A REVIEW ON PATHOPHYSIOLOGY AND TREATMENT OF TUBERCULOSIS

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ABSTRACT

A hypersensitive granulomatous infectious illness that mainly affects the lungs is tuberculosis. More than one-third of the world's population today has tuberculosis, which is caused by the bacteria Mycobacterium tuberculosis (M. tuberculosis), which is also the disease's etiological agent. Therefore, it is important for society or the general public to be aware of T.B., its pathophysiology, and accessible therapies. According to pathophysiology, illness results from an organ's or body's function being abnormal or changing in an animal or human. Infections are spread from person to person by aerosolized droplets of bacteria. To effectively treat tuberculosis, several antibiotics, including isoniazid, rifampicin, pyrazinamide, and ethambutol, must be administered over an extended period. Antibiotic resistance is consequently becoming more and more of a problem in infections with MDR TB (multidrug-resistant tuberculosis). This review's main emphasis is on how to identify the pathology, research it, and choose the most appropriate course of action. It can be diagnosed with PPD, IGRA, sputum testing, X-rays, and biopsies. Antibiotics are often preferred for the initial course of treatment.

Keywords: Tuberculosis, Pathophysiology, Diagnosis, Treatment, Antibiotics, etc.

I. INTRODUCTION

Mycobacterium tuberculosis infections, often known as tuberculosis, are characterized by a concerted interaction of pathogenic and physiological processes. M. tuberculosis has evolved to flourish by invading a host and staying there for an extended period, exploiting the host's immune system. M. tuberculosis is an internal pathogenic bacterium that divides its cells once every 18 to 24 hours, has a mycolic acid coating, and is not mobile. The illness produced by M. tuberculosis is known as tuberculosis. [1-2]

This illness affects 1.7–2 billion people globally and kills over 4,000 individuals per day, amounting to 1.2–1.5 million deaths annually. [1-5] In fact, immunocompromised people, such as those who are co-infected with the human immunodeficiency virus (HIV), might experience the emergence of dormant mycobacteria (active TB). There are over 38 million people living with HIV, and they are at an 18-fold greater risk of contracting tuberculosis than HIV-negative individuals. [6-8] The TB epidemic appears to have continued unabated since its discovery and has spread to every country in the world. One of the leading causes of death globally and a disease spread through the air, TB is extremely contagious. Even though the illness most frequently affects the lungs (pulmonary TB), it can also spread to other sections of the body (extrapulmonary TB). [9]

Africa and Asia have the highest rates of TB infections. In 2011, India, China, South Africa, Indonesia, and Pakistan recorded the highest number of cases. China and India together accounted for 12% and 26% of all cases worldwide, respectively. Around 1.2 million of the 8.7 million TB incidence patients reported in 2011 also have HIV. 39% of TB cases in the African region are thought to also have HIV. Oropharyngeal and intestinal TB caused by consuming dairy milk contaminated with M. bovis is uncommon today and mostly occurs in nations with dairy cows that are infected with tuberculosis and unpasteurized milk. [10]

II. ETIOLOGY OF TUBERCULOSIS

Mycobacterium tuberculosis-most common cause Other than tuberculosis-includes:

- M. aviumintracellulare
- M. kansasii
- M. scrofulaceum
- M. marinum
M. ulcerence
M. fortuitum
M. chelonel

Sites involved:

a. Pulmonary tb-85% of all TB cases
b. Extra pulmonary sites
c. Lymph node

d. Genitourinary tract
e. Bones & joints
f. Meninges
g. Intestine
h. Skin

Characteristics of Mycobacterium Tb:

a. Rod shape, 0.2-0.5 in D, 2-4 in L
b. Mycolic acid present in its cell wall, makes it acid fast,
c. So it resists decolourization with acid & alcohol.
d. Aerobic and non-motile.
e. Multiplies slowly.
f. Can remain dormant for decades.

How is TB Transmitted:

a. Person-to-person through the air by a person with active TB disease of the lungs
b. Less frequently transmitted by
1. Ingestion of Mycobacterium bovis found in unpasteurized milk products or auto ingestion
2. Inoculation (in skin tuberculosis).
3. Trans placental route (rare route).

III. SIGNS AND SYMPTOMS OF TB

The clinical manifestations of active pulmonary TB may include pleuritic chest pain, low-grade fever, prolonged productive cough, haemoptysis, fatigue, loss of appetite, night sweat and weight loss.[11-12]
**Diagnosis of Tuberculosis:**

Clinical Clues [26]
- Cough > 2 weeks
- Fever > 2 weeks
- Exposure to TB
- Chronic immune suppression
- Endemic country
- Abnormal physical exam

**Pathophysiology of Tuberculosis:**

1. M. tuberculosis starts hypersensitivity immune reaction inside the lung which damages the lung tissue while killing the foreign microorganism. [13]
2. Pathologic manifestation of tuberculosis like caseating granuloma and cavitation are result of hypersensitivity that develops in concert with the protective host immune response.[13]
3. Macrophages are the primary cells infected by M. tuberculosis.[13]

![Figure No. 2: Seven Steps in the Pathophysiology of Active Tuberculosis. [21]](image)

This figure demonstrates the pathophysiology of active tuberculosis. These steps are aerosolization, macrophage phagocytosis, phagolysosome blockage and replication, TH1 response, granuloma formation, clinical manifestations, and transmission. [21]

(A) Aerosolization marks the start and finish of the TB pathophysiology cycle. While a person with active tuberculosis aggressively expires, such as while coughing, aerosolization happens. [14]

B) Monocytes, dendritic cells, and macrophages will be present in the alveolar sacs of a susceptible person who inhales aerosolized Mycobacterium tuberculosis and droplets small enough to fit there (seen in the first magnification). The macrophages will try to eliminate the invader by phagocytosing the bacteria (shown in the second magnification). T-helper cells will be activated by dendritic cells when they travel to lymph nodes. [2,15,16]

C) M. tuberculosis stops the fusion of the phagolysosome, avoids being destroyed, starts to replicate, and releases lipids, DNA, RNA, proteases, and other substances. Vascular endothelial growth factor (VEGF) and cytokines will

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also be released by the macrophages. Angiogenesis will be sparked by VEGF, increasing vascularization around the lesion. Natural killer (NK) cells, dendritic cells (DC), neutrophils, and macrophages will all be recruited by the cytokines to start the innate response. [17-18]

D) The immunological response is mediated by TH1 cells. This response comprises stimulating effector T cell populations, activating the endothelium, and—most importantly for granulomas—using interferon gamma (IFN) and the CD40 ligand to stimulate macrophages. [19]

E) The TH1 response’s IFN will lead the macrophages to create nitric oxide through nitric oxide synthase, mature their phagolysosomes, and trigger autophagy. [15] TNF alpha (TNF) will be released by the activated macrophages because they are no longer able to get rid of the pathogen. To contain M. tuberculosis, TNF stimulates the development of monocytes into epithelioid histiocyte cells, which create caseating granulomas. [20]

F) Immune compromise, either recent or current, inhibits the granuloma from holding the germs. The bacteria will grow and spread across a variety of clinical symptoms. [19-20] (G) During this stage, the initially vulnerable, now-infected host has the ability to aerosolize the germs and restart the cycle. [21]

IV. TREATMENT OF TUBERCULOSIS

First Line Anti-TB Drugs:
First-line medications like isoniazid (INH), rifampicin (RIF), pyrazinamide (PZA), and ethambutol (EMB) are typically used in a standard chemotherapeutic regimen for the treatment of tuberculosis (TB) during an initial 2-month phase, followed by a continuation phase with INH and RIF for 4 months (Table 2). Due to increasing rates of resistance, the bactericidal antibiotic streptomycin, which affects polypeptide synthesis, is no longer regarded as a first-line treatment. [22-23]

Second Line Anti-TB Drugs:
When treating TB under unique circumstances like extensively drug-resistant tuberculosis (XDR-TB) or multidrug-resistant tuberculosis (MDR-TB), second-line medications are frequently utilized. In (Table 3), various kinds of second-line medicines (SLDs) used to treat TB are listed. The second-line medications differ from the first-line medications in that they might be less effective (like p-amino salicylic acid) or might have hazardous side effects (like cycloserine) or might not be available in many developing nations (like fluoroquinolones). [23-24]

Antibiotics used to treat “TBs” of all kinds. [10]
- Rifampicin.
- Rifabutin.
- Ciprofloxacin.
- Amikacin.
- Ethambutol.
- Streptomycin.
- Clarithromycin.
- Azithromycin.

Table No. 1. Adverse reactions of commonly used Anti-TB drugs.[25]
Pyrazinamide

- Joint aches, Hepatitis,
- Rashes, Stomach upset,
- Gout (rarely)
- Avoid in pregnancy
- Disruption of Mycobacterium tuberculosis membrane transport and energetics by pyrazinonic acid.

Ethambutol

- Visual Problems
- Should not be used in young children whose vision can’t be tested unless there is drug resistant TB
- Inhibit Arabinosyl transferase-III enzyme thus cause disruption of microbial cell wall formation.

V. CONCLUSION

Tuberculosis (TB) is an infectious disease caused by the bacillus Mycobacterium tuberculosis (M-Tb). Tuberculosis is a chronic granulomatous infectious disease. Infection occurs via aerosol and the inhalation of a few droplets containing M. tuberculosis bacilli. Most cases of TB are pulmonary and acquired by person-to-person transmission of airborne droplets of organisms. It can be diagnosed by PPD, IGRA, sputum studies, X-rays, and biopsies. Some antibiotics, such as Isoniazid (INH), Rifampicin, Pyrazinamide (PZA), Ethambutol are therapeutically used.

VI. REFERENCES

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