ejpmr, 2023, 10(12), 263-268

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

A REVIEW ON TUBERCULOSIS

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Article Received on 06/10/2023 **Article Revised on 26/10/2023** **Article Accepted on 16/11/2023**

ABSTRACT

Tuberculosis treatment remains a challenge due to the need to consider, when approaching it, the context of individual and collective health. In addition, social and economic issues have been shown to be variables that need to be considered when it comes to treatment effectiveness. In a small proportion of cases, the bacillus is transmitted to humans from infected cows through drinking non-sterilized milk. This mode of transmission plays only a minor role in the natural history of the disease in humans. This review article will focus on the epidemiology, diagnosis, symptoms, treatment of TB, and provide a knowledge on current epidemiology, pathogenesis, and immune response, proper treatment and control of TB.

KEYWORDS: Tuberculosis, Introduction, epidemiology, pathogenesis, immune response, symptoms, diagnosis, treatment, prevention, diet.

INTRODUCTION

Tuberculosis 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. Tuberculosis can affect any organ in the body. Pulmonary tuberculosis is the most frequent site of involvement; extrapulmonary tuberculosis is less frequent. Only pulmonary tuberculosis is infectious**.** Tuberculosis (TB) remains a leading infectious killer globally. In contrast, TB remains out of control in many developing countries—to the point that one-third of the world's population currently is infected.1 Estimates suggest that 1 person dies of TB in India each minute (Times of India, August 29, 2003). M. tuberculosis preferentially infects humans, and the closely related M. bovis causes a similar disease in cattle and other livestock. Although uncommon today, humans frequently developed TB by drinking milk contaminated with M. bovis—a threat that spurred the development of pasteurization. Today, airborne M. tuberculosis is the main threat to humans. Evidence of TB has been found in ancient human remains, and ancient texts describe it.1−3 TB commonly was known as "consumption".

EPIDEMIOLOGY

Globally, roughly 2 billion people are infected by M. tuberculosis, and roughly 2 to 3 million people die from active TB each year despite the fact that it is curable. In the United States, about 13 million people are latently infected with M. tuberculosis, meaning that they are not currently sick but that they could fall ill with TB at any time.

The annual incidence of TB in the United States declined by about 5% per year from 1953 to 1983. In 1984, this decline slowed, and then the incidence of TB rose from 1988 to 1992, reaching 10.5 cases per 100,000 population. Since 1992, more effective infection control practices and treatment protocols have reduced TB rates to 5.2 per 100,000 population as of 2002. Despite this good news, the eradication of TB from the United States will remain very difficult. One reason is that we continue to import new cases from countries where TB remains out of control.

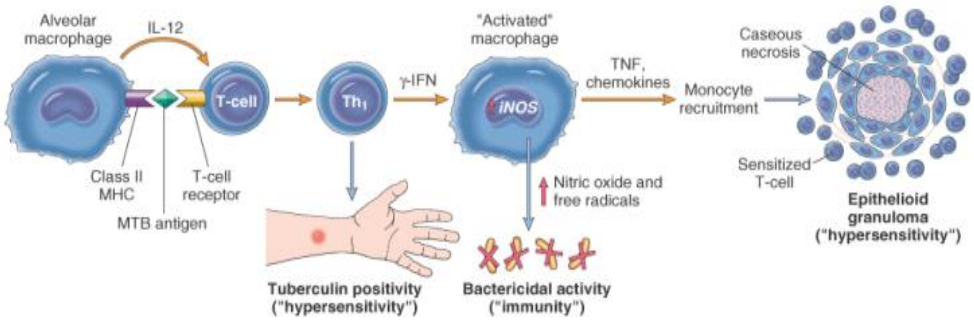
PATHOGENESIS

The outcome of infection in a previously unexposed, immunocompetent person depends on the development of antimycobacterial T cell-mediated immunity. These T cells control the host response to the bacteria and also result in development of pathologic lesions, such as caseating granulomas and cavitation. Early in infection, M. tuberculosis replicates essentially unchecked within macrophages, and later in infection, the cell response stimulates macrophages to contain the proliferation of the bacteria.

The steps in infection are as follows

M. tuberculosis enters into macrophages by phagocytosis mediated by several receptors expressed on the phagocyte, including mannose-binding lectin and type of

3 complement receptor (CR3). M. tuberculosis inhibits maturation of the phagosome and blocks formation of the phagolysosome, allowing the bacterium to replicate unchecked within the vesicle, protected from the microbicidal mechanism of lysosomes. The bacterium blocks phagolysosome formation by recruiting a host protein called coronin to the membrane of the phagosome. Coronin activates the phosphatase calcineurin, leading to the inhibition of the phagosome-lysosome fusion. Thus, during the earliest stage of primary tuberculosis the nonsensitized individual, bacteria proliferate in the pulmonary alveolar macrophages and air spaces, resulting in bacteraemia and seeding of multiple sites. Multiple pathogen associated molecular patterns made by M. Tuberculosis are recognized by innate immune receptors. Mycobacterial lipoarabinomannan binds TLR2, and unmethylated CpG nucleotides bind TLR9. About 3 weeks after injection, a Th1 response is mounted that activates macrophages, enabling them to become bactericidal. The response is initiated by mycobacterial antigens that enter draining lymph nodes and are displayed to T-cells. Differentiation of Th1 cells depends on IL-12 and IL-18, which are produced by antigen- presenting cells that have encountered the bacteria. Stimulation of TLR2 by mycobacterial ligands promotes production of IL-12 by dendritic cells. Th1 cells, both in lymph nodes and in the lung. In addition to stimulating macrophages to kill mycobacteria, Th1 response orchestrates the formation of granulomas and caseous necrosis. Macrophages activated by IFN-γ differentiate into the "epithelioid histiocytes" that aggregate to form granulomas; some epithelioid cells may fuse to form giant cells. In many people the infection progresses due to advanced age or immunosuppression, and the on-going immune response results in caseous necrosis. Activated macrophages also secrete TNF and chemokine's, which promote recruitment of more monocytes.



RISKFACTORS

Once infected with M. tuberculosis, a person's lifetime risk of active TB is about 10%. The greatest risk for active disease occurs during the first 2 years infection. Children younger than 2 years and adults over 65 years of age have 2 to 5 times greater risk for active disease compare with other age groups. Patients with underlying immune suppression (e.g., renal failure, cancer, and immunosuppressive drug treatment) have 4 to 16-time greater risk than other patients. Finally, HI-infected patients with M. tuberculosis infection are 100 time more likely to develop active TB than a normal host. HIV-infected patients have an annual risk of active TB of about 10% rather than a lifetime risk at that rate. Therefore, all patients with HIV infection should be screened for tuberculosis infection, and those known to be infected with M. tuberculosis should be tested for HIV infection.

SYMPTOMS

A person with latent, or inactive, TB will have no symptoms. You may still have a TB infection, but the bacteria in your body is not yet causing harm.

Symptoms of active TB include

- A cough that lasts more than three weeks
- Loss of appetite and unintentional weight loss
- Fever
- Chills
- Night sweats

DIAGNOSIS

1. TUBERCULOSIS SKIN TEST

In the TST test, tuberculin protein derivative from TB is inject intradermally into the patient which caused a delayed hypersensitivity skin reaction. If the patients has mycobacterial infection. To determine the infection of TB, the size of the skin reaction is measured; the usual standardize 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 response in the patient who are BCG vaccinated and negative in immunosuppressed persons.

2. INTERFERON-GAMMA RELEASE ASSY

The IGRAs is a more sensitive and specific diagnostic test for TB but IGRAs are costly and specific technique is used. In IGRAs the released of cytokine IFN-g from tells that react to antigens not available in vaccine. A blood sample is collected from is measured.

3. CHEST RADIOGRAPHY

Chest radiography is indicated for all persons being evaluated for LIBI or active TB. Pulmonary TB as result of endogenous reactivation of latent infection classically presents with infiltrates in the apical and posterior 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.

SITE	DIAGNOSTIC PROCEDURE
Tuberculosis 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
Tuberculosis pericarditis	Pericardiocentesis with culture
Skeletal TB	Needle biopsy and culture
Genitourinary TB	Biopsy and culture of masses culture of urine

TREATMENT

The desired outcomes for the treatment of tuberculosis are:

1. Rapid identification of a new TB case.
2. Isolation of the patient with active disease to prevent spread of the disease.
3. Collection of appropriate samples for smears and cultures.
4. Initiation of specific anti-tuberculosis treatment.
5. Prompt resolution of the signs and symptoms of disease.
6. Achievement of a non-infectious state in the patient, thus ending isolation.
7. Adherence to the treatment regimen by the patient.
8. Cure of the patient as quickly as (generally at least 6 months of treatment)

Secondary goals are identification of the index case that infected the patient, identification of all persons infected by both the index case of TB, and completion of appropriate treatments for those individuals.

ADULTS

In the 1940s, the Brazilin National Campaign against tuberculosis was started, and during that period, two anti-tuberculosis drugs were used: streptomycin and para-amino salicylic acid. In the 1950s, Brazil chose to use q twice-weekly regimen with isoniazid and streptomycin.

- In the 1940 streptomycin and para-amino salicylic acid are used in the treatment of tuberculosis.
- In 1950 isoniazid and streptomycin are used in a week.
- In 1960 due to increasing the bacterial resistance isoniazid, streptomycin and pyrazinamide for 18 months was implement as treatment for adults. (HSZ regimen)
- In the mid of 1970 rifampicin, isoniazid and pyrazinamide are used for 6 months as shorter anti-tuberculosis chemotherapy. (RHZ)
- In 1980 combination of rifampicin and isoniazid capsules were implement to prevent acquired. (RH regimen)
- In 2009 the Brazil introduce use of SDC tablets (fixed dose combination) and added ethambutol to the RHZ regimen.

CHILDREN

Tuberculosis is children is difficult to diagnose, even in its pulmonary form; children rarely produce sputum, so sputum smear examination can therefore not be used to obtain bacteriological proof, which is the cornerstone of diagnosis in adults. In Brazil, patients under 10 years of age are treated with three medications: rifampicin (10 mg/kg), isoniazid (10 mg/kg), and pyrazinamide (35mg/kg). This decision is based on the lower risk of resistance to isoniazid in patients with a low bacterial load, as is more common in children with tuberculosis, and on the risk of ethambutol-related visual impairment, the diagnosis of which can be difficult in children.

Infants and children may be infected within the family circle. There are two key factors in diagnosing tuberculosis in children

- Identification of an infection adults close to the child;
- Loss of weight or failure to thrive.

Doses of tuberculosis Drugs for Adults and Children

Drug	preparation	Adult/children	Dose			
			Daily	11x/wk.	2x/wk.	3x/wk.
First-Line Drugs:						
Isoniazid	Tablets (50 mg,100 mg, 300 mg); elixir (50 mg/ml); aqueous solution (100 mg/ml) for IV or IM injection	Adults (max.)	5 mg/kg (300 mg)	15 mg/kg (900 mg)	15 mg/kg (900 mg)	15 mg/kg (900 mg)
		Children (max.)	10-15 mg/kg (300 mg)	–	20-30 mg/kg (900 mg)	–

Rifampicin	Capsule (150 mg, 300 mg); powder may be suspended for oral administration; aqueous solution for IV injection	Adults (max.)	10 mg/kg (600 mg)	–	10 mg/kg (600 mg)	10 mg/kg (600 mg)
		Children (max.)	10–20 mg/kg (600 mg	–	10–20 mg/kg (600 mg	–
Rifabutin	Capsule (150 mg)	Adults (max.)	5 mg/kg (300 mg	–	5 mg/kg (300 mg)	5 mg/kg (300 mg)
		Children	Appropriate dosing for children is unknown	Appropriate dosing for children is unknown	Appropriate dosing for Children is unknown	Appropriate dosing for children is unknown
Rifapentine	Tablet (150 mg, film coated	Adults	–	10 mg/kg (continuation phase) (600 mg)	–	–
		Children	The drug is not approved for use in children	The drug is not approved for use in children	The drug is not approved for use in children	The drug is not approved for use in children
Pyrazinamide	Tablet (500 mg, scored)	Adults	Tablet (500 mg, scored) 1500 mg (56–75 kg) 2000 mg (76–90 kg)	– – –	2000 mg (40–55 kg) 3000 mg (56–75 kg) 3000 mg (56–75 kg)	1500 mg (40–55 kg) 2500 mg (56–75 kg) 3000 mg (76–90 kg) k
		Children	15–30 mg/kg (2.0 g)	–	50 mg/kg (2.5 g)	–
Ethambutol	tablet (500 mg, scored)	Adults	800 mg (40–55 kg) 1200 mg (56–75 kg) 1600 mg (76–90 kg)k	– – –	2000 mg (40–55 kg) 2800 mg (56–75 kg) 4000 mg (76–90 kg) k	1200 mg (40–55 kg) 2000 mg (56–75 kg) 2400 mg (76–90 kg) k
		Childrens	15–20 mg/kg daily (1.0 g)	–	50 mg/kg (2.5 g)	–
Second-Line Drugs:						
Cycloserine	Capsule (250 mg)	Adults	10–15 mg/kg/day (1.0 g in two doses), usually 500–750 mg/d in two doses	There are no data to support intermittent administration	There are no data to support intermittent administration	There are no data to support intermittent administration
		Childrens	10–15 mg/kg/day (1.0 g/day	–	–	–
Ethionamide	Tablet (250 mg)	Adults	15–20 mg/kg/day (1.0 g/day), usually 500–750 mg/day in a single daily dose or two divided doses	There are no data to support intermittent administration	There are no data to support intermittent administration	There are no data to support intermittent administration
		Children	15–20 mg/kg/day (1.0 g/day)	There are no data to support intermittent administration	There are no data to support intermittent administration	There are no data to support intermittent administration

Streptomycin	Aqueous solution (1-g vials) for intravenous or intramuscular administration	Adults	g	g	g	G
		Children	20–40 mg/kg/day (1 g)	–	20 mg/kg	–
Amikacin/ kanamycin	Aqueous solution (500-mg and 1-g vials) for intravenous or intramuscular administration	Adult	g	g	**g**	G
		Children	15–30 mg/kg/day (1 g) intravenous or intramuscular as a single daily dose	–	15–30 mg/kg	–
Capreomycin	Aqueous solution (1-g vials) for intravenous or intramuscular administration	Adults	g	g	g	G
		Children	15–30 mg/kg/day (1 g) as a single daily dose	–	15–30 mg/kg	–
p-Amino salicylic acid (PAS)	Granules (4-g packets) can be mixed with food; tablets (500 mg) are still available in some countries, but not in the United States; a solution for intravenous administration is available in Europe	Adults	8–12 g/day in two or three doses	There are no data to support intermittent administration	There are no data to support intermittent administration	There are no data to support intermittent administration
		Children	200–300 mg/kg/day in two to four divided doses (10 g	There are no data to support intermittent administration	There are no data to support intermittent administration	There are no data to support intermittent administration
Levofloxacin	Tablets (250 mg, 500 mg, 750 mg); aqueous solution (500-mg vials) for intravenous injection	Adults	500–1000 mg daily	There are no data to support intermittent administration	There are no data to support intermittent administration	There are no data to support intermittent administration
		Children	h	h	h	h

PREVENTION

As TB is an airborne infection, TB bacteria are released into the air when someone with infection TB coughs or sneezes. The risk of infection can be reduced by using a few simple precautions:

- Good ventilation: as TB remain suspending in the air for several hours with no ventilation.
- Natural light: UV light kills off TB bacteria.
- Good hygiene: converting the mouth and nose when coughing or sneezing reduces the spread of TB bacteria.

DIET

Food To Eat	Food To Avoid
• Balanced diet with fruits, vegetables, lean protein sources • Protein foods are more required for TB patients like meat, fish, eggs, beans • Eating meals in small amount and maintaining weight and energy levels • Drinking plenty of fluids • Eat food rich in vitamins and minerals	• Avoid Tobacco consumption and Alcohol intake • Avoiding coffee and caffeinated drinks • Avoid deep fried food, junk food, refined products • Limit consumption of red meat or food items • Avoiding soft drinks instead of these drink like water or coconut water

REFERENCES

1. Horsburgh Jr CR, Barry III CE, Lange C. Treatment of tuberculosis. New England Journal of Medicine, 2015 Nov 26; 373(22): 2149-60.
2. Natarajan A, Beena PM, Devnikar AV, Mali S. A systemic review on tuberculosis. Indian Journal of Tuberculosis, 2020 Jul 1; 67(3): 295-311.
3. Handa U, Mundi I, Mohan S. Nodal tuberculosis revisited: a review. The Journal of Infection in Developing Countries, 2012; 6(01): 6-12.

4. Bansal R, Sharma D, Singh R. Tuberculosis and its treatment: an overview. Mini reviews in medicinal chemistry, 2018 Jan 1; 18(1): 58-71.
5. Perez-Velez CM, Marais BJ. Tuberculosis in children. New England Journal of Medicine, 2012 Jul 26; 367(4): 348-61.
6. Khan MK, Islam MN, Ferdous J, Alam MM. An Overview on Epidemiology of Tuberculosis. Mymensingh medical journal: MMJ., 2019 Jan 1; 28(1): 259-66.
7. Maher D, Raviglione M. Global epidemiology of tuberculosis. Clinics in Chest Medicine, 2005 Jun 1; 26(2): 167-82.
8. Nyarko RO, Prakash A, Kumar N, Saha P, Kumar R. Tuberculosis a globalized disease. Asian Journal of Pharmaceutical Research and Development, 2021 Feb 15; 9(1): 198-201.
9. Doherty AM, Kelly J, McDonald C, O'Dywer AM, Keane J, Cooney J. A review of the interplay between tuberculosis and mental health. General hospital psychiatry, 2013 Jul 1; 35(4): 398-406.
10. Murray JF. A century of tuberculosis. American journal of respiratory and critical care medicine, 2004 Jun 1; 169(11): 1181-6.
11. Sumartojo E. When tuberculosis treatment fails. Am Rev Respir Dis., 1993; 147(1311): e20.
12. Cohn DL, Bustreo F, Raviglione MC. Drug-resistant tuberculosis: review of the worldwide situation and the WHO/IUATLD global surveillance project. Clinical infectious diseases, 1997 Jan 1; 24(Supplement_1): S121-30.
13. Leung AN. Pulmonary tuberculosis: the essentials. Radiology, 1999 Feb; 210(2): 307-22.
14. McCray E, Weinbaum CM, Braden CR, Onorato IM. The epidemiology of tuberculosis in the United States. Clin Chest Med, 1997; 18: 99–113.
15. Haas DW. Mycobacterium tuberculosis. In: Mandell GL, Bennett JE, Dolin R, eds. Principles and Practice of Infectious Diseases, 5th ed. New York, Churchill-Livingstone, 2000; 2576–2607.