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Tuberculosis: Current Diagnosis and Management

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Abstract

Tuberculosis is an airborne disease caused by the bacterium *Mycobacterium tuberculosis* (M. tuberculosis). *Mycobacterium tuberculosis* is carried in airborne particles, called droplet nuclei, of 1– 5 microns in diameter. Infectious droplet nuclei are generated when persons who have pulmonary or laryngeal TB disease cough, sneeze, shout, or sing. Depending on the environment, these tiny particles can remain suspended in the air for several hours. *Mycobacterium tuberculosis* is transmitted through the air, not by surface contact. Transmission occurs when a person inhales droplet nuclei containing *Mycobacterium tuberculosis*, and the droplet nuclei traverse the mouth or nasal passages, upper respiratory tract, and bronchi to reach the alveoli of the lungs. Tuberculosis (TB) is a major cause of morbidity and mortality worldwide. It is estimated that 25% of the world's population are infected with *Mycobacterium tuberculosis*, with a 5–10% lifetime risk of progression into TB disease. Early recognition of TB disease and prompt detection of drug resistance are essential to halting its global burden. Culture, direct microscopy, biomolecular tests and whole genome sequencing are approved methods of diagnosis; however, their widespread use is often curtailed owing to costs, local resources, time constraints and operator efficiency. TB disease most commonly affects the lungs; this is referred to as pulmonary TB disease. Patients with pulmonary TB disease usually have a cough and an abnormal chest radiograph, and may be infectious. Although the majority of TB cases are pulmonary, TB can occur in almost any anatomical site or as disseminated disease.

Keywords*: tuberculosis, current diagnosis, management*

introduction

TB is an airborne disease caused by the bacterium Mycobacterium tuberculosis (M.tuberculosis). M. tuberculosis and seven very closely related mycobacterial species (M. bovis, M. africanum, M. microti, M. caprae, M. pinnipedii, M. canetti and M. mungi) together comprise what is known as

the M. tuberculosis complex. Most, but not all, of these species have been found to cause disease in humans. Tuberculosis organisms are also called tubercle bacilli.[1-6] Tuberculosis (TB) is a major cause of morbidity and mortality worldwide. TB is caused by the bacillus *Mycobacterium tuberculosis (Mtb*), which is spread *via* airborne droplets. Approximately one in four people worldwide demonstrate an immunological response to *Mtb* infection, which can remain dormant or progress into active disease forms. Patients infected with TB who have no active signs or symptoms of disease were previously deemed to have latent TB, more recently changed to TB infection. Whereas patients with active disease are termed to have TB disease. Patients with TB infection have a 5–10% lifetime risk of developing TB disease, which increases in varying states of immunodeficiency up to a 16% annual risk of activation of TB infection into TB disease in HIV patients.[7-12]

Tuberculosis generally affects the lungs, but it can also affect other parts of the body. Most infections show no symptoms, in which case it is known as latent tuberculosis. Around 10% of latent infections progress to active disease which, if left untreated, kill about half of those affected. Typical symptoms of active TB are chronic cough with blood-containing mucus, fever, night sweats, and weight loss. It was historically referred to as consumption due to the weight loss associated with the disease. Infection of other organs can cause a wide range of symptoms.[13-17]

Tuberculosis is spread from one person to the next through the air when people who have active TB in their lungs cough, spit, speak, or sneeze. People with latent TB do not spread the disease. Active infection occurs more often in people with HIV/AIDS and in those who smoke. Diagnosis of active TB is based on chest X-rays, as well as microscopic examination and culture of body fluids. Diagnosis of Latent TB relies on the tuberculin skin test (TST) or blood tests. Prevention of TB involves screening those at high risk, early detection and treatment of cases, and vaccination with the bacillus Calmette-Guérin (BCG) vaccine.[18-23] Those at high risk include household, workplace, and social contacts of people with active TB. Treatment requires the use of multiple antibiotics over a long period of time. Antibiotic resistance is a growing problem, with increasing rates of multiple drug-resistant tuberculosis (MDR-TB).[24]

Tuberculosis

Tuberculosis (TB) is an infectious disease that most often affects the lungs and is caused by a type of bacteria. It spreads through the air when infected people cough, sneeze or spit. About a quarter of the global population is estimated to have been infected with TB bacteria. About 5–10% of people infected with TB will eventually get symptoms and develop TB disease. A total of 1.6 million people died from TB in 2021 (including 187 000 people with HIV). Worldwide, TB is the 13th leading cause of death and the second leading infectious killer after COVID-19 (above HIV and AIDS). In 2021, an estimated 10.6 million people fell ill with tuberculosis (TB) worldwide. Six million men, 3.4 million women and 1.2 million children. TB is present in all countries and age groups. But TB is curable and preventable. Multidrug-resistant TB (MDR-TB) remains a public health crisis and a health security threat. Only about 1 in 3 people with drug resistant TB accessed treatment in 2021.[25-28]

Transmission of TB, M. tuberculosis is carried in airborne particles, called droplet nuclei, of 1– 5 microns in diameter. Infectious droplet nuclei are generated when persons who have pulmonary or laryngeal TB disease cough, sneeze, shout, or sing. Depending on the environment, these tiny particles can remain suspended in the air for several hours. M. tuberculosis is transmitted through the air, not by surface contact. Transmission occurs when a person inhales droplet nuclei containing M. tuberculosis, and the droplet nuclei traverse the mouth or nasal passages, upper respiratory tract, and bronchi to reach the alveoli of the lungs.[29]

Factors that determine the probability of m. tuberculosis transmission

The transmission of Mycobacterium tuberculosis (M. tuberculosis), the bacterium that causes tuberculosis (TB), depends on various factors. TB is primarily transmitted from person to person through the air when an infectious individual with active TB disease coughs or sneezes, releasing respiratory droplets containing the bacteria. Several factors influence the probability of M. tuberculosis transmission.[30]

Infection of the index case

The degree of infectiousness of the person with active TB (the index case) plays a significant role. Individuals with higher bacterial loads in their respiratory secretions are more contagious. Factors such as the presence of cavities in the lungs and the extent of disease can also affect infectiousness.[31]

Duration of contact

The longer a susceptible individual is in close contact with an infectious person, the greater the risk of transmission. Prolonged exposure in confined spaces, such as households, healthcare settings, or crowded public places, increase likelihood of transmission.[32]

Ventilation and Air Exchange

Adequate ventilation and air exchange in indoor settings can help reduce the concentration of infectious droplets in the air. Poorly ventilated spaces can facilitate transmission, especially in crowded areas.[33]

Immune Status of contact

People with compromised immune systems, such as those with HIV infection or certain medical conditions (e.g., diabetes), are more susceptible to TB infection when exposed. Their weakened immune response may lead to a higher risk of progression to active disease.

Drug-Resistant Strains

The presence of drug-resistant strains of M. tuberculosis, such as multidrug-resistant TB (MDR-TB) or extensively drug-resistant TB (XDR-TB), can increase transmission risk, as these strains are more challenging to treat and may require longer periods of exposure to transmit.[34]

Behavioral Factor

Behaviors such as close contact with infectious individuals, substance abuse, and poor adherence to TB treatment regimens can contribute to transmission dynamics.

Geographic and socioeconomic

TB transmission can vary by geographic region and socioeconomic conditions. Factors such as poverty, overcrowding, and inadequate access to healthcare can facilitate transmission.[35]

HIV Coinfection

The presence of HIV/AIDS increases the risk of TB transmission, as HIV weakens the immune system and makes individuals more susceptible to TB infection and progression to active disease.

Pathogenesis of Tuberculosis

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 intracellularly 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). This process of dissemination primes the immune system for a systemic response.[36]

Stages of tb infections

TB infection can be manifest in different stages, depending on the infection between the bacterium and the host's immune system. There are three stages of Tb infection

Exposure

This happens when a person has been in contact with, or exposed to, another person who has TB. The exposed person will have a negative skin test, a normal chest X-ray, and no signs or symptoms of the disease.[32]

Latent TB Infection (LTBI)

In this stage, the bacteria are present in the body, but the immune system is able to control their growth and prevent the person from becoming sick. People with LTBI do not feel sick and cannot spread the disease to others. LTBI is typically diagnosed through a positive tuberculin skin test (TST) or interferon-gamma release assay (IGRA) blood test. While most individuals with LTBI do not progress to active TB disease, they are at risk of developing active TB if their immune system weakens, such as due to other illnesses or medications.[37]

Active TB Disease

This stage occurs when the immune system fails to control the growth of the TB bacteria, allowing them to multiply and cause symptoms. Active TB disease can affect the lungs (pulmonary TB) or other parts of the body (Extrapulmonary TB). Common symptoms of active TB include persistent cough, fever, night sweats, and weight loss. Active TB is contagious and can be spread to others through respiratory droplets when an infected person coughs or sneezes. Diagnosis is typically made through a combination of clinical evaluation, chest X-ray, Sputum or other bodily fluid tests, and sometimes molecular tests to identify the presence of the bacteria.[38]

Current diagnosis of tuberculosis

Improving the efficiency and accuracy of TB diagnosis contributes to treatment efficacy. Pulmonary TB should be suspected when patients present with classical symptoms such as non-resolving cough, haemoptysis, fevers, night sweats and weight loss. Extrapulmonary TB, including TB lymphadenitis, TB meningitis, laryngeal TB, Pott's disease and abdominal TB, presents in a variety of manners. Special consideration should always be given to patients who have potential TB exposure, as well as immunocompromised patients who may present atypically. The diagnosis must be made by confirming the presence of the causative pathogen, Mtb. A variety of methods are employed to confirm the diagnosis.[39]

Clinical Evaluation

A healthcare provider will start by taking a detailed medical history and conducting a physical examination. They will ask about symptoms, such as persistent cough, fever, night sweats, weight loss, and fatigue.[40]

Chest Radiograph

With pulmonary TB being the most common form of disease, the chest radiograph is useful for diagnosis of TB disease. Chest abnormalities can suggest pulmonary TB disease. A posterior-anterior radiograph of the chest is the standard view used for the detection of chest abnormalities. In some cases, especially in children, a lateral view may be helpful. Abnormalities seen on chest radiographs may be suggestive of, but are never diagnostic of, TB disease.[41]

Sputum Smear Microscopy

If TB is suspected, a sample of sputum (mucus coughed up from the lungs) may be examined under a microscope to check for the presence of acid-fast bacilli (AFB), which are characteristic of Mycobacterium tuberculosis, the bacteria that causes TB; This procedure is done for developing country where other machine for diagnosis of TB is absence.

Tuberculin Skin Tests

Tuberculin skin test and interferon-gamma release assay are currently recommended for the diagnosis of LTBI, but have a marginal role in the detection of TB cases, as they cannot distinguish between active and latent infection and may be influenced by the patient's immune status. This is an initial screening test that involves injecting a small amount of purified protein derivative (PPD)

under the skin, usually on the forearm. The site is then checked after 48-72 hours for a reaction. A positive reaction indicates exposure to TB but does not confirm active disease.[42]

Sputum culture

A sputum sample is cultured in a laboratory to grow and identify Mycobacterium tuberculosis. This is the definitive test for confirming TB and can also help determine drug susceptibility.[43]

Biopsy and Molecular Tests

In cases where TB may affect other parts of the body (extrapulmonary TB), a biopsy or other specific tests may be performed to confirm the diagnosis.[44]

GeneXpert MTB/RIF

This molecular diagnostic test can detect both TB and drug resistance to rifampicin, a key TB drug. It provides rapid results and is particularly valuable in regions with high rates of drug-resistant TB The World Health Organization (WHO) today recommended the use in all settings of a next-generation Xpert® MTB/RIF assay (called Xpert® MTB/RIF Ultra) as a replacement for the current Xpert MTB/RIF® cartridge. The Xpert MTB/RIF test for use with the Cepheid GeneXpert® System is a semi-quantitative nested real-time PCR in vitro diagnostic test for:

(1) the detection of Mycobacterium tuberculosis complex (MTB complex) DNA in sputum samples or concentrated sediments prepared from induced or expectorated sputa that are either acid-fast bacilli (AFB) smear positive or negative;

(2) the detection of rifampin resistance associated mutations of the rpoB gene in samples from patients at risk for rifampin resistance.[45]

Current management of tuberculosis

Anti-TB treatment aims to cure the patient, prevent complications and death, avoid relapses, reduce the transmission potential to susceptible individuals, and limit the emergence and spread of drug-resistant strains. The management of tuberculosis is divided into two phase

Initial phase

The initial phase of treatment is crucial for preventing the emergence of drug resistance and determining the ultimate outcome of the regimen. Four drugs

(i) Isoniazid (H)
(ii) Rifampin (R)
(iii) Pyrazinamide (Z)
(iv) Ethambutol (E)

Should be included in the initial treatment regimen until the results of drug-susceptibility tests are available. Each of the drugs in the initial regimen plays an important role. Isoniazid (H) and Rifampin (R)allow for short-course regimens with high cure rates. Pyrazinamide (Z) has potent sterilizing activity, which allows further shortening of the regimen from 9 to 6 months. Ethambutol (E) helps to prevent the emergence of RIF resistance when primary INH resistance is present. If drug-susceptibility test results are known and the organisms are fully susceptible, EMB need not be included. For children whose clarity or sharpness of vision cannot be monitored, EMB is usually not recommended except when the risk of drug resistance is high or for children who have "adult-type" (upper lobe infiltration, cavity formation) TB disease.

Continuation phase

The continuation phase of treatment is given for either 4 or 7 months. The 4-month continuation phase should be used in patients with uncomplicated, noncavitary, drug-susceptible TB, if there is documented sputum conversion within the first 2 months. The 7-month continuation phase is recommended only for • Patients with cavitary or extensive pulmonary TB disease caused by drug-susceptible organisms and whose sputum culture obtained at the time of completion of 2 months of treatment is positive; • Patients whose initial phase of treatment did not include PZA; or • Patients being treated with once-weekly INH and RPT and whose sputum culture at the time of completion of the initial phase (i.e., after 2 months) is positive

Completion treatment

Treatment completion is defined primarily as the ingestion of the total number of doses prescribed within the specified time frame. The duration of therapy depends on the drugs used, the drug susceptibility test results of the isolate, and the patient's response to therapy. Most patients with previously untreated pulmonary TB disease can be treated with either a 6-month or a 9-month regimen, although the 6-month regimen is used for the majority of patients. All 6-month regimens must contain INH, RIF, and initially, PZA. The goal is to complete all doses within 1 year.

Conclusion

The diagnosis and management of tuberculosis (TB) have evolved significantly over the years, with ongoing research and advancements in medical science. here are some key points regarding the current state of TB diagnosis and management. Early detection of TB remains the cornerstone of effective management. Various diagnostic tools such as molecular tests (e.g., PCR), radiological imaging, and the Mantoux tuberculin skin test are employed to identify TB infection. The Bacillus Calmette-Guérin (BCG) vaccine remains a vital tool in preventing severe forms of TB in children.

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