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An Update Review On Tuberculosis

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Abstract:

Tuberculosis is a hypersensitive granulomatous infectious disease caused by Mycobacterium Tuberculosis (M.TB).In India 40% people are affected by T.B. So need of knowledge about T.B. and the pathogenesis of T.B is more important to People or society. Pathophysiology means, when a human being is suffering from a disease this is Because of change in function on that organ or human body. Infection is caused by air- borne droplets Of organisms person to person. The main objective of this review is how to diagnose and how it is cure or treat the tuberculosis . It is Diagnosed by PPD, IGRA, Sputum studies, X-rays and Biopsies. Mostly antibiotics are preferred.

Introduction to Tuberculosis:

Tuberculosis is a widespread infectious disease which was enters into our body through the inhalations of few drops of the bacteria from the infected person (by sneezing, coughing) is mycobacterium The main cause of tuberculosis is mycobacterium tuberculosis bacteria which will majorly spread through out the body after infection The TB is known as chronic granulomatous disease TB was mainly discovered by Robert Koch in 1882 The tuberculosis is environmental born disease and it is also known as air born disease The Mycobacterium bacteria was rod Shaped bacteria needs oxygen to Survive The general Symptoms weight toss, fatigue, fever.

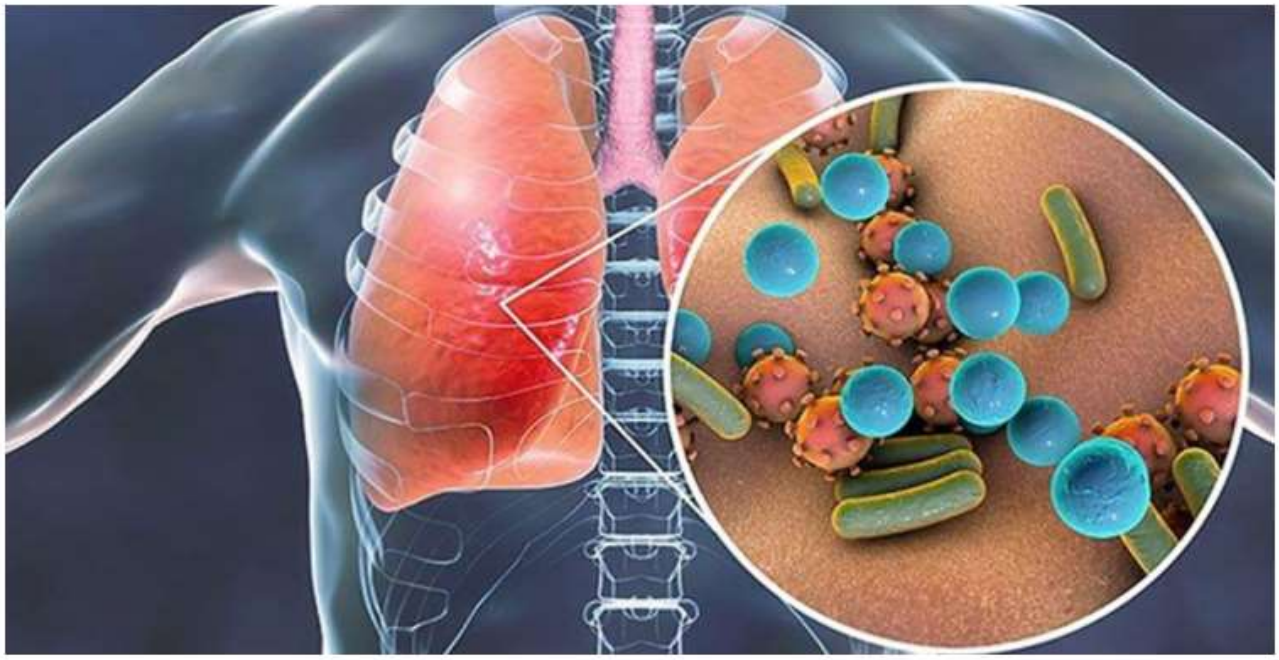


Fig-1:PULMONARY TUBERCULOSIS

The Majorly used drugs for tuberculosis are rifampicin, Isoniazid, pyrazinamide The patient who have the low immunity level are more likely to develop T-B Every year 9.0 million people were infected in which 2 million people were died due to TB In the year 1993 WHO i.e world health organization was declared that TB was global health emergency The tuberculosis was majorly occurred in low and middle income countries like Africa and Nigeria.

The burden of TB is highest in Asia and Africa. In 2011, largest number of cases was reported from India, China, South Africa, Indonesia and Pakistan. India and China alone accounted for 26% and 12% of global cases, respectively. Of the 8.7 million TB Incident cases reported in 2011, about 1.2 million People are also suffering from HIV. In the African Region, 39% of TB cases were estimated to be coinfected with HIV. Most cases of TB are caused by M. Tuberculosis and the reservoir of infection is humans with active TB.Most cases of TB are pulmonary and acquired by person to person transmission of air-borne droplets of organisms. The intestinal TB contracted by drinking dairy milk contaminated with M. Bovis rarely seen nowadays and usually in countries with tuberculosis dairy cows and unpasturised milk. Tuberculosis is a common disease prevalent through out the world. It is a chronic specific inflammatory infectious disease caused by Mycobacterium tuberculosis in humans. Tuberculosis usually attacks.

There four a we can say that tuberculosis is a common disease throughout the world Tuberculosis remains a global health problem leading to mortality as well as morbidity.In 2015, 10.4 million people, globally, had tuberculosis and 1.8 million died from it.Over 95% of tuberculosis-related deaths occur in low- and middle-income countries. Six countries that account for more than 60% of the total tuberculosis cases worldwide include

India (top most country) followed by Indonesia, China, Nigeria, Pakistan, and South Africa.[1]The total number of tuberculosis cases notified in India in the year 2015 were 1,740,435.Approximately 18% cases were of extrapulmonary tuberculosis. Human immunodeficiency virus (HIV) infect.

HISTORY:

The burden of TB is highest in Asia and Africa. In 2011, largest number of cases was reported from India, China, South Africa, Indonesia and Pakistan. India and China alone accounted for 26% and 12% of global cases, respectively. Of the 8.7 million TB incident cases reported in 2011, about 1.2 million people are also suffering from HIV In the African region, 39% of TB cases were estimated to be coinfected with HIV. (Kaufman, 2014)Most cases of TB are caused by M. Tuberculosis and the reservoir of infection is humans with active TB.Most cases of TB are pulmonary and acquired by person to person transmission of air-borne droplets of organisms. Oropharyngeal and intestinal TB contracted by drinking dairy milk contaminated with M. Bovis rarely seen nowadays and usually in countries with tuberculosis dairy cows and unpasturised milk.

Characteristics of mycobacterium Tuberculosis

- Rod shape, 0.2-0.5 in D, 2-4 in L.
- My colic acid present in its cell wall, makes it acid fast,
- So it resists depolarization with acid & alcohol.
- Aerobic and non motile.
- Multiplies slowly.
- Can remain dormant for decades.

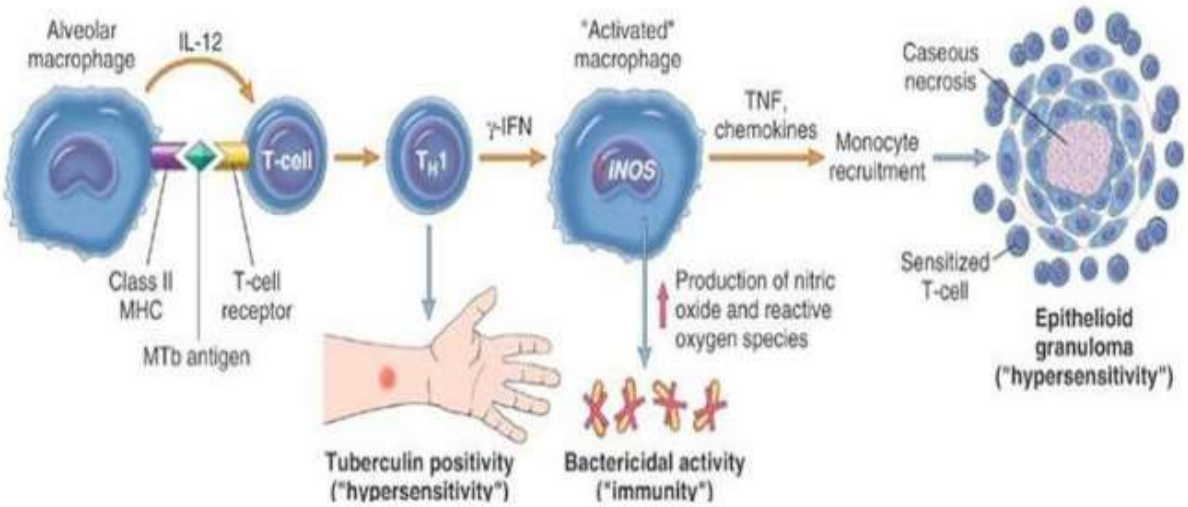


Fig- 2: primary pulmonary tuberculosis.

How is TB Transmitted

Mycobacteria are a group of bacteria that can cause a variety of diseases. Some mycobacteria are grouped As Mycobacterium tuberculosis complex because they cause TB or diseases similar to TB. In the United States, The vast majority of TB cases are caused by an organism called Mycobacterium tuberculosis. M. tuberculosis Organisms are also called tubercle bacilli. Other mycobacteria that can cause human tuberculosis disease Include M. bovis, M. africanum, M. microti, and M. canetti

TB spreads person to person through air :

If another person inhales air that contains these droplet nuclei, infection may result from this transmission.Transmission is the spread of an organism such as M. tuberculosis from one person to another.

Not everyone who is exposed to an infectious TB patient becomes infected with M. tuberculosis.

- **The probability that TB will be transmitted depends on four factors:**

- Infectiousness of the TB patient
- Environment in which the exposure occurred
- Frequency and duration of the exposure
- Susceptibility (immune status) of the exposed individual

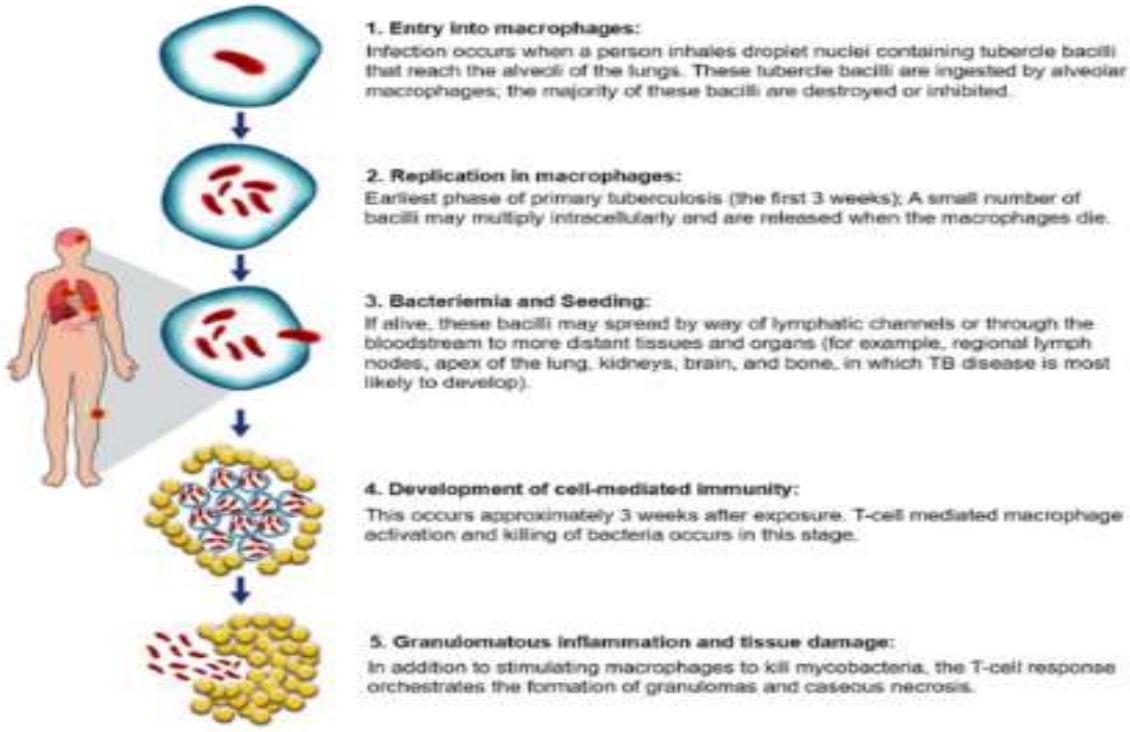
- The risk of developing TB disease is highest in the first 2 years after infection:

Some conditions increase the risk that LTBI will progress to disease. These conditions increase the risk By negatively impacting the ability of the body's immune system to control the spread of tubercle Bacilli. The risk may be about 3 times higher (as with diabetes) to more than 100 times higher (as with Human immunodeficiency virus [HIV] infection) for people who have these conditions than for those Who do not. Some of these conditions that increase the risk are

- Infection with HIV
- History of untreated or inadequately treated TB disease
- Recent TB infection (within the past 2 years)
- Abusing drugs or alcohol or smoking cigarettes

PATHOGENESIS OF TUBERCULOSIS

The mycobacterium tuberculosis starts a iv hypersensitive immune reaction inside the lungs which the lungs tissue while killing the micro organisms Pathologic manifestation of tuberculosis like caseating granuloma and cavitation are the results of hyper sensitivity that develops in concert with the protective host immune response The pathogenic life cycle of M.tb illustrated in Tuberculosis and it is transmitted via M.tb containing aerosol droplets propelled by active TB patients when they Sneezing ,cough or talk patients after new host inhale the TB bacteria, they travel through the respiratory tract and reach the lungs at this point the host innate immune system comes into play to quell the infection where upon the tubercle bacilli are internalized by alveolar macrophages when the macrophages fail to inhibit or destroy the bacteria multiple with in their intracellular environment. The tuberculosis patient relapse if treatment is not continue for 6 months because chemotherapy failed to convert the patient response from the necrotizing pattern characteristics of disease to the non necrotizing bacterial function required for optimal immunity The process of infection is initiated when the bacterium delivered in a water droplet into an alveolar in the lungs is ingested by an alveolar macrophages. Hence we can say that macrophages are the primary cells infected by mycobacterium tuberculosis



MORPHOLOGY OF TUBERCULOSIS:

Primary tuberculosis:

- Form of disease that develops in a previously unexposed person.
- Almost always begins in lungs.
- Inhaled bacilli implant in the distal airspaces of lower part of upper lobe or upper part of lower lobe.
- It forms a small sub pleural parenchymal lesion in the mid zone of the lung (ghon focus inflammation + caseous necrosis)
- Tubercle bacilli drain to the regional lymph node which also often undergo caseous necrosis.
- Parenchymal lung lesion + Nodal involvement= Ghon's complex.

ETIOLOGY OF TUBERCULOSIS:

Mycobacterium tuberculosis is a most common cause bacteria for tuberculosis and there are some other causes that can cause the tuberculosis

- Mycobacterium avium intracellular
- Mycobacterium Kansasi
- Mycobacterium scrofulaceum
- Mycobacterium Marinum

Introduction	Treatment	Symptoms
Mycobacterium avium intracellulare: It is a type of infection and It's commonly found in people who are immunocompromised, such as those with AIDS, hairy cell leukemia, or who are undergoing immunosuppressive chemotherapy and it can be found in water, soil, and dust, and can be transmitted to people through inhalation of respiratory droplets of bacteria.	Doctors are typically treat NTM infections with a combination of three to four antibiotics such as the azithromycin and streptomycin, rifampicin	Symptoms include are : weight loss, abdominal pain,vomiting,fever, nightsweats,
Mycobacterium kansasii : It is a type of infection that is infrequently isolated from natural water and sources or soil. The major reservoir appears to be tap water. Infection is	The doctors typically treat with a combined drugs of antibiotics includes rifampin &	Symptoms of these infection Mycobacterium kansasii can include are the pulmonary symptoms

likely acquired through the aerosol route, with low infectivity and in regions of endemicity. Human-to-human transmission is thought not to occur.	ethambutol,isoniazid **Rifampin**:600mg per day	like cough,fever ,sputum production,chestpain and weight loss
Mycobacterium scrofulaceum: It is a non-tuberculous mycobacteria (NTM) that is acid fast and scotocromogenic. It's a slow-growing bacteria that's resistant to isoniazid, para-aminosalicylic acid, and kanamycin.	Two antibiotics, such as ethambutol and macrolide, are used typically Rifampin is added if the infection is in the deeper such as osteomyelitis	The Symptoms of these infection mycobacterium scrofulaceum can cause a variety of symptoms they includes: Lungs parenchymal infect and also the cervical lymphadenopathy in the children & Symptomatic lung infection in the immunocompetent patients.
Mycobacterium Marinum: It is an atypical mycobacterium and it is worldwide distributed pathogen living in salt or fresh water: it is responsible for infections in oyster workers, swimmers, individuals with aquariums at home [14–16]. It usually consists in skin infection, forming cutaneous nodules which may be indolent and unrecognized [17]. But it may also involve deeper structures and progress to tenosynovitis, arthritis, and osteomyelitis.	Ethambutol and also rifampicin with the combination of the minocycline	The Symptoms of these Mycobacterium marinum infection include: The reddish or purplish bump (papule) that slowly grows into a painful nodule A non-healing red sore on the skin Localized pain and firmness at the site of the infection

Types of tuberculosis disease:

Tuberculosis can be classified into different types depending upon the various factors based on :

The sequence of the exposure

Location

There are mainly three types of tuberculosis arise when the disease is classified according to the sequence of the events following the first exposure, such as :

Primary tuberculosis

Progressive primary tuberculosis

Post primary tuberculosis

Primary tuberculosis:- Occurs in the person exposed to Mycobacterium TB for the first time .

Progressive primary tuberculosis:- It was occurs when there is impaired immunity it was mostly seen in the infants and in elderly people.

Post primary tuberculosis:- Generally seen in the adults due to endogenous reactivation in a previously sensitised patient who has retained some degree of acquired immunity.

Based on the location, two types of Tuberculosis are seen, such as:

Pulmonary tuberculosis

Extra pulmonary tuberculosis

Pulmonary tuberculosis:- Tuberculosis is seen in the lungs

Extra pulmonary tuberculosis:- Occurs in the organs other than the lungs. The most common sites are lymph nodes, pleura, bone and joints.

Epidemiology

Ninety percent of people infected with TB develop latent infection. Approximately 5% of people infected with TB develop active disease within the first 2 years after infection; an additional 5% develop the infection later. The risk factors associated with the development of active TB are immunocompromised state, tobacco use, and excessive alcohol use. The immunocompromised state may be due to the following:

Immune senescence of older age

Genetic diseases causing immunodeficiency

Human immunodeficiency virus (HIV)

Transplantation

Prolonged corticosteroid use

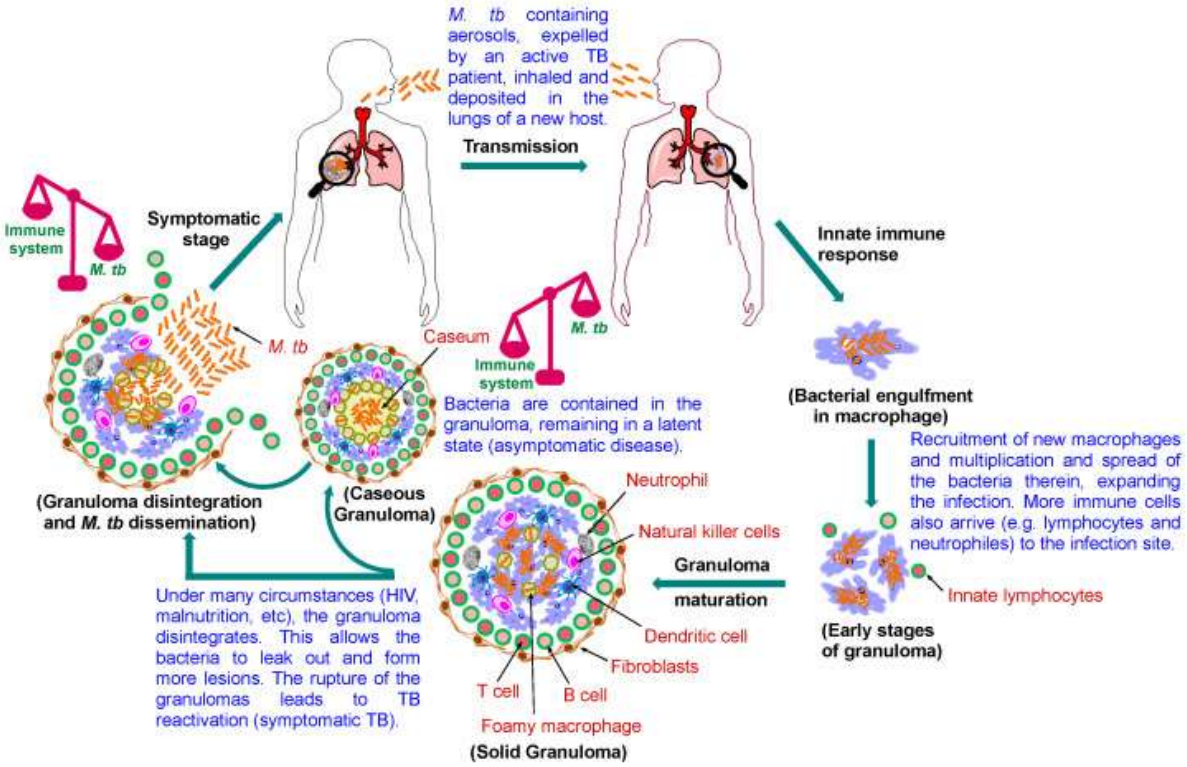
Cytoreductive chemotherapy

Tumor necrosis factor (TNF) antagonists

Malnutrition

Diabetes

The WHO publishes an annual report outlining the current epidemiology and progress towards the WHO End TB Strategy goals. In 2022, TB caused 1.3 million deaths worldwide, a decrease from 1.4 million estimated deaths in both 2020 and 2021. TB is the leading cause of mortality in patients with HIV, causing 167,000 deaths in 2022. Approximately 7.5 million people were diagnosed with TB in 2022, 46% of whom live in Southeast Asia, 23% in Africa, and 18% in the Western Pacific. This is the highest number since global TB monitoring began in 1995. About 10.6 million people globally are currently living with active TB, of which 5.8 million are men, 3.5 million are women, and 1.3 million are children. In addition, approximately 25% of the world's population is infected, of which 5% to 10% develop active TB.



In the United States (US), in 2023, the Centers for Disease Control (CDC) reported 9615 new cases of TB (approximately 2.9 cases/100,000 persons), up from 8300 cases in 2022. This 16% increase is in addition to increases seen yearly since 2020, after 27 years of decreasing numbers. The increases occurred across age groups, in US- and non-US-born persons, 40 states, and the District of Columbia. The largest relative increase in case numbers and the rate was in children (ages 5 to 14; 42% and 45%, respectively), although the numbers are small (68 cases). Seventy-six percent of cases are among persons born outside the US, representing a 16% increase. While Th causes a minimal risk among US- born individuals, higher rates exist among Native Hawaiians, Pacific Islanders, American Indians, Alaska Natives, and Black individuals, reflecting persistent health disparities. Approximately 85% of reported cases are associated with the reactivation of latent TB infection rather than recent transmission. HIV coinfection existed in 5% of patients Within the US and globally, years of progress towards TB eradication have been lost since the COVID-19 pandemic. Due to the focus on diagnosing and treating COVID-19, healthcare professionals in public health and the acute healthcare systems identified fewer cases of latent and active TB. The 2020 decrease in latent and active infections is likely due to these healthcare disruptions. In some jurisdictions, including the US, decreased migration also led to a lower incidence of infections in 2020. Globally, COVID-19 disruptions caused an estimated half million excess deaths due to TH between 2020 and 2022, compared to the number of deaths that would have occurred had prepandemic trends continued. The increased incidences of latent and active infections since 2021 or 2022 likely reflect a backlog of people whose diagnosis of TB was delayed. Between 1995 and 2014, TB control efforts prevented approximately 300,000 people from developing TB, saving 14.5 billion in costs. Drug-resistant TB is a serious public health concern. Globally, approximately 13% of new cases and 17% of previously treated cases of TB are isoniazid (INH)-resistant and rifampin-susceptible.

The categories of drug resistance include:

Rifampicin-resistant TB

May be resistant to isoniazid

May he resistant to other TB drugs

Rifampicin-susceptible, isoniazid-resistant TB

Multidrug-resistant TB (MDR-TB)

Resistant to both rifampin and INH

Extensively drug-resistant TB

Resistant to rifampin, INH, a Fluoroquinolones, and at least 1 of the second-line injectable drugs, such as capreomycin, kanamycin, and amikacin.

Drug-resistant TB poses a threat to global public health control efforts. In 2018, the global Estimate of MDR-TB was approximately half a million new cases, of which only 30% were started on second-line therapy. The complexity of treatment and management led to the establishment of strategies to intensify treatment programs.

LABORATORY TESTING :

TB test is the Monteux skin test (PPD) - a small amount of fluid (called tuberculin) is injected into the forearm just under the skin. –A health professional should read the test 48 to 72 hours after it is administered to check for a reaction. –If there is a reaction (swelling), more testing is done. –The Tine test (which uses a 4-pronged device) is no longer recommended because it is not as effective in delivering the proper amount of tuberculin under the skin.

Mycobacterial Examination- Mycobacterial examination has 6 stages:

- Proper specimen collection
- Examination of acid-fast bacilli (AFB) smears
- Direct identification (NAAT- nucleic acid amplification test)
- Specimen culturing and final identification
- Drug susceptibility testing

Specimen Sources

- Sputum(primary)
- Pulmonary aspiration (secondary)
- Body fluids (CSF, pleural, peritoneal, etc.)
- Tissue biopsy
- Blood
- Urine
- Gastric aspirate
- Stool (special request)

Acid-fast Bacilli (AFB) smear

- Least sensitive of all AFB Tests (20-75% positivity)
- Requires 10,000 AFB/ml to be positive
- Positive slide does not differentiate TB from atypical mycobacteria (i.e. M. avium)
- Reported within 24 hours of receiving the specimen in the laboratory.

Fluorescent AFB Smear Using Auramine-O Staining

- Very sensitive, takes minutes to read
- Not all that is fluorescent is AFB (need a care ful eye)
- Chemical fluorescence, notan immune stain or Direct Fluorescent Antibody
- Can be confirmed with Ziehl Neelson (ZN) smear.
- "NAA testing should be performed on at least one respiratory specimen from each patient with signs and symptoms of pulmonary TB for whom a diagnosis of TB is being considered but has not yet been established, and for whom the test result would alter case management or TB control activitie
- NAAT should be performed on all new AFB+ sputum specimens.
- NAA tests are available that are not FDA approved, such as real time PCR assays. MDHHS performs a real time lab developed PCR test to detect Mtband MAC using the ABI 7500

Img :

AFB Culture Test

- More sensitive than AFB smear
- 10 AFB/ml can produce a positive result, whereas

AFB smear needs 10,000 AFB/ml

Culture may be AFB positive even if smear was negative

Drug	Adverse Reactions	Comments
Izoniazid	Hepatitis, drug interactions, numbness, tingling, pain in extremities, fatigue	Raises Dilantin and INH blood serum levels if taken together; this may lead to toxicity
Rifampin	Stomach upset, Symptoms of Flu, Bleeding, Rashes, Hepatitis	If you are taking other drugs (such as birth control pills) consult your doctor. Rifampin can turn body fluids orange but this is temporary.
Pyrazinamide	Joint aches, Hepatitis, Rashes, Stomach upset, Gout (rarely)	Avoid in pregnancy
Ethambutol	Visual Problems	Should not be used in young children whose vision can't be tested unless there is drug resistant TB

Short-term medication regimen for tuberculosis :

Standard Short-Term Regimens:

- **Rifampicin-based regimens* (6 months):**

- 2 months of rifampicin , isoniazid, pyrazinamide, and ethambutol

- 4 months of rifampicin ,isoniazid

- **Intensive Phase (2 months):**
  Rifampicin , isoniazid , pyrazinamide , and ethambutol

- **Continuation Phase (4 months):**
  Rifampicin, isoniazid

Shorter Treatment Regimens (new developments):

- **4-month regimen(BPaL):**
  Bedaquiline, pretomanid, and linezolid

- **6-month regimen (HRZE):**

- Isoniazid, rifampicin, pyrazinamide, and ethambutol

Common Short-Term Medications:

- **First-line medications:**

- Rifampicin (RMP)

- Isoniazid (INH)

- Pyrazinamide (PZA)

- Ethambutol (EMB)

- **Second-line medications (for drug-resistant TB):**

- Fluoroquinolones (e.g., levofloxacin)

- Aminoglycosides (e.g., kanamycin)

Effective short-term medication management is crucial for TB treatment success. Healthcare providers must balance treatment efficacy with potential side effects and patient adherence. Ongoing research aims to improve treatment outcomes and reduce treatment duration.

Long term medication for tuberculosis :

Duration: 6-24 months, depending on disease severity and drug resistance

Pill burden: Multiple medications, often 3-5 pills/day

Adverse effects: Hepatotoxicity, nephrotoxicity, peripheral neuropathy, and others

Drug interactions: Potential interactions with concomitant medications

Adherence: Critical for treatment success, requiring patient education and support

Monitoring: Regular check-ups, liver function tests, and blood counts

Common Long-term Medications:

- **First-line medications:**

- Isoniazid (INH)
- Rifampicin (RMP)
- Pyrazinamide (PZA)
- Ethambutol (EMB)

- **Second-line medications (for drug-resistant TB):**

- Fluoroquinolones (e.g., levofloxacin, moxifloxacin)
- Aminoglycosides (e.g., kanamycin, amikacin)
- Cycloserine
- Terizidone

Tuberculosis Treatment for pediatric infection:

Children account for up to 20% of incident cases of tuberculosis in high-burden settings and have a higher risk than do adults of developing severe and rapidly progressive forms of the disease, such as disseminated disease and meningitis. However, the study of anti tuberculosis treatment in children is difficult in Evidence to support dosing recommendations in children is inadequate, and results from studies suggest that internationally recommended doses of first-line drugs result in suboptimum drug exposure and there is even less information available to guide the use of second-line drugs. Uncertainties about the safety of ethambutol and fluoroquinolones in children also restrict their use. Development of paediatric drug formulations to suit high-burden settings, and specific studies for investigation of the appropriate dosing and safety in children are important.

Uses of isotopes in tuberculosis :

Isotopes are used in tuberculosis research and diagnosis to help identify the disease, assess its extent, and differentiate it from other conditions:

Radioisotope Therapy is a form of treatment that involves using therapeutic radioisotopes, such as beta or alpha emitters, to target TB cells by binding to specific molecules like antibodies. This allows for direct radiation delivery to the TB effected cells, although neighboring cells may also be affected

Img: 4 Radio pharmaceutical kit for the treatment of tuberculosis

Current uses:

Radioisotopes are used in tuberculosis diagnosis and treatment in a various ways

- **Technetium**

A radioactive isotope of technetium (Tc) binds to the bacillus Mycobacterium tuberculosis, which causes tuberculosis. The compound accumulates in the TB lesion and can be detected.

- **Gallium68**

This radioisotope has a half-life of 68 minutes, which is similar to the pharmacokinetics of many peptides and molecules. It's used in imaging neuroendocrine tumors and infection imaging.

- **Terbium**

Terbium radioisotopes have a number of uses in tuberculosis, including:

149Tb: This radioisotope emits alpha particles and gamma rays, and can be used for targeted alpha therapy.

152Tb: This radioisotope is a multiple beta-plus emitter, and can be used for dosimetry and monitoring.

155Tb: This radioisotope can be used for pre-therapeutic imaging and dosimetry.

161Tb: This radioisotope has decay characteristics that make it a promising radionuclide in nuclear oncology.

These are some various uses of radioactive isotopes which was majorly used in the treatment of the Tuberculosis

Complications of tuberculosis in pregnancy:

The complications which can be seen in the pregnancy includes:

Increased the rate of spontaneous abortion

Reduced birth weight

Increased neonatal mortality

Weight gain in the pregnancy

Conclusion:

Tuberculosis (TB) is an infectious disease caused by the bacillus Mycobacterium tuberculosis (Mtb). Tuberculosis Is a chronic granulomatous infectious disease. Infection occurs via aerosol, and inhalation of a few droplets Containing M. tuberculosis bacilli. Most cases of TB are pulmonary and acquired by person to person Transmission of air-borne droplets of organisms. It can be diagnosed by PPD, IGRA, Sputum studies and X-rays.