INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACY AND CHEMISTRY

Available online at www.ijrpc.com

Review Article

DOI: https://dx.doi.org/10.33289/IJRPC.9.4.2019.966

A RECENT REVIEW ON TUBERCULOSIS AND ITS TREATMENT

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ABSTRACT

Tuberculosis (TB) is a fatal disease that is transmitted through air and is caused by *Mycobacterium tuberculosis* that generally affects the pulmonary portion of the human body and leading to severe coughing, fever and chest pain. Although the ongoing research on tuberculosis from few past years has provided valuable information about tuberculosis transmission, detection and treatment. Tuberculosis puts stress on public health because of its high mortality rates after HIV/AIDS. WHO (World Health Organisation) is working closely with countries, partners and civil societies in scaling up the TB response. This review article will focus on the epidemiology, diagnosis, symptoms, treatment of TB and provide a knowledge on the current epidemiology, pathogenesis and immune response, proper treatment and control of TB. Interferon-gamma release assay are whole blood tests in diagnosing TB but unable to distinguish tuberculosis infection from tuberculosis disease. Thus, Tuberculin skin test are used around all over the world for tuberculosis diagnosis. To fight against this fatal disease that has no boundaries, it is necessary to clear and understand all the mechanisms of TB overall with giving better information about its treatment.

Keywords: *Mycobacterium tuberculosis,* WHO, Epidemiology, Tuberculin Skin Test.

INTRODUCTION

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

HISTORY OF TB

"Just sleep and eat nutritious foods" was advice given to TB patients in the 1800s infected with *Mycobacterium tuberculosis*, an airborne disease that usually affects the pulmonary region leading to severe coughing, fever and chest pains[3]. German microbiologist Robert Koch reported that *Mycobacterium tuberculosis* cause TB in humans in 1882[4]. This revolutionary finding along with the later invention of tuberculin in 1890[3-5]. With the starting of AIDS, TB rates increase once again, and with that, it attracts the interest of

scientists for its research and prevention[3]. Now a days, the diagnostic and treatment tools needed to fight against TB were largely decreased and planning to control the disease were arises, including the Directly Observed Treatment Short-Course (DOTS) therapy in early 1993, with the addition of a DOTS-plus program to address multidrug-resistant (MDR) TB in 1998[3-5]. Although, ongoing research on TB reported valuable data about TB transmission, detection, and its full treatment, much remains to be evolved to effectively decrease the incidence of TB[3-6].

The Bacillus Calmette Guerin (BCG) vaccine was invented to prevent TB during the interval of the 20th century but, even with outspread coverage, has failed to control the spread of TB in high populated areas. The continued increase of infections in such poor areas even after vaccination is in part due to the BCG vaccine's different effectiveness in preventing the expansion of adult pulmonary TB. Transmission of *Mycobacterium tuberculosis*, by active pulmonary disease, follows the continuing transmission of TB. There is an urgent need for a more potent vaccine against TB[7].

WHO Global Tuberculosis Report (2017), concluded 4,90,000 cases of multidrug resistant (MDR) TB, with only 50% survival in patients who received recommended WHO treatment regimens[6-7]. The report explains the need for new therapies and access for elaborating TB treatment delivery and management conclusion. Many challenges remain in developing optimal tuberculosis treatment regimens. Combined attempts by stakeholders, advocates and researchers are promoting further development of shorter courses, more potent, safer and better tolerated treatment regimens. Only three novel drugs are in an advanced phase of evolution for MDR TB and nine are being analysed in phase 1 and 2 trials. Rather than new drugs, a bunch of immune based therapy and host directed therapies are under expansion aimed to wipe off *Mycobacterium tuberculosis* infection, reducing the duration of treatment, preventing permanent lung damage and avoiding the development of new drug resistance[8-10].

The International Union against TB is one of the most ancient unions dealing with health issues related to TB. It was first registered in 1902 and started its publication 'Tuberculosis' in French, German and English. Its main aim to provide care to an innumerable number of TB patients in poorer countries through the National Tuberculosis Program (NTP). This program is aimed at providing the skill to the person responsible for the task at the Basic Management Unit (BMU) of NTP, often a paramedical professional pharmacist, and nurse. This is done with the objective of transferring this knowledge to the general public suffering from TB[11].

EPIDEMIOLOGY

It is reported that 1/3rd of the entire world's population is infected with MTB[9]. 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 TB[12].

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[5]. In 2004, only TB was responsible for more than 2.5% of all deaths in the world[9], the infection rates are very higher in areas such as hospitals or prisons[6]. 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 TB[6-10]. 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[3]. 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[6].

TRANSMISSION

TB infection transmitted by inhalation of infectious particles released by the TB patient through cough or sneezing. A majority of persons who intake MTB bacteria through air, can cause an effective response in the lungs which lead to inhibition in the growth of MTB, result in the bacteria becoming dormant; this condition is known as latent tuberculosis or LTBI; immunocompetent latent patient is infected with MTB but do not shows signs & symptoms and do not transmit the disease to other person[6-7].

There are certain persons that are more sensitive to getting infected which include:

adults (commonly in males), those in developing countries, health care workers who are around this disease and those which have a very weak immune system, in those who have AIDS. In fact, TB is the main cause of death in those patients who are infected with HIV and HIV-TB combination has been widely observed. Additionally, foreign-born persons and those who live in poor areas or where malnutrition is common are more likely to get TB infection[7].

TB also transmitted through droplet aerosolization from an individual who has active TB. AFB positive patient has the highest chance to easily infected with TB. However, patients with negative smears but positive cultures may still transmit the disease[13-14].

There are other conditions that may arise a high-risk for susceptibility to MTB infection such as diabetes, long term use of corticosteroids, TNF-alpha blockers, polymorphism in vitamin D receptors, polymorphism in IL-12 and IFN-g genes[8] **(Fig. 1: Image explaining the transmission of TB (Courtesy: www.healthnavigator.com) and Table 1: Factors determine the probability of transmission of *M.* tuberculosis)**.

TUBERCULOSIS INFECTION CONTROL[15]

Administrative controls

Assign responsibility for TB infection control.

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

Environmental controls[16]

Reduce the concentration of infectious droplet nuclei through the following technologies:

- Ventilation technologies, including natural ventilation.
- Mechanical ventilation.
- High-efficiency particulate air filtration (HEPA).
- Ultraviolet germicidal irradiation (UVGI)

Respiratory protection control[17-20]

- Implement a respiratory protection program.
- Train health care workers on respiratory system protection.
- Educate patients on respiratory hygiene and the importance of covering their cough.
- Wear mask for protection.

DIAGNOSIS OF TUBERCULOSIS[21]

Hence research on new diagnostic and screening tools and standards has become very necessary in planning to control TB[7,9]. 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[9]. The mechanism behind TST and IGRA is by analyzing the response of immune T cells to the TB antigens.

1. Tuberculin skin test[22-25]

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[29-33]

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[6]. 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 TB **(Table 3: Test for TB: Strength and limitations)**.

3. Chest Radiography[39]

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]

(Table 4: Diagnosis procedure of Common Extrapulmonary TB).

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SIGNS AND SYMPTOMS[41]

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[42]

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 **(Fig. 2: Image shows general symptoms of TB (Courtesy-www.dovemed.com).**

TREATMENT OF TUBERCULOSIS

Latent TB Infection

Treatment for LTBI is recommended for persons who are at a relatively very high risk of developing active TB and should be initiated only after active TB has been diagnosed by clinical and radiographic techniques. Failure to treat TB may result in inadequate treatment and development of drug resistance which is a great problem now a days. For most patients, treatment with Isoniazid (INH) for 9 months is preferred[16]. Pyridoxine supplementation (25 mg/d) to INH is recommended for patients at an increased risk of neuropathy, including those with pre-existing peripheral neuropathy, nutritional deficiency, diabetes mellitus, HIV infection, renal failure, alcoholism or thyroid disease and those who are pregnant or breastfeeding. Intermittent treatment (i.e., a twice-weekly regimen) should only be performed as directly observed therapy (DOT). Due to the high rates of hospitalization and death from liver injury, the combination of Rifampin (RIF) and Pyrazinamide (PZA) is no longer recommended for the treatment of LTBI[41-44].

Active TB

Patients with active TB should be treated with multiple drugs to achieve bacterial killing, to reduce the risk of transmission and to prevent the drug resistance by bacteria. Directly observed therapy (DOT), which involves direct observation of patients taking antitubercular medications, is the preferred management strategy for all patients being treated for TB. For treatment to be successful, patient-centred case management and a close combination between health care professionals and local public health programs are important. Medications for treating TB are classified as first and second-line drugs. First-line drugs are INH, RIF, Ethambutol (EMB) and PZA. The rifamycin derivatives rifapentine and rifabutin are also considered among the first-line drugs[42-43].

Second-line drugs include the aminoglycosides streptomycin, kanamycin and amikacin and several fluoroquinolones (e.g. Moxifloxacin, levofloxacin and gatifloxacin). The American Thoracic Society, the Centers for Disease Control and Prevention, and the Infectious Diseases Society of America have issued a joint statement on the treatment of TB in the United States[39-40].

Four treatment regimens are recommended for patients with the drug-susceptible disease. Although these regimens are broadly applicable, treatment must be individualized on the basis of each patient's clinical situation. Each of the four TB treatment regimens has an initial phase of 2 months followed by a continuation phase of 4 or 7 months. Treatment in the initial phase is usually empirical because susceptibility data may not be available. To guard against drug resistance and to ensure maximal effectiveness, the initial phase of treatment should include 4 drugs (INH, RIF, PZA, and EMB). If the isolate is susceptible to INH and RIF, EMB can be discontinued. Depending on the regimen

chosen, medication in the initial phase may be given daily throughout treatment, daily for 2 weeks then twice weekly thereafter, or 3 times weekly throughout. Susceptibility data should direct treatment in the continuation phase, which lasts for 4 months in most patients[40]. The continuation phase of treatment should be extended to 7 months for the following 3 groups of patients: those with cavitary pulmonary TB whose sputum culture remains positive after 2 months of treatment; those in whom the initial phase of treatment did not include PZA (e.g., those who have severe liver disease or are pregnant); and those being treated with once-weekly INH and rifapentine whose sputum culture remains positive after 2 months of treatment. Extending the continuation phase of treatment in these situations reduces the rate of relapse. During the continuation phase, medications may be given daily or 2 to 3 times a week with DOT. The minimum duration of treatment for culture-positive TB is 6 months. If PZA is not included in the initial phase, treatment should be given for 9 months. Smear-negative, culture-negative pulmonary TB may be treated successfully with 4 months of a combination INH-RIF regimen. Completion of anti-TB treatment is determined by both the total number of doses taken and the duration of therapy[41]**(Table 5: Treatment Regimens of TB)**.

REVIEW OF LITERATURE ON TUBERCULOSIS

Leitch A.G. *et al.,* 1995 stated that disease due to *Mycobacterium tuberculosis* is less common than expected in HIV-positive patients. He experienced that tuberculosis is reported to complicate HIV infection in those dually infected with Mycobacterium tuberculosis and HIV at the rate of approximately 10% per annum. Therefore, this study determines the outcome in HIV-positive patients known to have been tuberculin skin test positive. On the basis of similar historical skin test data appropriate to the age groups of the HIV-positive patients, to predict the total number of cases of tuberculosis expected yearly[18].

Collazos J. *et al.,* 1995 discussed the chemotherapy of tuberculosis from ancient to recent. His article provides an overview of the past, present, and future aspects of chemotherapy for TB. The reported efficacy of rifampin was a major breakthrough because the regimens which included rifampin were able to treat TB in all patients[19].

Mouroux J. *et al.,* 1996 reported about Surgical Management of Pleuropulmonary Tuberculosis and analysed the result of procedures. He concluded that the morbidity and mortality rates in his group of patients were 31.25% and 12.5%, respectively. The surgery had both therapeutic and diagnostic indications for the management of pleuropulmonary tuberculosis[20].

Keith P.W.J. *et al.,* 1997 stated that Bacille Calmette-Guerin (BCG) is the most widely used vaccine worldwide. However, its efficacy varies from 80% to zero among studies. A meta-analysis of all the published prospective trials and case-control studies indicates approximately 50% efficacy against all forms of tuberculosis, but it is even more effective against the invasive forms of the disease, meningitis and miliary tuberculosis. Geographic latitude accounts for 41% of the variance between studies. The variability between different BCG preparations and the role of environmental nontuberculous mycobacteria are discussed as major factors in the inconsistent results of BCG vaccine trials[21].

Wilcke J.T.R. *et al.,* 1998 concluded that if the diagnosis of pulmonary TB missed the risk may be high if patients present with an X-ray unusual for TB, but this is fortunately seen only in approximately 8% of cases of pulmonary tuberculosis. Unusual X-ray is more commonly found in patients with the related disease, such as diabetes and cancer. If the chest X-ray shows cavities, but the smear is negative for Mycobacterium, TB is unlikely and further diagnostic procedures should be performed without waiting for culture results[22].

Lounis N. *et al.,* 1999 studied and stated the impact of iron loading and iron chelation on murine tuberculosis. Iron loading in mice enhanced the multiplication of *M. tuberculosis* in the spleens but not in the lungs. Deferoxamine exhibited significant activity against *M. tuberculosis* in iron-loaded mice and isoniazid therapy was strongly bactericidal in both iron-loaded and non-iron-loaded mice[23].

Sierra C. *et al.,* 2000 reported that extra laryngeal head and neck tuberculosis has a slow duration of action but it is difficult to diagnose due to no involvement of lung[24].

John J.T. *et al.,* 2001 described the risk factor involved during post-transplant tuberculosis and stated in his article that diabetes mellitus and chronic liver disease are risk factors for

post-transplant TB. He also concluded that any type of infection, liver problem and hyperglycaemia can be fatal in the case of transplantation tuberculosis[25].

Nguyen V. H., 2002 illustrated that intestinal obstruction due to tuberculosis is uncommon in comparison to other causes of mechanical bowel obstruction, but it is common in the course of intestinal tuberculosis, with or without treatment. The aims of the study were to determine some clinical and pathological features and to evaluate the role of surgery and also to suggest the best procedure for the management of this disease[26].

Rizzo P.B. *et al.,* 2003 stated that laryngeal tuberculosis almost disappeared after 1950 but, related to the increase in pulmonary forms, may still be found and, being uncommon, is often misdiagnosed[27].

Esteban J. *et al.,* 2004 confined in his studies about Drug resistance among *Mycobacterium tuberculosis* strains in immigrants, he determined the impact of drug resistance in tuberculosis among immigrant patients in Madrid, Spain. During the time period of 1995-2001, the relative proportion of isolates from immigrant patients increased from 4.4% to 24.2%. and concluded that no differences between immigrants and Spanish-born patients were detected for resistance to any first-line anti-tuberculous drug. More studies are required to determine the actual incidence of resistant tuberculosis in immigrants[28].

Abal A.T. *et al.,* 2005 described the effect of cigarette smoking on sputum smear conversion in adults with active pulmonary tuberculosis. In conclusion, he stated that smoking did not influence sputum smear conversion in tuberculosis. However, as expatriate smokers and smokers with advanced disease showed a delay in smear conversion, smoking should be discouraged in patients with pulmonary tuberculosis[29].

Saltini C., 2006 concluded that rifampicin, isoniazid, and pyrazinamide as the first line drugs for short course in his article chemotherapy and diagnosis of tuberculosis[30].

Arnold C., 2007 stated that different genetic markers indicate that the species *M. tuberculosis* have different strained families, each with a single ancestor. An analysis of genetic marker deviation from the common ancestor of each of these families will improve understanding of the individual marker evolution rates and the degree of convergence within genetic families[31].

Bukhary Z.A. *et al.,* 2008 illustrated in his review article that relation between TB and diabetes mellitus, there is a need to alert all physicians about the potential impact of diabetes mellitus on the control of tuberculosis and its treatment. It is important to check fasting blood sugar in new patients with tuberculosis and to screen all patients with diabetes mellitus for latent *Mycobacterium tuberculosis* infection. Patients with combined diabetes mellitus and tuberculosis require close monitoring for the control of both diseases[32].

Gopinath K. *et al.,* 2009 narrated that specific PCR and culture examination of spot urine samples from suspected pulmonary TB patients significantly improved the detection rate of Pulmonary TB and should be encouraged in resource-limited settings and where multiple pulmonary specimens are not feasible[33].

Schirmer P. *et al.,* 2010 stated in his article that between 50% and 75% of patients with osteoarticular TB and approximately 33-50% of patients with spinal TB have an associated primary lung focus or have a reported history of pulmonary TB. In one study of spinal TB, MTB was found elsewhere in the body in approximately 40% of cases, and 50% of those cases had pulmonary involvement. Most reports suggest that spinal TB results from a primary focus outside of the spine, and spread is postulated to be via hematogenous or lymphatic dissemination[34].

Chen T.C. *et al.,* 2011 described in his article Fluoroquinolones are associated with delayed treatment and resistance in tuberculosis: a systematic review and meta-analysis that Empirical fluoroquinolone prescriptions for pneumonia are associated with longer delays in diagnosis and treatment of pulmonary TB and a higher risk of developing fluoroquinolone resistant in *M. tuberculosis*[35].

Sneh S. *et al.,* 2012 stated that primary hepatic TB is fatal if remained undiagnosed and its result from tubercular bacilli gaining access to the portal vein from a microscopic tubercular focus in the bowel with subsequent healing taking place at the site of entry leaving no trace of it[36].

Naha K. *et al.,* 2013 described that in developing countries with a high prevalence of TB in the general population, the possibility of

incidental TB in a patient with HIV should always be considerd[37].

Sugarman J. *et al.,* 2014 estimated that 2,16,500 (95% uncertainty range) active tuberculosis cases existed in pregnant women globally in 2011. The greatest burdens were in the WHO African region with 89,400 cases and the WHO South East Asian region with 67,500 cases in pregnant women. Chest radiography proves that[38].

Aziza R. *et al.,* 2015 ascertained that it raised the harmful impact of smoking on the clinical and radiological presentation of tuberculosis, and late bacteriological negativity, therefore we need to integrate smoking control into the national TB control program to completely obsolete TB[39].

Mehraj J. *et al.,* 2016 confirmed that there is a need to focus on extrapulmonary TB among female populations to document the epidemiology in South Asia, and examine the risk factors, diagnostic modalities, treatment strategies, and outcomes to carry out preventive and controls[40].

Cataldi A.A. *et al.,* 2017 illustrated that there is a number of drugs that can cure TB but his article focuses on azole compounds and All azole compounds tested in his study showed inhibitory activity against MDR *M. tuberculosis* clinical isolates bacterias[41].

Wakamatsu K. *et al.,* 2018 concluded in his article that Prognostic factors in patients with miliary tuberculosis that in patients with miliary tuberculosis, old age, ARDS (Acute Respiratory Distress Syndrome) and consciousness disturbance were factors associated with poor prognosis[42-45].

Singh A. *et al.,* 2019 stated about the abdominal TB in Indians that although the burden of the disease remains the same, the availability of newer investigations has aided in its early diagnosis and availability of good drugs has reduced the mortality and morbidity[46].

CONCLUSION

Tuberculosis remains a deadly disease throughout the world. Many efforts to remove TB have been hampered due to poverty, lack of health care access, drug resistance, immunosuppressed populations (e.g. HIV infected persons, Diabetes patient or any other infection) and global migration. Effective management is carried out by using a combination of clinical, radiographic, microbiological, histopathologic methods and initiation of appropriate multidrug therapy. In addition to the effective treatment of patients with active TB, public health management strategies include diagnosis, contact investigation, and testing of persons who came into close contact with patients with active TB. The increasing population, poverty, improper treatment is the main reason behind the growth of TB. Short course chemotherapy has been considered to be very effective and fruitful in the treatment of TB. Some mandatory steps might be taken to minimising the resistance problem in antitubercular drugs and to provide better efficacy and potent therapeutic effect.

FUTURE ASPECTS

TB is spreading very fast all over the world. The main reason behind this is the drug resistance developed by the bacteria. But newer drugs, diagnosis, treatment and prevention are under research. WHO has played an important role to control the spread of TB and WHO promotes a number of the new plan and program to completely eradicate TB. Every year WHO updates Guidelines for treatment of drug-susceptible tuberculosis and patient care which includes objective, methods, policies and recent research. WHO plans to completely eradicate the TB from the world in the future.

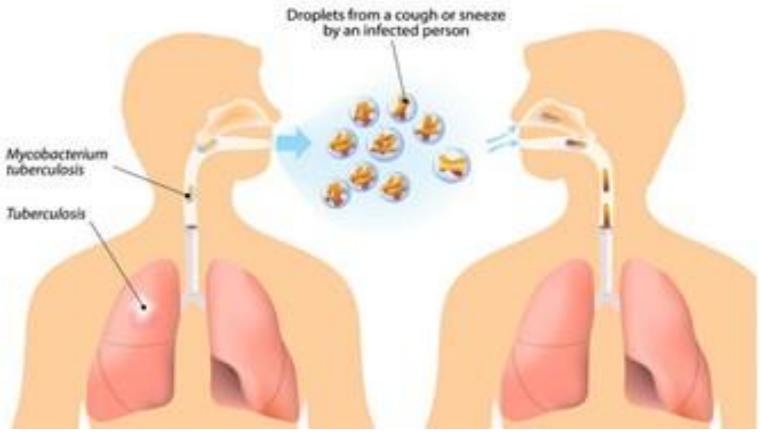

Fig. 1: Image explaining the transmission of TB (Courtesy: www.healthnavigator.com)

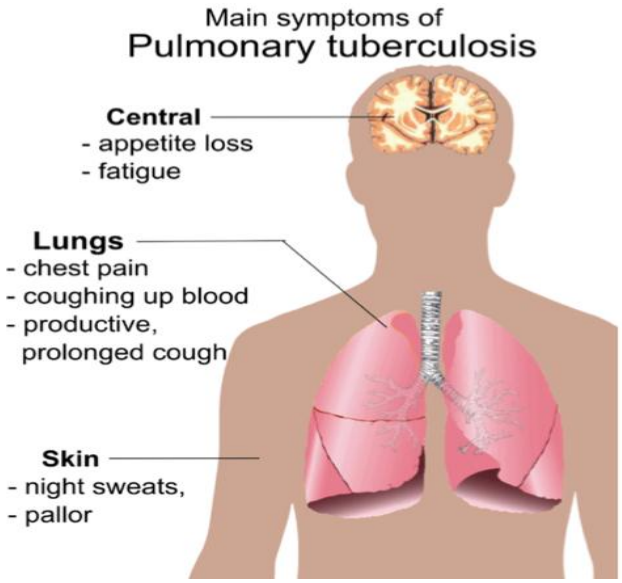

Fig. 2: Image shows general symptoms of TB (Courtesy- www.dovemed.com)

Table 1: Factors determine the probability of transmission of *M.* tuberculosis[14-15]

Factors	Description
Susceptibility	Susceptibility (immune status) of the exposed individual.
Infectiousness	Infectiousness of the person with TB disease directly related to the number of tubercle bacilli that he or she expels into the air.
Environment	Environment factors that affect the concentration of *M. tuberculosis* organisms.
Exposure	Proximity, frequency and duration of exposure.

Table 2: TST Results for Populations at Risk of TB[26-28]

At-risk populations	Positive TST reaction size (mm)
Patients with HIV infection Patients receiving immunosuppressive therapy Abnormal findings on chest radiography consistent with previous TB infection Persons who have come in close contact with and actively contagious patient	≥5
Patients with certain chronic conditions Patients with certain malignancies Foreign-born persons from high-incidence regions (>25/100,000) Employees and residents of high-risk facilities	≥10
Healthy people at low risk of TB	≥15

Table 3: Test for TB: Strength and limitations[34-38]

Test	Strengths	Limitations
TST test	High specificity in non-BCG-vaccinated populations Cost-effectiveness	Training required for administration and interpretation Return visit required in 48-72 h for test result Possible booster effect Possible false-positive and false-negative results
Interferon-gamma release assays	High specificity Only 1 patient visit required No confounding by BCG vaccination High cost	Blood withdrawal required Indeterminate results in those who are immunosuppressed and in those aged <5 year No capacity to differentiate between latent and active TB High cost
Chest X-ray	Ready availability Capacity to differentiate latent infection from active TB Not confirmatory	Low sensitivity and specificity Not confirmatory
Smear microscopy	Ease, speed, and cost-effectiveness of the technique A quantitative estimate of the number of bacilli Usefulness in determining infectiousness and in monitoring treatment progress	Low sensitivity No capacity to differentiate from nontuberculous mycobacteria

Table 4: Diagnosis procedure of Common Extrapulmonary TB[40]

Site	Diagnostic procedure
Tuberculous lymphadenitis	Excisional biopsy with culture
CNS TB	Characteristic CSF exam AFB smear and culture of CSF Polymerase chain reaction for TB of CSF
Pleural TB	Pleural biopsy with pathology and culture
Tuberculous pericarditis	Pericardiocentesis with culture
Skeletal TB	Needle biopsy and culture
Genitourinary TB	Biopsy and culture of masses Culture of urine

AFB = acid-fast bacilli, CNS = central nervous system,
CSF = cerebrospinal fluid, TB = tuberculosis.

Table 5: Treatment Regimens of TB[42-45]

Regimen	Drugs	Interval and Dose (duration)
1	INH, RIF, PZA, EMB	7 day/week for 56 doses (8 week)
2	INH, RIF, PZA, EMB	7 day/week for 14 doses (2 week), then twice weekly for 12 doses (6 week)
3	INH, RIF, PZA, EMB	3 times weekly for 24 doses (8 week)
4	INH, RIF, EMB	7 day/week for 56 doses (8 week)

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