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Tuberculosis

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ABSTRACT

Tuberculosis is a bacterial infection, which is the dominant cause of death all over the world. It is the chronic infectious disease caused by the tubercle bacillus. It is regarded as oldest disease. Tuberculosis is the infection occurs by inhaling the droplet nuclei containing Mycobacterium tuberculosis organisms by susceptible person. New methods have been evolved in diagnosing, treatment and prevention. The disease remains as an important public health problem in developing countries. Extra pulmonary TB became more common with the advent of infection with human immunodeficiency virus and by the increase in the number of organ transplantation, which also leads to immunosuppression of thousand of persons. Urogenital TB represents 27% of extrapulmonary cases. Renal involvement in TB can be part of a disseminated infection or a localized genitourinary disease. Renal involvement by TB infection is underdiagnosed in most health care centers. Most patients with renal TB have sterile pyuria, which can be accompanied by microscopic hematuria. The diagnosis of urinary tract TB is based on the finding of pyuria in the absence of common bacterial infection. The first choice drugs include isoniazide, rifampicin, pirazinamide, ethambutol, and streptomycin. Awareness of renal TB is urgently needed by physicians for suspecting this disease in patients with unexplained urinary tract abnormalities, mainly in those with any immunosuppression and those coming from TB-endemic areas.

Keywords: Tuberculosis, Micobacterium Tuberculosis, Discover, Symptoms, Type, Diagnosis, Treatment.

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INTRODUCTION

TB is a contagious disease that is transmitted from person to person through coughing and breathing in airborne droplets that contain bacteria. TB primarily affects the lungs, but can affect any part of the body. As one of the most common infections in the world, TB remains a major problem in many countries and among vulnerable populations

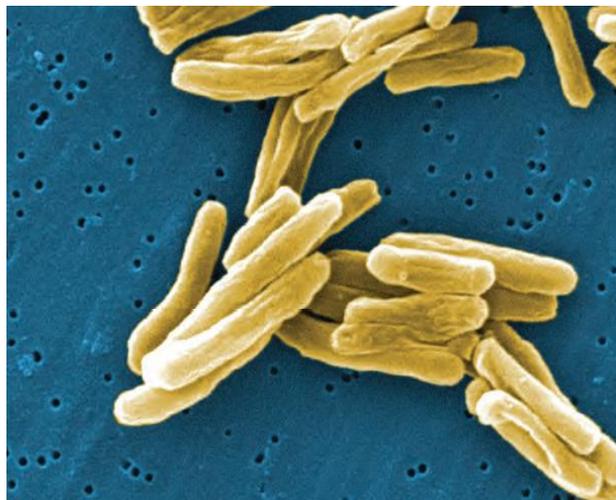


Figure: Micobacterium Tuberculosis

Tuberculosis (TB) is known to be recorded as one of the oldest form of human disease. Accordingly it's known to be the major reason for mortality of nearly two million people each year. In spite of the effective treatment strategies, the disease still remains to be the major cause of death among the different curable infectious diseases]. TB could be seen through different instances like it can affect the bones, the nervous system or many other organ systems, but basically it's characterized as pulmonary disease which occurs due to accumulation of Mycobacterium tuberculosis (MTB) onto the lungs alveolar surfaces. Mycobacterium tuberculosis is a constrained pathogenic bacterial species which belong to the family of mycobacteriaceae first discovered by Robert Koch in 1882. It is the chronic infectious disease caused by the tubercle bacillus]. It can form acid stable complexes made up of peptidoglycan. It mainly infects the lungs of humans.^[2] There are many methods to diagnose the tuberculosis among them tuberculin skin test, acid-fast stain, and chest radiographs are commonly used to detect the mycobacterium pathogen. Tuberculosis (TB) is one of the major public health threats, competing with the human immunodeficiency virus (HIV) as the cause of death due to infectious diseases worldwide. Although a declining trend in TB incidence, prevalence and mortality has been observed over the last decade, elimination of the disease at global level is still out of reach, and massive resource investment is still required.^[3]

Discovered:

Robert Koch, a German physician and scientist, presented his discovery of *Mycobacterium tuberculosis*, the bacterium that causes tuberculosis (TB), on the evening of March 24, 1882. He began by reminding the audience of terrifying statistics: "If the importance of a disease for mankind is measured by the number of fatalities it causes, then tuberculosis must be considered much more important than those most feared infectious diseases, plague, cholera and the like. One in seven of all human beings dies from tuberculosis. If one only considers the productive middle-age groups, tuberculosis carries away one-third, and often more."

Symptoms:

The bacterium that causes TB is called *Mycobacterium tuberculosis*. Inactive tuberculosis means that one can even unconsciously and unknowingly acquire the bacteria for tuberculosis within them but not even know about it because it is *inactive*. Whereas, active tuberculosis is the start of the bacteria developing, and the signs and symptoms begin to be visible. This is when tuberculosis is *active* within you, and is a serious issue leading to even more serious results. Although the TB bacteria can infect any organ (e.g., kidney, lymph nodes, bones, joints) in the body, the disease commonly occurs in the lungs.^[3] Around 80% of all TB cases are related to pulmonary or lung.^[5]

Common symptoms include:

Coughing that lasts longer than 3 weeks with green, yellow, or bloody sputum

Weight Loss

Fatigue

Fever

Night Sweats

Chills

Chest Pain

Shortness of Breath

Loss of Appetite

Stage:

As discussed in the earlier section most of the TB infection is pulmonary. This could be because of the use of the use of pasteurized milk in the modern times. In record to the studies carried out in 1978, 85% of the registered TB cases are diagnosed to be pulmonary. Since mostly all the cases of TB follows a general pattern, it was divided into four different stages by Wallgren.

Stage 1:

This stage is dated to be after 3-8 weeks of the inhaled MTB infected aerosol which becomes implanted on the alveoli surface. This occurs when the bacteria dissimilates from the lymphatic circulation system to regional lymph nodes which leads to the formation of the Ghon-complex. This aids to the conversion of tuberculin reactivity.

Stage 2:

During this stage the hematogenesis of bacteria to different organs and also different areas of the lungs occurs. During this time some acute or fatal diseases like tuberculosis meningitis or military tuberculosis occurs to some individuals. This stage nearly lasts for a period of about 3 months.

Stage 3:

The identification of this stage is characterized by the onset of Pleurisy or inflammation of the pleural surfaces along with severe chest pains. These stage last for a period of about 3-7 months but can also be prolonged to about 2 years. The inflammation is thought to be due to the dissipation of bacteria to the pleural surfaces from subpleural areas. These free circulating bacteria interact with the sensitized CD4 T lymphocytes, thus leading to its proliferation and release of inflammatory cytokines.

Stage 4:

The last stage is the liquefaction of the primary complex which is accompanied with the slow development of the extra pulmonary lesions like those on bones and joints.

In most cases the individuals infected with the TB do not exhibit disease progression. This indicates that normally an individual infected with TB will have MTB in the body but the immune system of the individual keeps the bacteria under control by the production macrophages against these bacteria.^{[6][7]}

Type:

Tuberculosis(TB) is divided into two categories: pulmonary and extrapulmonary.

Pulmonary Tuberculosis Types:

Primary Tuberculosis Pneumonia

Tuberculosis Pleurisy

Cavitary Tuberculosis

Miliary TB

Laryngeal Tuberculosis

Primary Tuberculosis Pneumonia:

This **uncommon type** of TB presents as pneumonia and is **very infectious**. Patients have a high fever and productive cough. It occurs most often in extremely young children and the elderly. It is

also seen in patients with immunosuppression, such as people with HIV/AIDS, and in patients on long term corticosteroid therapy.

Tuberculosis Pleurisy:

This usually develops soon after initial infection. A granuloma located at the edge of the lung ruptures into the pleural space, the space between the lungs and the chest wall. Usually, a couple of tablespoons of fluid can be found in the pleural space.

Once the bacteria invade the space, the amount of fluid increases dramatically and compress the lung, causing shortness of breath (dyspnea) and sharp chest pain that worsens with a deep breath (pleurisy). A chest x-ray shows significant amounts of fluid. Mild- or low-grade fever commonly is present. Tuberculosis pleurisy generally resolves without treatment; however, two-thirds of patients with tuberculosis pleurisy develop active pulmonary TB within 5 years.^[8]

Cavitary TB:

Cavitary TB involves the upper lobes of the lung. The bacteria cause **progressive lung destruction** by forming cavities, or enlarged air spaces. This type of TB occurs in reactivation disease. The upper lobes of the lung are affected because they are highly oxygenated (an environment in which *M. tuberculosis* thrives). Cavitary TB can, rarely, occur soon after primary infection.

Symptoms include productive cough, night sweats, fever, weight loss, and weakness. There may be hemoptysis (coughing up blood). Patients with cavitary TB are highly contagious. Occasionally, disease spreads into the pleural space and causes TB empyema (pus in the pleural fluid).^[9]

Miliary TB:

Miliary TB is disseminated TB. "Miliary" describes the appearance on chest x-ray of very small nodules throughout the lungs that look like millet seeds. Miliary TB can occur shortly after primary infection. The patient becomes **acutely ill** with high fever and is in danger of dying. The disease also may lead to chronic illness and slow decline.

Symptoms may include fever, night sweats, and weight loss. It can be difficult to diagnose because the initial chest x-ray may be normal. Patients who are immunosuppressed and children who have been exposed to the bacteria are at high risk for developing miliary TB.

Laryngeal TB:

TB can infect the **larynx, or the vocal chord area**. It is extremely infectious.

Extrapulmonary Tuberculosis:

This type of tuberculosis occurs primarily in **immune compromised patients**.

Lymph Node Disease

Tuberculosis Peritonitis

Osteal Tuberculosis

Renal Tuberculosis

Adrenal Tuberculosis

Tuberculosis Meningitis

Lymph Node Disease:

Lymph nodes contain macrophages that capture the bacteria. Any lymph node can harbor uncontrolled replication of bacteria, causing the lymph node to become enlarged. The infection can develop a fistula (passageway) from the lymph node to the skin.

Tuberculosis Peritonitis:

M. tuberculosis can involve the outer linings of the intestines and the linings inside the abdominal wall, producing increased fluid, as in tuberculosis pleuritis. Increased fluid leads to **abdominal distension and pain**. Patients are moderately ill and have fever.

Tuberculosis Pericarditis;

The **membrane surrounding the heart** (the pericardium) is affected in this condition. This causes the space between the pericardium and the heart to fill with fluid, impeding the heart's ability to fill with blood and beat efficiently.

Osteal Tuberculosis:

Infection of any bone can occur, but one of the most common sites is the spine. **Spinal infection** can lead to compression fractures and deformity of the back.

Renal Tuberculosis:

This can cause asymptomatic pyuria (white blood cells in the urine) and can spread to the reproductive organs and affect reproduction. In men, epididymitis (inflammation of the epididymis) may occur.

Adrenal Tuberculosis:

TB of the adrenal glands can lead to adrenal insufficiency. **Adrenal insufficiency** is the inability to increase steroid production in times of stress, causing weakness and collapse.

TB Meningitis:

M. tuberculosis can infect the meninges (the main **membrane surrounding the brain and spinal cord**). This can be devastating, leading to permanent impairment and death. TB can be difficult to discern from a brain tumor because it may present as a focal mass in the brain with focal neurological signs.

Headache, sleepiness, and coma are typical symptoms. The patient may appear to have had a stroke.^{[10][11]}

What is the difference between latent TB and active TB?

Although your body may harbour the bacteria that cause tuberculosis, your immune system can help prevent you from getting sick. To distinguish between latent TB and active TB:

Latent TB refers to the condition when you have a TB infection but the bacteria remains inactive in your body and causes no symptoms. Latent TB isn't contagious but has a chance of becoming active.

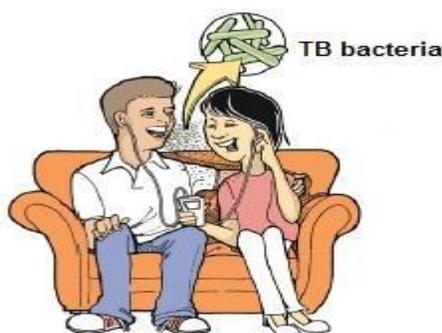
Active TB is when the TB bacteria multiply in your body, causing you to develop the symptoms of tuberculosis. If your lungs get infected with active TB, you can easily spread the disease to others.

Who gets TB infection and TB disease?

People who are more likely to acquire **TB infection** are the following: (1) People recently exposed to someone who has symptomatic TB disease; (2) People who live in congregate settings with high risk persons; (3) People who live or have lived in countries where TB is common; or (4) People who are health care workers who are in contact with TB patients when proper infection control procedures are not followed. Many people who acquire TB infection do not have symptoms and may never develop TB disease. These people have **latent TB infections (LTBI)**. However, people with TB infection who have weaker immune systems due to diabetes, HIV infection, kidney failure, or take certain immunosuppressive medications such as TNF-alpha blockers may be more likely to develop active **TB disease** with symptoms.^[12]

Transmission

Infection with TB bacteria almost always happens from inhalation of tiny droplets of moisture (droplet nuclei) that contain TB bacteria. People with active respiratory TB disease (TB in the lungs or airways) expel TB bacteria when they cough, sneeze, laugh, sing, or play wind instruments. People with laryngeal TB disease (TB laryngitis) can expel TB bacteria when they talk.^[13]



Transmission of tuberculosis

To a large degree, a person's risk for becoming infected with TB bacteria during an exposure to an infectious case depends on the concentration of TB bacteria in the air s/he breathes. This concentration is influenced by:

How infectious the case is.

The degree of air circulation and ventilation.

Whether the person is appropriately protected against inhaling TB bacteria (e.g., wearing a

How close (physical proximity) the person is to the infectious case.

fit-checked, disposable N95 respirator).

How infectious a case is (the degree of infectiousness) is influenced by:**Site and extent of TB disease;**

Cases with laryngeal involvement and/or cavities on their chest x-rays are considered highly infectious before treatment. Cases with sputum-smear positive/culture-positive pulmonary TB are considered relatively more infectious before treatment than smear- negative/culture-positive cases. Cases with non-respiratory TB disease are not infectious under most circumstances.

Strength and frequency of coughing and other behaviors/activities that produce infectious droplet nuclei;

Forceful expiration (e.g., coughing, sneezing, singing, playing wind instruments) can cause TB bacteria to be released into the surrounding airspace, as can certain medical procedures (e.g., sputum induction, bronchoscopy, autopsy, high- pressure wound irrigation of a non-respiratory site of TB disease). TB transmission has also been linked to smoking crack cocaine or marijuana

Pathogen factors;

Some strains of TB bacteria might be more transmissible. Other factors that can influence the risk of transmission include: ^{[14][15]}

Frequency and duration of exposure(s) to the case.

Susceptibility of the exposed person; people with pre-existing TB infection, such as those with LTBI or a history of TB disease, might have some innate immunity to reinfection.

Table: 4-1 summarizes factors that can increase the risk of transmission from cases to contacts.

Risk Factors for Infection with TB Bacteria

Groups at increased risk for being infected with TB bacteria include: Known contacts to infectious cases (TB contacts) Canadian-born elderly people (related to risk for exposure when TB disease was more prevalent in Canada)

Foreign-born immigrants, refugees, students, and visitors from countries where TB is prevalent. TB incidence of specific countries is available from WHO, Canadian-born Aboriginal peoples from communities with high rates of TB Staff and residents of congregate settings, particularly those that house persons from the risk groups mentioned above, such as correctional facilities and shelters for the homeless/under-housed Staff of facilities where people with undiagnosed active TB disease could present for care (e.g., acute care hospitals)

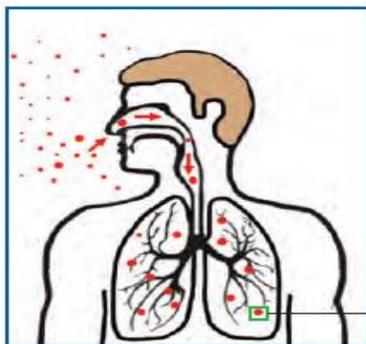
Some travelers to countries where TB is prevalent ^[16]

Pathogenesis of TB

Infection occurs when a person inhales droplet nuclei containing tubercle bacilli that reach the alveoli of the lungs. These tubercle bacilli are ingested by alveolar macrophages; the majority of these bacilli are destroyed or inhibited. A small number may multiply intracellular and are released when the macrophages die. If alive, these bacilli may spread by way of lymphatic channels or through the bloodstream to more distant tissues and organs (including areas of the body in which TB disease is most likely to develop: regional lymph nodes, apex of the lung, kidneys, brain, and bone).^[17] This process of dissemination primes the immune system for a systemic response. Further details about pathogenesis of latent tuberculosis infection (LTBI) and TB disease are described in Figure 2.

Pathogenesis of LTBI and TB Disease

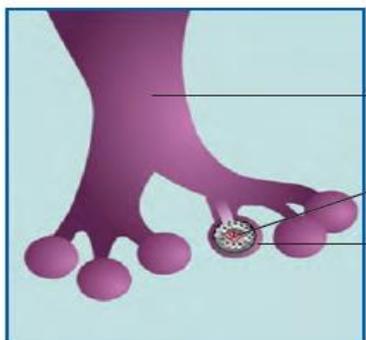
1.



Area of detail for boxes 2, 4, and 5

Droplet nuclei containing tubercle bacilli are inhaled, enter the lungs, and travel to the alveoli.

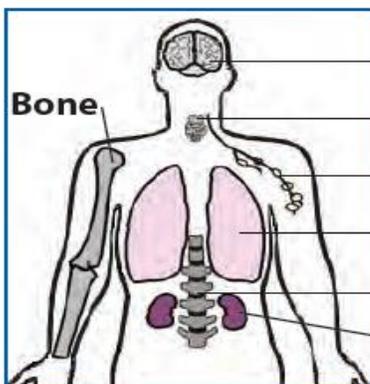
2.



Bronchiole
Tubercle bacilli
Alveoli

Tubercle bacilli multiply in the alveoli.

3.



Brain
Larynx
Lymph node
Lung
Spine
Kidney
Bone

A small number of tubercle bacilli enter the bloodstream and spread throughout the body. The tubercle bacilli may reach any part of the body, including areas where TB disease is more likely to develop (such as the brain, larynx, lymph node, lung, spine, bone, or kidney).

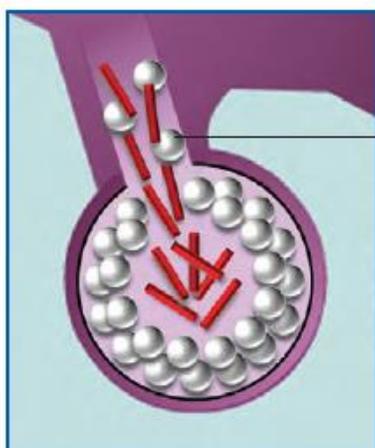
4.



Special immune cells form a barrier shell (in this example, bacilli are in the lungs)

Within 2 to 8 weeks, special immune cells called macrophages ingest and surround the tubercle bacilli. The cells form a barrier shell, called a granuloma, that keeps the bacilli contained and under control (LTBI).

5.



**Shell breaks
down and
tubercle
bacilli escape
and multiply**

If the immune system **cannot** keep the tubercle bacilli under control, the bacilli begin to multiply rapidly (**TB disease**). This process can occur in different areas in the body, such as the lungs, kidneys, brain, or bone (see diagram in box 3).

Figure 2: Pathogenesis of LTBI and TB Disease

How is TB diagnosed?

- Bacteriological confirmation
 - Sputum smear microscopy
 - Culture
- Non-bacteriological
 - Symptom screen
 - TST or Mantoux or PPD
 - Chest X-ray
 - Diagnostic algorithm

How is TB treated?

Treatment of **latent TB infection** consists of 1 or 2 oral medications that kill the bacteria and greatly reduces the risk of the infection progressing to TB disease immediately and later in life. There are several treatment options that include isoniazid taken daily for six to nine months, rifampin taken daily for 3 to 4 months or isoniazid plus rifapentine taken once weekly for 12 weeks. If you have or are at risk for liver disease, your doctor may need to follow your liver blood tests to ensure these medications do not cause any harm.

TB disease is usually treated with 4 anti-TB medications for at least six months.^[18] If TB is in the bones, brain or other hard-to-reach areas, treatment will be longer. This can mean taking 6-12 pills per day! Many patients find this difficult without the support of workers trained in providing directly observed treatment (DOT). DOT is the universal standard for treating TB worldwide. DOT helps detect side effects early and prevents missed doses and breaks in treatment that reduce the benefit of treatment and can lead to drug-resistant strains of bacteria.

PREVENTION OF TUBERCULOSIS:

Control programmes that is the NATIONAL TUBERCULOSIS PROGRAM(NTP) district Tuberculosis Programme (DTP) must be adapted to the need of community. These are often limited by financial allocations.

Raising the resistance of the population to the disease by :

- a) Good social conditions including satisfactory housing and an adequate diet
- b) BCG (bacille calmette Guerin) vaccination: BCG vaccination is usually performed by intradermal injection of 0.05 ml or 0.1 ml of the vaccine, just after birth or with the first dose of DPT vaccine respectively.

Reduction of the human infection by:

- a) Detection and isolation of maximum number of cases: It is required in cases giving history of persistent cough, continuous fever, chest pain and haemoptysis. This can be done by sputum examination mass miniature radiography and tuberculin test
- b) chemoprophylaxis: the chemoprophylaxis or preventive treatment is done by giving INH alone for one year or INH plus ethambutol for nine month.

Elimination of tuberculosis infection in milk:

Pasteurization kills the tubercle bacilli by heat while preserving the nutritive components of the milk with the exception of vit-c^{[19][20]}

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