INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA):IJPS00]
Journal Homepage: https://www.ijpsjournal.com

Review Article

Review Of Tuberculosis Caused By Bacteria

Tekchand Manohar Pawar*, Vikram Jaysingh Pansare, Akash Vitthal Kaulange, Yogesh Ankush Narute

Department of Pharmaceutics, Saikrupa Institute of pharmacy Ghargaon 414728

ARTICLE INFO

Received: 26 Sep 2024
Accepted: 29 Sep 2024
Published: 01 Oct 2024

Keywords:
Tuberculosis (TB): drug-resistance; pathogenesis; drug therapy; infectious diseases

DOI:
10.5281/zenodo.13871749

ABSTRACT

Tuberculosis (TB), which is caused by bacteria of the Mycobacterium tuberculosis complex, is one of the oldest diseases known to affect humans and a major cause of death world-wide. Tuberculosis continues to be a huge peril disease against the human population and according to WHO, tuberculosis is a major killer of the human population after HIV/AIDS. Tuberculosis is highly prevalent among the low socioeconomic section of the population and marginalized sections of the community. In India, National strategic plan (2017-2025) has a national goal of elimination of tuberculosis by 2025. It requires increased awareness and understanding of Tuberculosis. In this review article history, taxonomy, epidemiology, histology, immunology, pathogenesis and clinical features of both pulmonary tuberculosis (PTB) and extra-pulmonary tuberculosis (EPTB) has been discussed. A great length of detailed information regarding diagnostic modalities has been explained along with diagnostic algorithm for PTB and EPTB. Treatment regimen for sensitive, drug resistant and extensive drug resistant tuberculosis has been summarized along with newer drugs recommended for multi drug resistant tuberculosis. This review article has been written after extensive literature study in view of better understanding and to increase awareness regarding tuberculosis, as a sincere effort that will help eliminate tuberculosis off the face of the earth in near future.

INTRODUCTION

allows us to breathe. TB is caused by a bacterium called Mycobacterium tuberculosis. It spreads from person to person when an infected person coughs, sneezes, laughs, or spits. Tiny droplets of fluid from the lungs are carried in the air and can be breathed in by someone nearby. Although it can affect many parts of the body, TB usually occurs in the lungs. One third of the world's people are infected with TB, and along with HIV, TB is one of the world's leading causes of death due to disease. The World Health Organization (WHO) estimates that over three million women became

***Corresponding Author:** Tekchand Manohar Pawar
Address: *Department of Pharmaceutics, Saikrupa Institute of pharmacy Ghargaon 414728*
Email : sachinkadam4041@gmail.com
Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

sick with TBin 2014.Of the almost ten million that Tuberculosis (TB) is an infection of the lungs and respiratory system, which isthe organsystem new cases of tuberculosis in 2014, over one millionoccurred in people living with HIV (HIV+). The risk of developing TB is estimatedto be 26 to 31 times greater for people living with HIV than for those who are HIV-negative. The largest numbers of TB infection occur in southeast Asia and the Western Pacific (58 percent of global total), while Africa had the most severe TB burden in relation to its population. The good news is that the number of people living with TB across the globe in 2015 was 42 percent lower than in 1990.

In the US, the number of new TB cases reported declined each year from 1993to 2014; there was a slight increase in the number of cases in 2015 (1.6 percent morethan in 2014). According to the Centers for Disease Control and Prevention (CDC), the number of TB cases reported in 2014 was the lowest that is has been since reporting began in 1953. Worldwide, TB is the leading cause of death in people living with HIV in Africa, and a leading cause of death elsewhere. The WHO estimates that one third ofthe 35 million people living with HIV worldwide are infected with TB. The CDC recommends that people living with HIV be screened for TB when they are first diagnosed with HIV; in addition, yearly screening is recommended for people living with HIV who have repeated exposure to others with active TB (see "Diagnosing TB, "below).[1,2]

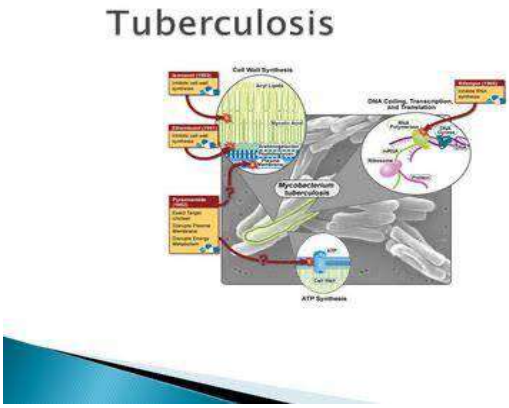

Fig.no 1 Tuberculosis

LITERATURE REVIEW:

1. Keertan Dheda, Clifton E Barry, Gary Maartens, Tuberculosis, 2015, Tuberculosis is also a major problem in health-care workers in both low-burden and high-burden settings. The ideal preventive agent, an effective vaccine, is still some time away, several new diagnostic technologies have emerged, Efforts towards an effective vaccine have been thwarted by poor understanding of what constitutes protective immunity. New interventions and investment in control programmes will enable control, eradication will only be possible through substantial reductions in poverty and overcrowding, political will and stability, and containing co-drivers of tuberculosis, such as HIV, smoking, and diabetes.
2. Thomas M. Daniel, The history of tuberculosis, Respiratory Medicine (2006) 100, 1862-1870, has described history of tuberculosis and studied of the pathogenesis of tuberculosis began with the work of The ophile Laennec at the beginning of the 19th century and the demonstration of the transmissibility of Mycobacterium tuberculosis infection by Jean-Antoine Villemin in 1865 and theidentification of the tubercle bacillus as the etiologic agent by Robert Koch in 1882. Clemens von Pirquet

developed the tuberculin skin test in 1907 and 3 yearslater used it to demonstrate latent tuberculous infection in asymptomatic children. In the late 19th and early 20th centuries sanatoria developed for the treatment of patients with tuberculosis. The modern era of tuberculosis treatment and control was heralded by the discovery of streptomycin in 1944 and isoniazid in 1952.

3. Stephen d lawn, Tuberculosis, 2011 Has present the current perspectives on thescale of the epidemic, the pathogen and the host response present and emerging methods for disease control including diagnostics, drugs, biomarkers, and vaccines and the ongoing challenge of tuberculosis control in adult in the 21st century.
4. Kartik kumar, onn min kon, diagnosis and treatment of tuberculosis; latest development and future priorities, 2017, This article provide an update on resistant and latent TB. The global epidemiology of the disease, clinical presentation and approaches to management of Tuberculosis are discussed. Feature research and clinical priorities are considere. [3,4,5].

OBJECTIVE:

1. Cure the individual petient
2. To Minimize risk of death and disability
3. To reduce transmission of M. tuberculosis to other person
4. To improve TB patients health

History

TB or illnesses resembling TB have been described from different civilization since ancient times. The earliest such description can be found in Vedas, where TB was referred to as Yakshma meaning wasting disease. Greek, Chinese and Arabic literature also describes TB like disease.2 Mycobacte- rium exists on earth since last 150 million years. Typical tubercular vertebral lesions were seen in mummies from the Egyptian pre-dynastic era and Peruvian pre-Colombian era. The first weak evidence of TB in humans is from a bone lesion found in a 500 thousand year old skull in Turkey. Human TB detection using PCR sequencing in a Neolithic infant and women from 9 thousand year old settlement in the Eastern Mediterranean is the oldest strong evidence available. Galen first suspected that TB could be contagious. It took many centuries until Girolamo Fracastorius showed that some diseases could be transmitted through 'particles' by direct or indirect contact between humans. Thomas Willis first described miliary TB. Calm- ette extracted a protein (tuberculin) from large cultures of the bacillus and first used for therapy known as 'tuber- culinisation', which failed as treatment for TB. The Tuberculin was also used for intradermal skin test which was described by Charles Mantoux & used in the diagnosis of TB. Later this intradermal skin test was named after Charles Mantoux and is known as Mantoux test. 15 Benjamin Marten hypothesized that TB is caused by 'wonderfully minute living creatures' in his theory of 'contagious living fluid'. It was Jean Antoine Villemin a French army doctor who successfully demonstrated the transmission of TB from humans to animals and from animals to animals. In 1834, Johann Lukas Schonlein proposed the name 'Tuber- culosis' which is derived from Latin word 'tubercula' meaning 'a small lump' seen in all forms of the disease. 15 On 24th March 1882, Robert Koch announced in the meeting of the Berlin Society of Physiology that he had discovered causative agent responsible for pulmonary TB and named it as 'tuberkel virus' in his paper published 2 weeks later. First innovative decision of staining tuberculosis bacilli and second innovative decision of culturing it on solidified cow or sheep serum gave Robert Koch the Nobel prize of medi- cine in 1905. Leon Charles Albert Calmette and Camille Guerin developed vaccine against TB by sub-culturing Mycobacterium bovis for more than 200

times in the Guinea pig model between Arvid Wallg- ren, a professor from Royal Caroline medical institute, Sweden described clinical manifestations of tuberculous infection in an article titled 'The timetable of Tuberculosis' which helped in better understanding course of TB illness. The effective treatment for TB became a reality after the discovery of antitubercular drugs like Streptomycin, Para- amino salicylic acid (PAS) and isoniazid by the mid-1940s. By late 1970 it was believed that TB may no longer be a public health problem in the developed world. But the emergence of Acquired Immune Deficiency Syndrome (AIDS) in the early 1980s has ended this optimism and led to the resurgence of TB worldwide.[6,7]

EPIDEMIOLOGY

It is reported that 1/3rd of the entire world's population is infected with MTB. From latent infection, the infection can arise to change in active state 7-8. About 5 to 10% of LTBI cases are at very high risk due to evolving from normal infection to active (primary) TB. Those with HIV and other immunocompromised patients, such as a patient with cancer or currently taking medication of immunosuppressive drug have a very higher risk of developing active TB12. Robert Koch's gives a statement that TB is much fatal than the plaque or cholera about 9 million people from all over the world were infected with TB and about 1.5 million stops fighting to TB in 2013. In 2004, only TB was responsible for more than 2.5% of all deaths in the world, the infection rates are very higher in areas such as hospitals or prisons. Expansion of TB in such areas depends on virulence, innate immunity and sensitivity 7-8.

While TB can occur in any area in any country but the majority of deaths reported that about 95% occurred in poor countries where resources are finite and it majorly includes India and China 4.6. Patients with HIV+ve are very sensitive to getting TB infection and 80% of HIV+ve patients live in sub-Saharan Africa and have TB6-10. The United States, a less populated country has only 10% of TB patients with HIV+ve. 12,904 TB cases were reported in 2008 with a ratio of 4.2 per 100,000. While diagnostic advancements have been made in the past four years, 80% of TB cases worldwide are concentrated in more than twenty-two countries which include India, Pakistan, Nigeria, Bangladesh, China, Indonesia, South Africa and Russias.[8,9,10]

Treatment of Tuberculosis

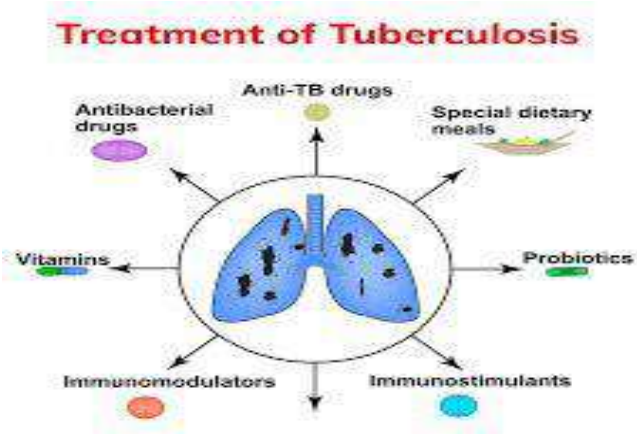

Fig.no 2 Treatment of Tuberculosis

MANAGEMENT OF TUBERCULOSIS:

There are two types of treatment for TB:

Preventive Treatment:

If you have latent or inactive TB (infected but no symptoms), your health careprovider will likely suggest that you start treatment to help your body get rid of the TB germ. This treatment is intended

to prevent active TB (TB with symptoms) fromdeveloping. Treatment typically involves nine months of an antibiotic called isoniazid (INH) plus vitamin B6 supplements. Although it is recommended that all people living with HIV begin taking HIV drugs as soon as possible, there may still be rare instances in which people living with HIV and TB are not yet taking HIV drugs. Those people living withHIV who are not taking HIV drugs may be treated with INH and B6 plus rifapentine orrifampin for only three months. The INH, B6, and rifapentine or rifampin treatment combination is not recommended for people on HIV treatment because rifapentine and rifampin can interact negatively with some HIV drugs. Your health care providerwill help you decide which treatment option is best for you. During INH and B6 treatment, your provider will draw lab tests to check for anyside effects from the INH medication, such as liver inflammation. The first set oflab tests will be done after you have taken the medication for one month. Also, your provider will question you regularly about any side effects you may be having from the INH. Possible side effects from INH include: loss of appetite nausea and/or abdominal pain jaundice (yellowing of the skin, eyes, and mucous membranes) dark urine rashnumbness and tingling of your hands and/or feet (peripheral neuropathy) fever and weakness for more than three days muscle sorenessLong lasting fatiue(extreme tiredness) The pyroxidine or B6 medication is taken to prevent the peripheral neuropathysymptoms that INH can cause. It is important not to drink alcohol while you are taking INH, or your liver may become badly damaged.

Treatment of Active Disease

Treatment of active TB requires combination therapy. The usual regimen is:

Isoniazid (INH)

Rifampin (also known as rifampicin, Rifadin, or Rimactane) Pyrazinamide

Ethambutol (Myambutol)

These four drugs are taken daily for two months. Tests can be done to see how well the drugs are fighting the TB. If the drugs are fighting the TB well, then the treatment changes to just two drugs: isoniazid plus rifampin for four more months. Sometimes the treatment will last longer, depending on whether or not the TB is resistant to these drugs, or if the TB disease has spread through the bloodstream toother parts of the body. Some TB drugs can interact with HIV drugs. Rifampin, forexample, can interfere with protease inhibitors and non-nucleoside reverse transcriptase inhibitors. This can make it difficult to treat both diseases at the sametime. If you are taking a protease inhibitor, your health care provider may make changes to your TB drugs. Your provider may also adjust your drug doses when you are being treated for both TB and HIV. Some people living with HIV may needlonger TB treatment thanpeople without HIV. As with HIV, taking your TB drugs exactly as prescribed (good adherence) is very important. Even though symptoms usually improve after three to four weeks andyou feel better before you have finished taking all your drugs the full course of treatment must be completed. This helps prevent TB from coming back and becoming resistantto drugs.[11,12,13]

T.B Symptoms:

After TB bacteria inhaled, they settle in the lungs. People with healthy immune systems can usually fight the bacteria and keep it from multiplying. The immune system may build structures that wall off or contain the bacteria. These structures can burst, leaving scars in the lungs. If a person's immune system is too weak and the structures burst, the bacteria can get out and enter the bloodstream. Oncein the bloodstream they travel to other parts of the body including the brain, kidneys, bones, and reproductive organs, where they can cause infertility. This is called "extrapulmonary TB" because is has spread

outside the lungs. ExtrapulmonaryTB is more likely in people with advanced HIV disease. People with active TB disease may develop symptoms including: Cough lasting more than two to three weeks Coughing up sputum (phlegm) or bloodUnexplained weight loss Fever or chillsNight sweats Fatigue (unusual tiredness) Loss of appetite Chest pain. [14]

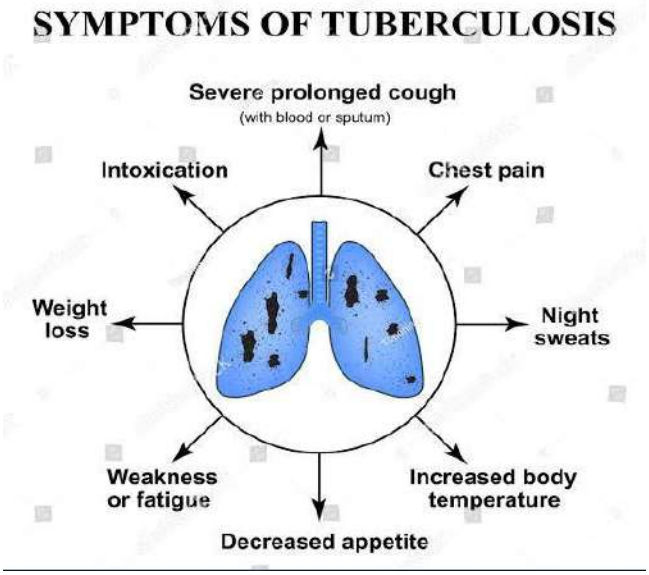

Fig. no 3 Symptoms of Tuberculosis

Pathogenesis

The majority of droplet nuclei containing MTB from infec- tious patients are trapped in upper airway and expelled by ciliated mucosal cells: only a fraction reaches alveoli. The mycobacteria then bind to cell surface of alveolar macro- phages through complement receptors, mannose receptor or type A scavenger receptor. Following phagocytosis, myco- bacteria reduce acidity in phagosome and a cell wall component (i.e. lipoarabinomannan) impairs Ca+/calmod- ulin pathway thus inhibiting phagosome-lysosome fusion. Following successful arrest of phagosome maturation, the multiplication of bacilli begins and the macrophage even- tually ruptures to release its bacilli, which are taken up by macrophages and continues infection cycle further expanding the spread.22 During primary infection, MTB bacilli undergo hematogenous and lymphatic dissemination involving hilar and mediastinal lymph nodes forming pri- mary Ghon's complex. Eventually bacilli enter blood stream and reach various organs. This lympho-hematogenous dissemination results in extrapulmonary tuberculosis dur- ing primary infection or later in life during reactivation of disease. 23 EPTB can involve any site in the body & the most common site is lymph node. However pleural, neurological, synovial, pericardial, abdominal, genitourinary involvement has been described.[15]

a. Tubercular Lymphadenitis

From ancient times, lymph node TB has been called Scrofula or King's evil. It constitutes nearly 35% of EPTB cases. Cervical lymphadenitis is the most common and reported in 60-90% of tuberculous lymphadenitis cases. Involvement of cervical lymph node is due to spread of bacilli from primary focus of infection in Ghon's complex or from tonsils, adenoids, sinonasal/osteomyelitis of the ethmoid bone. Initially, MTB bacilli multiply in lymph node causing marked hyperemia, swelling, necrosis and caseation of involved lymph node. The inflammation, progressive swelling and matting of other nodes around, resulting in adhesion to adjacent skin and rupture into surrounding tissue or through skin

forming si- nuses. Mediastinal lymphadenitis can compress major blood vessels, phrenic nerve or recurrent laryngeal nerve or cause erosion of bronchus which is commonly seen in children.

Peripheral tuberculosis of lymph nodes is classified by Jones and Campbell into-

1. STAGE I:-Enlarged, firm, motile discrete nodes.
2. STAGE II:-Large rubbery nodes fixed to surrounding tissue.
3. STAGE III:-Central softening due to abscess formation.
4. STAGE IV:-Collar stud abscess formation.
5. STAGE V:-Sinus tract formation.

b. Pleural TB

The incidence of pleural TB is as high as 30% of all EPTB cases in high burden countries. The patients usually presents with acute febrile illness with nonproductive cough and pleu- ritic chest pain; associated with night sweats, chills, weakness, dyspnea, weight loss. The pathogenesis in pleural TB is pre- sumed to be due to delayed hypersensitivity rather than direct infection of pleural space. This space is infected from initial lung parenchymal lesions and results in immunological response predominated by neutrophils (first 24 hours). This is followed by lymphocyte driven immune response forming pleural granuloma formation and release of Adenosine Deam- inase (ADA). Neutrophils remain the first line of defense for first 24 hours, followed by macrophages which peak at 96 hours and then by lymphocytes. A strong T-helper type-1 (Th 1) response is necessary to contain MTB. Activated CD3+ and CD4+ Th1 cells release interferon γ (IFN- γ) thus activating macrophages to kill MTB. The Th1 immunity in pleural TB is confirmed by the high levels of IFN- γ, interleukin-12 (IL-12) and elevated helper T cells in pleural fluid as compared to serum/peripheral blood. The delayed hypersensitivity reaction to mycobacterial anti- gens affects pleura and increases the permeability of pleural capillaries, and thereby increasing fluid in pleural cavity. The fluid is drained through openings in the parietal pleura called stomata. Since diffuse involvement of parietal pleura with TB and damage to or obstruction of stomata leads to accumulation of pleural fluid. Chronic TB empyema resolve leaving thick- ened, scarred and calcified pleura causing chronic chest pain, dyspnea and impaired lung function. Pleural fibrosis, a well- documented complication has been reported in 5-55% of pleural TB cases.

c. Abdominal TB

The abdominal tuberculosis is diagnosed in 11% of patients with EPTB which was around 55-90% in era before effective ATT. The most common site of gastrointestinal tract involvement is the ileocecal region due to following reasons-

i. More lymphoid tissue (Peyer's patches)
ii. Increased physiological stasis
iii. Rate of fluid and electrolyte absorption is more
iv. Low digestive activity

Other sites of involvement in decreasing order are ascending colon, jejunum, appendix, duodenum, stomach esophagus, sigmoid colon and rectum. Hepatobiliary, splenic and pancreatic TB are rare and associated with miliary tuberculosis; often diagnosed in immunocompromised pa- tients. MTB bacilli gain entry to abdominal organs by two routes and cause disease due to reactivation of dormant focus. As a result of hematogenous spread from primary lung infection in children and as a part of miliary TB. Through ingestion of contaminated food and milk which infect Peyer's patches and are transported to mesenteric lymph node, where they remain dormant. 27,28 esophagus, sigmoid colon and rectum. Hepatobiliary, splenic and pancreatic TB are rare and associated with miliary tuberculosis; often diagnosed in immunocompromised pa- tients. MTB bacilli gain entry to abdominal organs by

two routes and cause disease due to reactivation of dormant focus. As a result of hematogenous spread from primary lung infection in children and as a part of miliary TB. Through ingestion of contaminated food and milk which infect Peyer's patches and are transported to mesenteric lymph node, where they remain dormant. 27,28esophagus, sigmoid colon and rectum. Hepatobiliary, splenic and pancreatic TB are rare and associated with miliary tuberculosis; often diagnosed in immunocompromised pa- tients. MTB bacilli gain entry to abdominal organs by two routes and cause disease due to reactivation of dormant focus. As a result of hematogenous spread from primary lung infection in children and as a part of miliary TB. Through ingestion of contaminated food and milk which infect Peyer's patches and are transported to mesenteric lymph node, where they remain dormant.

d.Central Nervous System (CNS) TB

It is serious and often fatal form of EPTB, predominantly affecting young children. CNS TB is difficult to diagnose. It presents in 2 major forms

i. TB meningitis- 0.5-1% of all TB cases
ii. Intra-cranial tuberculoma-accounting up to 40% of brain tumors

MTB bacilli reach CNS during dissemination that occurs in active pulmonary disease. These bacilli cross physiological Blood Brain Barrier (BBB) via infected monocytes/neutrophils and cause a caseating focus in brain parenchyma or meninges. These foci are termed as 'Rich foci'. Later, these foci rupture in subarachnoid space triggering inflammatory T cell response with elevated levels of INF y and TNF-a in CSF. The subsequent inflammation leads to production of inflamma- tory infiltrates which obstructs CSF outflow causing hydro- cephalus and vasculitis leads to infarction, causing potentially irreparable neurological damage.

e. Bone and Joint TB

It accounts for 10-15% of all EPTB cases. It arises from reactivation of dormant MTB bacilli lodged in any bone (spine or large joints) during bacteremia of primary lung infection. These bacilli have affinity for spine and large joints because of their rich vascular supply. An extension of initial infection focus from the bone to the joint results in tuberculous arthritis. Rarely the bacilli can reach spine from the lung along the Batson paravertebral venous plexus or by lymphatic drainage to the paraaortic lymph nodes. Non tuberculous mycobacteria (NTM) have been reported to cause osteo- articular TB following a traumatic injury or during surgical procedure like joint arthroplasty. NTM bone infection in pa- tients with AIDS or transpla…

f. Genito-urinary TB (GUTB)

It accounts for 15% of all EPTB cases and 3-4% of all PTB cases. Its occurrence is 20 times more in kidney transplant recipients than in general population. 12 After hematogenous spread of bacilli from active site of infection (usually lungs), bacilli gets lodged in kidney (most common site of GUTB) and form metastatic lesions (tubercles). These foci of infection may heal spontaneously/due to treatment, enlarge and rupture into nephrons or remain dormant for many years. Usually the spread of infection is descending from kidney to other genito-urinary organs. It develops between 2nd and 4th decades of life; usually 5-25 years of inactivity after primary lung infection.

g. Miliary TB

Miliary TB account for less than 2% of all tuberculosis cases and up to 20% of all EPTB cases among immunocompetent adults, however the autopsy studies have shown military TB ranges between 0.3% and 13.3%. TH2 response plays a central role in immunopathogenesis of military TB. It inhibits pro- tective response such as granuloma formation and fencing of the disease

activity at the site of infection. The production of interleukin 4 (IL-4) during TH2 response, downregulates nitric oxide synthase (NOS), tall like receptor 2 and macrophage activation; thus sabotaging protective response of TH1 cells. This process favors dissemination of MTB. from host's cell mediated immunity. These tubercles are microscopic to begin with and coalesce to become macro- scopically visible granulomas. The granulomas contain MTB bacilli within macrophages, fibrin rich alveolar exudate, lymphocytes and multinucleated giant cells which are enclosed within fibroblastic rim. These granulomas formed are both caseating and non-caseating granulomas.[16,17]

DIAGNOSIS OF TUBERCULOSIS :

Hence research on new diagnostic and screening tools and standards has become very necessary in planning to control TB7.9. LTBI is diagnosed with the help of Interferon- gamma release assays (IGRAs) but the tuberculin skin test (TST) is always cost effective for poor peoples. The mechanism behind TST and IGRA is by analyzing the response of immune T cells to the TB antigens.

1. Tuberculin skin test

In the TST test, tuberculin protein derivative from TB is injected intradermally into the patient which caused a delayed hypersensitivity skin reaction (Type 4), if the patient has mycobacteria infection 11. To determine the infection of TB, the size of the skin reaction is measured; the usual standard is between 2 to 3 days and value from 0.74 at 5 mm to 0.40 at 15 mm. However, the TST gives a false report that is positive responses in the patient who are BCG vaccinated and negative in immunosuppressed persons (Table 2: TST Results for Populations at Risk of TB).

2. Interferon-gamma release assays

The IGRAs is a more sensitive and specific diagnostic test for TB (81-88% compared to 70% sensitivity for the TST) 12, but IGRAs are costly and specific technique is used. In IGRAs the release of cytokine IFN-g from T cells that react to antigens not available in the BCG vaccine 12. A blood sample is collected from an individual and the release of cytokine IFN-g is measured. IGRAs have different Guidelines and constantly changing. In Canada and in some European countries, it has even been suggested that IGRAs and the TST be used together to detect LTBI, but these tests are not definitive 11-12. How the disease develops in individuals from a latent to active TB is a heavy task and to improve diagnostic tools we have to identify risk factors associated with high and low burden countries and will improve our understanding of the immune response in Test for TB: Strength and limitations

3. Chest Radiography

Chest radiography is indicated for all persons being evaluated for LTBI or active TB. Pulmonary TB as a result of endogenous reactivation of latent infection classically presents with infiltrates in the apical and posterior segments of the right upper lobe, the apical-posterior segment of the left upper lobe, and the superior segment of the lower lobe.

4. Smear Microscopy

Smear microscopy for the detection of AFB is the most rapid and cheap method for TB diagnosis 40.[18,19]

SIGNS AND SYMPTOMS

General clinical features of TB

Cough with or without sputum more than 3 weeks, Weight loss, Fever/Pyrexia, Sweating in night Haemoptysis (blood in sputum), Chest ache,Fatigue/Weakness.

Symptoms of tuberculous meningitis

Subtle mental status changes that may progress to coma over a period of days to weeks Low-grade fever.

Symptoms of skeletal TB may include the following

Back pain or stiffness, Lower body paralysis, (50% have Pott disease), Tuberculous arthritis, usually involving the only single joint (most often the hip or knee, followed by the ankle, elbow, wrist, and shoulder).

Symptoms of gastrointestinal TB

Ulcers of the mouth, anus or GIT, Difficulty in swallowing (with the oesophageal disease), Abdominal pain mimicking peptic ulcer disease (with gastric or duodenal infection), Malabsorption (with infection of the small intestine), Pain, diarrhoea, or haematochezia (with infection of the colon).

Signs of extrapulmonary TB

Confusion, Coma, Neurologic deficit, Chorioretinitis, Lymphadenopathy, Cutaneous Lesions.[20]

DRUG

First line

All first-line anti-tuberculous drug names have a standard three-letter and a single-letter Ethambutol is EMB or E, isoniazid is INH or H, pyrazinamide is PZA or Z, rifampicin is RMP First-line anti-tuberculous drug names are often remembered with the mnemonic "RIPE," referring to the use of a rifamycin (like rifampin), isoniazid, pyrazinamide, and ethambutol. The US uses abbreviations and names that are not internationally recognised: rifampicin is called rifampin and abbreviated RIF; streptomycin is abbreviated STM. In the US only, streptomycin is no longer considered a first line drug by ATS/IDSA/CDC because of high rates of resistance. The WHO have made no such recommendation. Drug regimens are similarly abbreviated in a standardised manner. The drugs are listed using their single letter abbreviations (in the order given above, which is roughly the order of introduction into clinical practice). A prefix denotes the number of months the treatment should be given for; a subscript denotes intermittent dosing (so means three times a week) and no subscript means daily dosing. Most regimens have an initial high-intensity phase, followed by a continuation phase(also called a consolidation phase or eradication phase): the high-intensity phase is given first, thenthe continuation phase, the two phases divided by a slash. So, 2 HREZ/4HR3 means isoniazid, rifampicin, ethambutol, pyrazinamidedaily for two months, followed by four months of isoniazid and rifampicin giventhree times a week.[21]

Isoniazid

General information

Isoniazid, the hydrazide of isonicotinic acid, is highly bactericidal againstreplicating tubercle bacilli. It is rapidly absorbed and diffuses readily into all fluids and tissues. The plasma half-life, which is genetically determined, varies from less than 1 hour in fastacetylators to more than 3 hours in slow acetylators. Isoniazid is largely excreted in the urine within 24 hours, mostly as inactive metabolites. Clinical information Administration and dosage Isoniazid is normally taken orally but may be administered intramuscularly orintravenously to critically ill patients.

Adults:

- 5 mg/kg (4-6 mg/kg) daily, maximum 300 mg
- 10 mg/kg (8-12 mg/kg) three times weekly, maximum 900 mg (1).

Contraindications

- Known hypersensitivity.
- Active, unstable hepatic disease (with jaundice)

Adverse effects

Systemic or cutaneous hypersensitivity reactions occasionally occur during the first weeks of treatment. Sleepiness or lethargy can be managed by reassurance or adjustmentof the timing of administration. The risk of peripheral neuropathy is excluded if vulnerable patients receivedaily supplements of pyridoxine. Other less common forms of neurological disturbance, including optic

neuritis, toxic psychosis and generalized convulsions, can develop in susceptible individuals, particularly in the later stages of treatment, and occasionally necessitate the withdrawal of isoniazid. Symptomatic hepatitis is an uncommon but potentially serious reaction that canusually be averted by prompt withdrawal of treatment. More often, however, an asymptomatic rise in serum concentrations of hepatic transaminases at the outset of treatment is of no clinical significance and usually resolves spontaneously as treatment continues. A lupus-like syndrome, pellagra, anaemia, and arthralgias are other rare adverse effect[22]

Drug interactions

Isoniazid inhibits the metabolism of certain drugs, which can increase their plasma concentration to the point of toxicity. Rifampicin, however, has the oppositeeffect for many of these drugs. For example, the available data indicate that administering both rifampicin and isoniazid causes a reduction in plasma levels of phenytoin and diazepam. Isoniazid may increase the toxicity of carbamazepine, benzodiazepines metabolized by oxidation (such as triazolam), acetaminophen, valproate, serotonergicantidepressants, disulfiram, warfarin and theophylline.[23]

Overdose

Gastric lavage may be of value if undertaken within a few hours of ingestion. Very large doses of rifampicin may depress central nervous function. There is no specific antidote and treatment is supportive.

Storage

Capsules and tablets should be kept in tightly closed containers, protected from light Pyrazinamide

General information

Pyrazinamide is a synthetic analogue of nicotinamide that is only weakly bactericidal against M. Tuberculosis but has potent sterilizing activity, particularly inthe relatively acidic intracellular environment of macrophages and in areas of acute inflammation. It is highly effective during the first 2 months of treatment while acuteinflammatory changes persist. Its use has enabled treatment regimens to be shortenedand the risk of relapse to be reduced. It is readily absorbed from the gastrointestinal tract and is rapidly distributed throughout all tissues and fluids. Peak plasma concentrations are attained in 2 hours and the plasma half-life is about 10 hours. It is metabolized mainly in the liver and excreted largely in the urine. Clinical information.[24,25]

Administration and dosage

Pyrazinamide is administered orally.

Adults (usually for the first 2 or 3 months of TB treatment):

- 25 mg/kg (20-30 mg/kg) daily
- 35 mg/kg (30-40 mg/kg) 3 times weekly.
- Contraindications
- Known hypersensitivity.
- Porphyria.
- Active, unstable hepatic disease (with jaundice)

CONCLUSIONS

Tuberculosis remains one of the most deadly infectious diseases and has claimed millions of lives for many years. While significant progress has been made towards controlling the global burden of TB over the past decade, more efforts are still needed. Emerging issues such as multi drug-resistance threatens to revert the progress made regarding TB care and control. The knowledge base for TB remains a rapidly expanding area and global guidelines are continually being refined for instance to incorporate new anti-tubercular drugs to tackle issues of resistance. Health professionals, policy makers, patients and the general public need to keep up-to-date with current trends in TB management and control. This will be essential for efficient adoption of global guidelines to country-level situation, particularly taking into

consideration issues such as disease burden, health system structures and available resources.

REFERENCE

1. Ryan KJ, Ray CG. Sherris Medical Microbiology. 5th ed. USA:
2. McGraw Hill company, Inc; 2010:489—505.
3. www.ncbi.nim.nih.gov.
4. 3.Kartik kumar, onn min kon, A diagnosis and treatment of tuberculosis; latestdevelopment and featu vol. 1, 2017.
5. Sharma SK, Mohan A. Tuberculosis: from an incurable scourge to a curable disease-journey over a Millennium. Indian J Med Res. 2013;137:455-493.
6. Pommerville JC. Alcamo's Fundamentals of Microbiology. 7th ed.
7. Canada: Jones and Bartlett; 2004:284-289.
8. Lee JY. Diagnosis and treatment of extrapulmonary tuberculosis. Tuberc Respir Dis. 2015;78:47-55.
9. World Health Organization. Definitions and Reporting Frame Work for Tuberculosis: 2013 Revision. Geneva: World Health Organization; 2013 (updated December 2014).
10. World Health Organization. Global Tuberculosis Report; 2018. Available from: http://www.who.int/tb/publications/global_ report/en.
11. Goldman L. Tuberculosis: disease overview. In: Goldman L, Schafer Al editors. Goldman's Cecil medicine: expert consult premium edition. 24th ed. St. Louis (MO): Saunders Elsevier. 2011.
12. Berry MPR. System approaches to studying the immune response in tuberculosis. Curr Opin Immuno. 2013;25(5):579-587.
13. Cruz-Knight W and Blake-Gumbs L. Tuberculosis: an overview. Prime Care. 2013;40(3):743-756.
14. De Martino M and Galli L. Reflections on the immunology of tuberculosis: will we ever unravel the skein. BMC Infect Dis. 2014;14(Suppl. 1):S1.
15. Sia IG. The current concept in the management of tuberculosis. Mayo Clin Proc. 2011;86(4): 348-361.
16. Kartik kumar, onn min kon, A diagnosis and treatment of tuberculosis; latestdevelopment and feature priorities, vol. 1, 2017.
17. 14.Dheda K, Gumbo T, Gandhi NR, Global control of tuberculosis: from extensively drug-resistant to untreatable tuberculosis. Lancet Respir Med2014, 321-38.
18. Cambau E, Drancourt M. Steps towards the discovery of Mycobacterium tuberculosis by Robert Koch, 1882. Clin Microbiol Infect. 2014;20:196-201.
19. Wallgren A. The time-table of tuberculosis. Tubercle. 1948;29:245-251.
20. Tille PM. Bailey & Scott's Diagnostic Microbiology. 13th ed. Mosby Inc; 2014:484-512.ta,on
21. Pfyffer GE, Palicova F. Mycobacterium: general characteristics, laboratory detection, and procedures. In: Versalovic J, Carroll KC, Funke G, Jorgensec JH, Landry ML, Warnock DW, eds. Mannual of Clinical Microbiology. 10th ed. ASN press; 2011:472-502.ualui
22. Bhardwaj AK, Kumar D, Raina SK, Sharma S, Chander V. Assessment of extra pulmonary tuberculosis (EPTB) cases from selected tuberculosis units (TUs) of Himachal Pradesh, India. Int J Health. 2015;3:29-33.
23. World Health Organization. (2015). Global tuberculosis report. 20th ed. World Health Organization; 2015. https://apps.who. int/iris/handle/10665/191102.
24. 21 Nguyen VH. Intestinal Obstruction due to Tuberculosis. Asian journal of surgery. 2002;25(2):146-150.
25. Rizzo PB. Laryngeal tuberculosis: an often forgotten diagnosis. International Journal of 2003;7:129-131. Infectious Disease.

26. Esteban J. Drug resistance among Mycobacterium tuberculosis strains in immigrants: is there a real threat everywhere. Clinical Microbiology and Infection. 2004;10(4):336-338
27. Abal AT. Effect of cigarette smoking on sputum smear conversion in adults with active pulmonary Tuberculosis. Respiratory Medicine. 2005;99:415-420.
28. Saltini C. Chemotherapy and diagnosis of tuberculosis. Respiratory Medicine.2006;100:2085-2097

HOW TO CITE: Tekchand Manohar Pawar , Vikram Jaysingh Pansare, Akash Vitthal Kaulange, Yogesh Ankush Narute, An Overview On Three Generation Beta Blockers , Int. J. of Pharm. Sci., 2024, Vol 2, Issue 10, 56-68. https://doi.org/10.5281/zenodo.13871749