosocial factors significantly impact TB treatment outcomes. Interventions addressing mental health issues, such as anxiety and depression, have been shown to improve treatment adherence and cure rates. Effective strategies include combating stigma, addressing socioeconomic disadvantages, and providing counseling to manage fear and guilt associated with TB.

3. Community Engagement and Support

Community-based activities are essential in TB control. Engaging community health workers and volunteers helps in raising awareness, reducing stigma, and facilitating access to diagnostic and treatment services. These activities are particularly effective when integrated with other health services, such as HIV care, to provide comprehensive support [61].

4. Use of Mobile Health (mHealth) Technologies

mHealth technologies, including video observation and mobile reminders, have shown promise in improving TB treatment adherence. These tools offer innovative ways to monitor patient progress and provide support, especially in remote or underserved areas [62].

5. Addressing Stigma and Social Determinants

Reducing TB-related stigma is vital for encouraging individuals to seek treatment and adhere to prescribed regimens. Interventions focusing on stigma reduction, education, and community sensitization can lead to better treatment outcomes and increased patient engagement.

Integrating non-pharmacological interventions into TB management enhances treatment adherence and addresses the multifaceted challenges patients face. These approaches, when combined with pharmacological treatments, contribute to more effective and sustainable TB control efforts [63].

Prevention Strategies for Tuberculosis

1. Tuberculosis Preventive Treatment (TPT)

TPT is a cornerstone of TB prevention, particularly for high-risk groups such as household contacts of TB patients, individuals living with HIV, and those with latent TB infection. The World Health Organization (WHO) recommends various regimens, including:

- 3 months of daily rifampicin and isoniazid (3HR)
- 3 months of weekly rifapentine and isoniazid (3HP)
- 4 months of daily rifampicin (4R)
- 6 months of daily levofloxacin for contacts of multidrug-resistant TB (MDR-TB)

In 2023, approximately 2.1 million household contacts aged 5 years and over initiated TPT, marking a 52% increase from 2022. However, global coverage remains below targets, with only 21% of household contacts and 56% of people living with HIV receiving TPT [64].

2. Vaccination

The Bacillus Calmette-Guérin (BCG) vaccine is administered to infants in many countries to prevent severe forms of TB, such as TB meningitis and disseminated TB. While BCG does not prevent pulmonary TB in adults, ongoing research aims to develop more effective vaccines to reduce TB transmission and progression from latent infection to active disease [65].

3. Infection Prevention and Control (IPC)

Implementing IPC measures in healthcare settings and congregate environments (e.g., prisons, refugee camps) is crucial to prevent TB transmission. WHO's operational handbook outlines strategies such as administrative controls, environmental measures, and respiratory protection to reduce the risk of TB spread [66].

4. Early Detection and Screening

Active case finding through systematic screening of high-risk populations, including household contacts and individuals with HIV, is essential for early TB detection. Rapid diagnostic tools like Xpert MTB/RIF Ultra and Truenat assays facilitate timely diagnosis, enabling prompt initiation of treatment and reducing transmission.

5. Addressing Social Determinants

Factors such as malnutrition, overcrowded living conditions, and limited access to healthcare contribute to TB risk. Addressing these social determinants through multisectoral approaches can enhance TB prevention efforts [67].

Future Directions

- **Development of New Vaccines:**
  Advancements in vaccine research aim to produce candidates with higher efficacy against pulmonary TB in adults, potentially reducing transmission rates.
- **Integration of Digital Technologies:**
  Leveraging digital tools for TB surveillance, contact tracing, and treatment adherence monitoring can improve program efficiency and reach.
- **Enhanced Implementation of the End TB Strategy:**
  WHO's End TB Strategy sets ambitious targets for 2030, including an 80% reduction in TB incidence and a 90% reduction in TB deaths. Achieving these goals requires intensified efforts in prevention, diagnosis, and treatment [68].

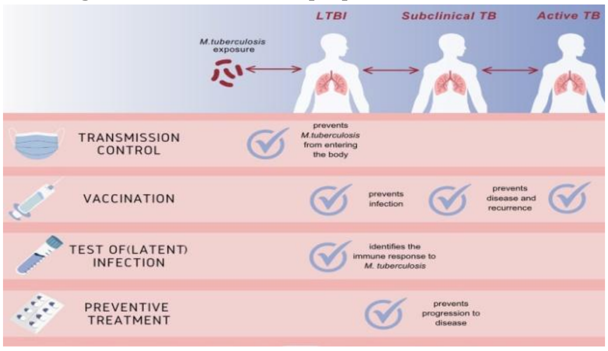

Fig 4: Image of Addressing Social Determinants.

Conclusion

The advanced management of tuberculosis (TB) represents a major step forward in combating this persistent global health challenge. Recent progress in pharmacological therapy, diagnostic tools, and patient-centered approaches has significantly improved treatment outcomes and reduced disease transmission. The development of new drugs such as bedaquiline, delamanid, and pretomanid, along with shorter, all-oral regimens, has revolutionized the management of multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB. These regimens not only enhance treatment efficacy but also improve patient adherence and safety.

Furthermore, the integration of molecular diagnostics, digital adherence technologies, and host-directed therapies offers a more comprehensive and personalized approach to TB care. Strengthening public health systems, ensuring early detection, and improving access to effective medications remain essential components of successful TB control programs.

In conclusion, advanced TB management combines innovation in pharmacology, diagnostics, and patient care strategies to move closer to the global goal of TB elimination. Continued investment in research, equitable access to novel therapies, and global collaboration are crucial to sustaining progress and ultimately ending the TB epidemic.

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