Tuberculosis: An Overview

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Purpose: To provide an overview of tuberculosis including its transmission, risk factors, signs and symptoms, diagnosis and treatment options.

Objectives

- List five risk factors for tuberculosis
- Discuss the use of the Mantoux test, QuantiFERON and chest x-ray in the diagnosis of tuberculosis
- List five signs and symptoms of tuberculosis
- Differentiate between latent and active tuberculosis
- Discuss treatment options for tuberculosis

Tuberculosis (TB) is caused by the bacteria *Mycobacterium tuberculosis*. The disease can affect any part of the body – such as the spine, brain and kidney - but it most commonly affects the lungs.

Public health efforts have significantly reduced the spread of the disease. TB is an airborne disease and is spread from person to person when respiratory droplets are breathed into the respiratory tract.

Latent vs. Active Tuberculosis
Latent TB is disease where one is infected with the bacteria but is not ill. Active TB is when disease is present, bacteria are growing and the patient has signs and symptoms of TB.

Latent TB occurs when the bacterium enters the body, but the immune response prevents the bacteria from proliferating. These individuals have a positive tuberculin skin test or a positive QuantiFERON blood test. Those with latent TB can progress to active TB. When the disease is in latency the individual cannot pass the disease on to others.

Active TB involves the proliferation of bacteria and symptoms suggestive of TB. Those with active TB can pass the disease to others.

Those who have latent TB are at risk to develop active disease. Five to 10 percent of untreated individuals with latent TB will develop symptoms at some point in their life (1). This often occurs when the immune system weakens such as if they develop cancer, HIV or go on corticosteroids.

Those with both active and latent disease typically have a positive skin tuberculin test and/or QuantiFERON blood test. Those with latent disease have a negative chest x-ray and no evidence of TB in the sputum. Those with active disease have a positive chest x-ray and evidence of tuberculosis growing in the sputum.

**Risk Factors**

Identifying who is at high risk to develop active disease is an important task of the nurse. Certain factors place individuals at high risk including:
• Individuals who immigrated from an area of the world with high TB rates including: South-East Asia and sub-Saharan Africa

• Close contact with individuals with infectious TB

• Individuals who live and work in prisons, homeless shelters and nursing homes

• Homelessness

• Injection drug users

• Those with weak immune systems such as individuals with human immunodeficiency virus (HIV), organ transplant, advanced renal disease, head or neck cancer, treatment with immunosuppressants or corticosteroids, diabetics, substance abusers or those with a low body weight

**Signs and Symptoms**

The types of signs and symptoms present depend on which area of the body is infected. Signs and symptoms may manifest shortly after infection or years later when their immune system weakens. The most commonly affected areas include the lungs and common signs and symptoms of pulmonary TB include:

• Chronic cough (longer than three weeks)

• Hemoptysis

• Chest pain
• Weight loss
• Night sweats
• Fever
• Weakness
• Fatigue
• Anorexia

When latent TB is present the individual is typically not ill and will have no symptoms.

**Diagnosis**

Multiple diagnostic modalities are used in the identification of tuberculosis. The most common initial method to evaluate for TB is the tuberculin skin test. This test uses a small needle to inject 5 tuberculin units of purified protein derivative. The test is read in 48-72 hours. A positive skin test indicates that there has been an infection at some point in the past – not that there is an active infection.

A skin test is positive at different sizes depending on the underlying issues with patients. The following individuals should be classified as a positive test if their Mantoux tuberculin skin test is more than 5 mm.

• HIV positive individuals
• Those who had an organ transplant
• Those taking more than 15 mg of prednisone per day for at least 30 days
• Those on TNF-alpha antagonists
• Recent close contact with a person with TB
• Chest x-ray that shows fibrotic changes suggestive of old TB

Those with a Mantoux tuberculin skin test of greater than or equal to 10 mm are considered to have a positive test if:

• They are injection drug users
• They immigrated from a high-prevalence country in the last five years
• They work in a laboratory with Mycobacterium
• They live or work in a nursing home, correctional facility, hospital or homeless shelter
• They are less than 4 years old
• They are children or adolescents who have had contact with adults in high-risk categories
• They have certain diseases or conditions (diabetes, end-stage renal disease, head or neck cancer, hematologic malignancies, jejunoileal bypass or gastrectomy) that put one at high risk
If none of the above criteria have been met, a test is classified as positive if the skin reaction is greater than or equal to 15 mm.

Another method to test for TB includes a blood test called a QuantiFERON-TB Gold test. This test is equally effective when compared to the tuberculin skin test in picking up infection. An advantage of the blood test is that a second appointment is not necessary like with the skin test. This test also only indicates that there has been infection in the past – not necessarily that the disease is active.

A chest x-ray should be used when there is a positive skin or QuantiFERON test. When a patient has a positive test no symptoms and a negative chest x-ray, the patient has latent TB.

When tuberculosis is present in the lungs the chest x-ray may mimic other conditions. The chest x-ray may show a patchy or nodular infiltrate in any part of the lung. The most common area of the infiltrate is the upper lobes of the lungs.

Checking the sputum for smear and culture is done in anyone thought to have TB. Sputum samples are taken on three consecutive days in the morning.

Blood tests that should be obtained in those with TB or suspected TB include a complete blood count, liver function tests (bilirubin, alkaline phosphatase, alanine aminotransferase and aspartate aminotransferase), kidney function and uric acid.
All patients who are positive for TB should be screened for HIV. Those who are at high risk for TB or those have close contact with TB should also be tested for HIV. HIV is one of the most important risk factors for latent TB to progress to active TB.

**Treatment**

In order to determine what type of treatment will be necessary to manage the disease it is important to label the disease. This section will break down treatment into latent disease, active disease and drug resistant tuberculosis.

Latent disease needs to be treated to prevent the progression of latent disease to active disease. Treatment is initiated after active disease has been ruled out. There is less bacteria present in latent TB than active disease and treatment is therefore less aggressive. Typically treatment only involves the use of one medication (usually isoniazid [INH] or rifampin). Individuals who have been exposed to multi-drug resistant TB or with contact to patients taking INH may need modification of therapy.

The long-term use of drugs to manage TB requires monitoring. INH increases the risk of liver problems. Prior to treatment with isoniazid or rifampin, baseline liver function tests should be carried out. Individuals with underlying liver pathology should be monitored closely for adverse reactions.

Active disease requires much more aggressive treatment. It involves multiple medications for 6-12 months. Compliance with therapy is a critical
point in the management of disease. Missing doses increases the risk of developing drug resistant TB.

Ninety to 95 percent of people infected with latent TB are able to prevent infection from progressing to active TB. This still leaves 5-10 percent of people with latent TB who will progress to active TB. Tuberculosis is a serious and infectious disease and it is critical to not allow this number of active cases. It is therefore essential to treat all cases of latent TB. Treatment for latent TB reduces the risk of active disease by 90% (1, 2). Treating infection before it becomes active is important because treatment of latent disease is much easier than treating active disease.

Patients who are treated for TB should work with the local health department and/or organizations within the community that can assure compliance with therapy. These programs can provide directly observed therapy for some high risk groups. They can offer case management to assure that therapy is completed as directed. Some organizations provide support in the form of incentives to provide motivation such as coupons and vouchers through local businesses.

The patient needs to understand the benefits and risks of treatment including side effects. The patient needs to be encouraged to adhere to therapy and a plan needs to be developed to assure compliance.

Active TB needs to be ruled out prior to initiating treatment for latent TB. Treatment strategies for latent TB include:
• Isoniazid which can be given as 900 mg twice a week for a total of 76 doses or 300 mg once a day for a total of 270 doses. The daily dosing regime is the preferred treatment. Individuals on INH should also take pyridoxine 50 mg daily to reduce the risk of neuropathy.

• INH given daily for 6 months or twice weekly for six months is another option with the daily treatment as the preferred treatment.

• Rifampin daily for 4 months can also be used.

INH is the preferred treatment for latent TB. Those less than 18 years-old and those with HIV should be treated for 9 months. Most cases of latent TB during pregnancy can be delayed until after delivery.

During treatment patients should be monitored on a routine basis to assure adherence as well as look for signs of toxicity from treatment. A common side effect is liver toxicity which is a higher risk in those who drink alcohol. INH should not be used in those with active liver disease.

Ten to 20 percent of individuals who take INH will have an increase in liver enzymes without any symptoms. Individuals who have an elevation of transaminases of three times the upper limit of normal in patients with symptoms and five times the upper limit of normal in those without symptoms should have the medication discontinued.
<table>
<thead>
<tr>
<th>Drug</th>
<th>Side effects</th>
<th>Drug interactions</th>
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<tbody>
<tr>
<td>Isoniazid</td>
<td>Hepatitis, peripheral neuropathy, agranulocytosis, thrombocytopenia, seizures, nausea, vomiting and epigastric discomfort</td>
<td>Increases levels of phenytoin and disulfiram</td>
</tr>
<tr>
<td>Rifampin</td>
<td>Orange discoloration of the urine and other body fluids, nausea, vomiting, fatigue, hepatitis, leukopenia, thrombocytopenia and agranulocytosis</td>
<td>Azole antifungals, some antiviral medications, protease inhibitors, acetaminophen, some cholesterol and blood pressure medications, corticosteroids, theophylline; decreases levels of oral contraceptives, methadone, sulfonylureas and warfarin</td>
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**Treatment of Drug Susceptible TB**

Initial treatment for TB should include the four drugs: isoniazid (INH), rifampin (RIF), ethambutol (EMB) and pyrazinamide (PZA). Sometimes streptomycin is substituted for ethambutol. The preferred regime includes an initial phase and a continuation phase. The initial phase includes two months of four drugs including INH, RIF, PZA and EMB. Than four months of daily IHN and RIF for 126 doses or twice weekly IHN and RIF for 36 doses.

An alternative regimen includes: daily IHN, RIF, PZA and EMB for 14 days than twice weekly for 12 doses than twice weekly IHN and RIF for 36 doses.
In all regimes EMB can be stopped if drug susceptibility labs show susceptibility to the first-line drugs.

Some individuals are candidates for longer treatment. Those who have a positive sputum culture after 2 months of treatment and/or cavitation on the initial chest film should have extended therapy.

**Monitoring**

During treatment of active TB the sputum should be examined microscopically every month until two back-to-back cultures are negative for TB. It is exceedingly important to determine if the patient has negative sputum after the first two months of therapy as this will affect the treatment options.

**Tuberculosis Disease and HIV**

Treatment for TB when HIV is present is similar to treatment without HIV, but there are some important points to note. Treatment of TB in HIV should be done in consultation with an expert in infectious disease.

Treatment should include two months of isoniazid (INH), a rifamycin (be careful with drug interactions), ethambutol (EMB) and pyrazinamide (PZA). After the first two months the INH and a rifamycin should be continued for 4 months.

Certain factors will affect treatment. It is important to monitor the CD4 count in those with HIV as CD4 counts less than 100 cells/mm$^3$ need to be treated with treatment three times a week or daily throughout treatment, but not twice weekly therapy. Twice a week therapy can be used in those with HIV and a CD4 count over 100 cells/mm$^3$, but once a week treatment should not be used in HIV.
Patients with TB should be treated for at least 6 months in the HIV positive patient and the treatment should be extended to 9 months in those who have a positive culture after 2 months of treatment.

**Drug-Resistant Tuberculosis**

Drug resistant TB is disease that does not respond to INH or RIF while multidrug-resistant TB does not respond to both INH and RIF. Those with drug resistant or multidrug resistant TB should be evaluated and treated by an infectious disease specialist.

Those with HIV pose a special problem for those with drug resistant TB as many of the antibiotics for treatment of TB interact with HIV medications. Those with HIV and TB should be managed by an infectious disease specialist.

The risk of developing drug resistant TB includes: living in areas where there is a lot of drug resistant TB, those born outside of the United States, having personal contact with drug-resistant TB, HIV co-infection, intravenous drug users, ethnic background that is not non-Hispanic white, those who have taken inappropriate therapy or did not complete the therapy as directed.

A new category of drug resistant TB has been called extensively drug resistant tuberculosis, which usually occurs when multi-drug resistant TB is not treated properly. It is resistance against both INH and rifampicin as well as resistance to any fluoroquinolone and at minimum one of the second-line medications to treat TB including: amikacin, capreomycin or kanamycin.
Vaccine

Bacille Calmette-Guerin vaccine (BCG) is the vaccine for TB. It is not routinely used in the United States but is used in other countries with a high prevalence of TB. Many of those born outside the United States may have been vaccinated for TB with the BCG vaccine. Two major drawbacks include: it has an unpredictable effect against adult pulmonary TB and it influences the results of the tuberculin skin test.

In the United States it is rare for an adult to be a candidate for the vaccine. Children who are persistently exposed and have a negative tuberculin skin test may be candidates for the vaccine. Some health care workers may also be candidates for vaccination. Those who are frequently exposed to multidrug resistant TB and infection is likely or when there is frequent transmission to health care workers despite all major prevention measures being implemented are candidates for vaccination after consultation with a TB expert.

Certain individuals should not be given the BCG vaccination. Those who are pregnant should not get the vaccine. Those who are immunosuppressed or those at high risk to become immunosuppressed should also not get the vaccine. This includes those with HIV, on chemotherapy or those who may need an organ transplant in the near future.

The BCG vaccination increases the rate of false-positive reactions on the tuberculin skin test and makes it more complicated for the clinician to determine if they have latent TB. The BCG vaccine does not affect the QuantiFERON test.

Conclusion
TB is a disease that is not very common in the United States, but has the potential to be very serious if active disease is not treated. Nurses need to be able to identify high risk individuals and implement screening on these groups. Being able to read the screening tests based on patient characteristics is a critical aspect in determining who is infected. Latent TB results when the individual has been infected with TB, but does not have symptoms. A small percentage of individuals will progress to active TB from latent TB. Active disease produces symptoms and has a high mortality rate if not treated.

Reference
