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Patient education: Tuberculosis (Beyond the Basics)

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TUBERCULOSIS OVERVIEW

Tuberculosis (TB) is a disease caused by a type of bacteria called *Mycobacterium tuberculosis*. It most commonly affects the lungs, although it can affect other parts of the body. Medications are available to treat TB and must be taken as prescribed by your provider. Depending on the medication(s) prescribed, the duration can be from four months to nine months or more.

Worldwide, TB remains a leading cause of death. In general, in the United States, TB has been on the decline since it became a reportable disease to the United States Centers for Disease Control and Prevention (CDC) in the 1950s. In 2023, more than 9600 new TB cases were reported in the United States, with cases reported from every state. However, unlike sharper declines in recent years, this represents a 16 percent increase over 2022 and the highest number reported since 2013.

TB can be fatal if not recognized and treated. It also can spread from person to person to infect others — at home, at work, or in the community. However, TB is treatable and preventable. Identifying and treating those who are infected but who have not yet become ill with TB disease can prevent the disease and thus eliminate the spread of TB in the community.

HOW DOES TUBERCULOSIS OCCUR?

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Usually the tuberculosis (TB) bacteria are spread through the air from a person who is ill with TB disease involving the lungs or airways. In these infectious individuals, bacteria are contained in small airborne droplets created by coughing or sneezing. Anyone who inhales these droplets is called a "contact." A contact can be someone who spends a lot of time with the person who has infectious TB, such as a family member, friend, or coworker.

The contact person does not usually become ill immediately. In many cases, the person's immune system is able to remove the bacteria and they do not become infected or develop the disease. In other cases, the person develops an immune response that controls the bacteria by containing them inside the body but it does not kill them. The person does not become ill at this time but is said to have "TB infection" (formerly called "latent TB infection"). Up to one-quarter of the world's population has TB infection. (See 'TB infection' below.)

A person also may become infected with TB by eating or drinking a TB-infected product, such as drinking unpasteurized milk from an animal with TB. This is rare; when it does occur, the immune system manages the infection much as it does when the bacteria are inhaled into the lungs.

TB infection — During this stage of TB, formerly known as "latent TB infection," the person is well and cannot spread the infection to others. If the person is treated at this stage, TB disease can usually be prevented. Treatment is recommended for people with TB infection who are at increased risk for the development of TB disease. (See 'Treatment of tuberculosis infection' below.)

Primary TB disease — In a small number of contacts, containment of inhaled TB bacteria by the immune system fails to occur and the initial infection progresses immediately to TB disease. This is termed primary TB and occurs most commonly in young children (<5 years of age) whose immune system may not yet be fully developed, or in otherwise immunosuppressed individuals.

Reactivation TB disease — Reactivation TB disease, also known as "active TB disease," may develop if TB infection is not fully treated. This is called reactivation TB, and it occurs in 5 to 10 percent of people with TB infection at a later time in their lives.

Reactivation TB may occur if the individual's immune system becomes weakened and no longer is able to control the bacteria. The bacteria then overwhelm the immune process and make the person sick with TB.

The greatest risk for developing reactivation TB disease is within the first two years following the initial infection as a contact to a person with infectious TB. Reactivation can also occur more readily in people with HIV, diabetes mellitus, malnutrition, or those who take medications that weaken the immune system, such as medications for rheumatoid arthritis, steroids, or cancer chemotherapy. It can also occur with aging and weakening of the immune system. Reactivation may also occur for other unknown reasons. (See 'Tuberculosis disease' below.)

HOW IS TUBERCULOSIS INFECTION DIAGNOSED?

Tuberculosis (TB) infection can be diagnosed with a positive skin test or blood test, followed by a clinical evaluation and imaging (usually a chest X-ray) to make sure the TB is not causing disease [1]. The skin test and the blood tests recognize the immune system's prior exposure and sensitization to the TB bacteria and result in a positive test that can be elicited shortly after TB infection has occurred.

Some reasons for testing — TB skin tests or blood tests generally are performed for persons who are at risk of having TB infection or who might be at high risk for developing TB disease if they already infected. Some of these risks include:

- If the person is a health care or laboratory worker who may be a new employee to a health care facility or have contact with patients with TB disease.
- If the person knows he or she was exposed to someone with TB disease. Two tests may be performed. If the first test is negative, a second test usually will be performed 8 to 10 weeks following the last date of exposure.
- Birth or extended stay in a region of the world where TB is common.
- If the person requires a medication that may weaken the immune system, such as steroids or medications for rheumatoid arthritis (eg, TNF-alpha inhibitors).

Blood tests — Blood tests, known as interferon-gamma release assays (IGRAs), are available for testing to identify TB infection and are becoming more widely used. The blood test may be offered instead of, or in addition to, the TB skin test. Blood tests may simplify TB testing because they do not require the person to make a return trip to read the test reaction as required for the skin test. In addition, blood test results for TB infection are not affected by prior immunization with BCG vaccine or by prior infection with most harmless bacteria from the environment that might affect the TB skin test. Like the skin test, IGRAs usually becomes positive within 4 to 10 weeks after exposure. Two blood tests, QuantiFERON TB Gold-Plus and T Spot TB, are approved by the United States Food and Drug Administration (FDA) in the United States.

Skin testing — The TB skin test is known as the tuberculin skin test (sometimes also called a purified protein derivative test [PPD]) and is one method of detecting TB infection. In a person who is newly infected, the skin test usually becomes positive within 4 to 10 weeks

after exposure to the person who is ill with TB. (See "Tuberculosis infection (latent tuberculosis) in adults: Approach to diagnosis (screening)".)

TB skin test is performed by injecting a small amount of PPD solution just beneath the surface of the skin, usually on the forearm. This solution contains an inactivated portion of the TB bacteria. Most individuals previously infected with TB develop a skin reaction (swelling) at this site that develops over the two to three days following test placement.

Skin test interpretation — The skin test must be examined 48 to 72 hours after the PPD solution is injected under the skin. The skin is examined to determine if there is swelling (a reaction) at the injection site and the size of the swelling is recorded. The area may also be reddened, but redness should not be measured.

A trained health care provider interprets the test as positive or negative based on the size of the reaction and criteria for what size of reaction is considered positive in certain patient groups. Anyone who has a reaction larger than 15 mm is considered to have a positive test, and some people with a reaction that is 5 mm (eg, HIV, close contact with someone with TB disease) or 10 mm (eg, recent immigrant from a region with a high rate of TB) are considered to have a positive test if they are at higher risk for developing TB.

- What does a positive TB skin test mean? The TB skin test indicates that the person has been infected with TB and TB bacteria still may be in the body. It cannot determine if a person has TB infection or TB disease; this requires further testing, usually a chest X-ray and a clinical examination. People who have TB disease usually have symptoms, such as a cough (usually persisting for several weeks), fevers, night sweats, and/or unexplained weight loss. (See 'Further testing' below.)
- Skin testing after a positive test in the past Anyone who has demonstrated a
 positive reaction to the TB skin test in the past usually will have a positive reaction in
 the future. Even after taking medication to treat TB, the reaction to the skin test will
 remain positive. Therefore, anyone who has a positive skin test does not need to have
 skin testing again. Skin testing can rarely cause a large and painful skin reaction at the
 injection site and should be avoided if it is unnecessary.
- BCG vaccine A TB vaccine called Bacillus Calmette-Guérin (BCG) is given in many countries to prevent infection with TB. It usually is given to infants, although it may be given again at other times. BCG offers protection against TB in young children but typically does not offer continuing protection. BCG is not routinely used to prevent TB in the United States.

This vaccine may or may not cause a positive skin test. In the United States, a positive reaction to a TB skin test is interpreted as positive, regardless of prior BCG vaccination.

Previous BCG vaccination should NOT stop a person from obtaining a TB skin test unless the person had a positive TB skin test reaction in the past.

Two-step skin testing – In some people, the TB skin test is falsely negative because the immune system's response to TB has faded over time. This may occur in people who were exposed to TB many years before. If a first skin test is negative, a second skin test may be done one to two weeks later. In this situation, performing the first test may "boost" the immune system if it has faded over time, allowing it to react on the repeat test if the person had been previously exposed and infected with TB.

If the person has two negative tests, this is considered a true negative. If the second test is positive, further testing will be done to determine if the person has TB infection or TB disease. (See 'Further testing' below.)

Two-step testing establishes a baseline in people who may need skin testing in the future (eg, some health care workers, employees and residents of institutions such as correctional facilities or nursing homes).

Further testing — If the TB skin test or blood test is positive, a health care provider will ask some specific questions, perform a physical examination, and obtain a chest X-ray to determine if person has TB disease, either currently or in the past. In some cases, the person will be referred to a TB specialist for this evaluation.

If these tests indicate that the person has TB **disease** rather than TB infection, the treatment regimen is different. (See 'Tuberculosis disease' below.)

TREATMENT OF TUBERCULOSIS INFECTION

Treatment approach — Tuberculosis (TB) infection, formerly known as latent TB, is treated with one or more medications to kill the live bacteria that have been contained (controlled) by the immune system. Treating TB infection greatly reduces the risk of the infection progressing to TB disease (reactivation TB disease) later in life. Prior to starting treatment, it's important to review all current medications with your health care provider in order to avoid any possible medication interactions.

While undergoing treatment, it is important to avoid drinking alcohol and taking acetaminophen (Tylenol). Both of these substances can make the liver work harder, potentially increasing the risk of liver injury from the medications.

There are several different drug regimens available for treating TB infection. Doctors typically recommend one of the following:

• Rifampin daily for four months

- Isoniazid plus rifapentine weekly for three months (usually given weekly by a trained health care worker)
- Isoniazid plus rifampin daily for three months

For people who cannot take rifampin or rifapentine, an alternative is:

• Isoniazid daily for six or nine months

The best regimen depends on potential medication interactions, concerns about side effects, and how likely the person is to take all of the medication. Each medication and regimen has its own risks for adverse effects, and it's important to discuss risks and potential drug interactions (eg, rifampin interacts with many drugs, including hormonal birth control, making them ineffective). It also is important to finish the entire course of treatment.

If there are concerns that a person may not be able to reliably take their medication on schedule and/or report any side effects, the health care provider might suggest "directly observed therapy" (see 'Tuberculosis and public health' below). In other cases, the person can take his or her medication at home without direct observation.

Nitrosamine impurities in rifampin and rifapentine — The US Food and Drug Administration (FDA) discovered elevated levels of nitrosamine compounds in rifampin and rifapentine. Nitrosamines are chemicals found in water and foods including cured and grilled meats, dairy products, vegetables, and some medicines. Everyone is exposed to some level of nitrosamines in daily life. If people are exposed above acceptable limits, nitrosamines may increase the risk of cancer. Also, the effects of nitrosamines on a developing fetus, if any, are not known.

The FDA is studying the problem and is working with manufacturers to reduce nitrosamine levels in these drugs. In the meantime, rifampin and rifapentine are still recommended for treating TB by the FDA and United States Centers for Disease Control and Prevention because the risk from TB, or of serious adverse effects from the alternative drug isoniazid, is greater than the possible cancer risk from these medicines. Nevertheless, if either rifampin or rifapentine is proposed for treating TB infection or disease, you should discuss this with your provider.

Monitoring during treatment — People who are being treated for TB infection must be evaluated by a health care provider **at least once per month** to monitor for adherence and for any signs of medication toxicity, such as liver injury. People who have active hepatitis, consume alcohol, take other medications that may injure the liver, or African American or Hispanic women in late pregnancy or in the postpartum period may be at higher risk for side effects from these drugs, especially isoniazid. Signs of liver injury may include unexplained tiredness, loss of appetite, nausea, vomiting, dark-colored urine, jaundice (yellowing of the skin or the white portion of the eye), fatigue, abdominal pain, or, rarely, unexplained bruises. Anyone who experiences one or more of these problems while taking any of these medications should stop their medication **immediately** and notify their health care provider.

In certain special cases, monthly monitoring may also include blood tests to monitor the function of the liver or blood counts.

TUBERCULOSIS DISEASE

Tuberculosis (TB) disease, formerly known as "active TB," occurs when the TB bacteria overwhelm the immune system and cause a person to become ill. This usually occurs in the lung, although TB can affect any part of the body, including the lymph nodes, brain, kidneys, or bones. (See "Treatment of drug-susceptible pulmonary tuberculosis in nonpregnant adults without HIV infection".)

If there is evidence on a chest X-ray or other signs that TB disease of the lungs (pulmonary TB) may be present, sputum smears (stained sputum examined on a microscope slide), cultures (to grow the bacteria in the laboratory), and or nucleic acid amplification test (NAAT; sometimes called polymerase chain reaction [PCR]) will be performed. This usually involves coughing up a "deep" specimen of phlegm from the chest. The phlegm is then sent to a laboratory and examined to determine if TB bacteria are present. Other tests, such as a bronchoscopy or biopsy, may also be needed to obtain specimens, especially if sputum does not provide a diagnosis. A tissue biopsy may be performed to obtain specimens for culture if TB is suspected in other organs (such as lymph nodes or kidney). (See "Patient education: Flexible bronchoscopy (Beyond the Basics)".)

While waiting for the results of laboratory tests (some laboratory results are positive within a day or two, but it may take as long as two months for the TB bacteria to grow in the laboratory), treatment with several (usually four) TB drugs may be recommended if TB disease is suspected. It is important to use more than one medicine to treat TB disease and to take the medicines exactly as prescribed to reduce the risk of treatment failure or of the bacteria becoming resistant to one (or more) of the medicines.

Infection caused by a strain of TB that has become resistant to standard TB drugs is more difficult to treat and may require four to six medications and a longer duration of treatment. (See "Treatment of drug-resistant pulmonary tuberculosis in adults".)

TUBERCULOSIS AND PUBLIC HEALTH

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Tuberculosis (TB) disease can easily be spread through the air. As a result, laws in the United States require that anyone with TB disease be reported to the health department. Health department staff will work with the patient's health care provider and the patient to make sure that a safe and effective treatment regimen is completed.

Directly observed therapy (DOT) is a program used by public health departments to ensure that a patient safely takes his or her medication exactly as prescribed. This requires daily interaction with a health care worker who makes sure medications are taken appropriately by watching the patient swallow the medications and assesses the patient for symptoms and signs of an adverse reaction to the medication or clinical worsening. This minimizes the risk of serious side effects. DOT may help to improve cure rates. (See "Adherence to tuberculosis treatment".)

The health department can also help to identify people who have been in contact with a person with TB disease. Contacts are advised to have TB testing and treatment if necessary.

Public health programs for TB are essential for several additional reasons:

- To reduce the number of new cases of TB (by identifying and treating people with TB infection in order to prevent disease from developing) and therefore
- To limit spread of the disease in the community (by monitoring and assuring safe, complete treatment of people with TB disease)

WHERE TO GET MORE INFORMATION

Your health care provider is the best source of information for questions and concerns related to your medical problem.

This article will be updated as needed on our website. Related topics for patients, as well as selected articles written for health care professionals, are also available. Some of the most relevant are listed below.

Patient level information — UpToDate offers two types of patient education materials.

The Basics — The Basics patient education pieces answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials.

Patient education: Tuberculosis (The Basics)Patient education: Isolation precautions (The Basics)Patient education: Tuberculosis screening tests (The Basics)Patient education: Endobronchial ultrasound (The Basics)

Beyond the Basics — Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are best for patients who want in-depth information and are comfortable with some medical jargon.

Professional level information — Professional level articles are designed to keep doctors and other health professionals up-to-date on the latest medical findings. These articles are thorough, long, and complex, and they contain multiple references to the research on which they are based. Professional level articles are best for people who are comfortable with a lot of medical terminology and who want to read the same materials their doctors are reading.

Adherence to tuberculosis treatment

Prevention of tuberculosis: BCG immunization and nutritional supplementation Pulmonary tuberculosis disease in adults: Clinical manifestations and complications Treatment of drug-resistant pulmonary tuberculosis in adults **Epidemiology of tuberculosis** Treatment of tuberculosis infection (latent tuberculosis) in nonpregnant adults with HIV infection Treatment of tuberculosis infection (latent tuberculosis) in nonpregnant adults without HIV infection Treatment of drug-susceptible pulmonary tuberculosis in nonpregnant adults with HIV infection: Initiation of therapy Treatment of drug-susceptible pulmonary tuberculosis in nonpregnant adults without HIV infection Tuberculosis transmission and control in health care settings Use of interferon-gamma release assays for diagnosis of tuberculosis infection (tuberculosis screening) in adults Diagnosis of pulmonary tuberculosis in adults Tuberculosis infection (latent tuberculosis) in adults: Approach to diagnosis (screening)

The following organizations also provide reliable heath information.

- National Library of Medicine
- (https://medlineplus.gov/tuberculosis.html, available in Spanish)
 - Centers for Disease Control and Prevention (CDC)

Toll-free: (800) 311-3435

- (www.cdc.gov/tb/)
 - National Institute of Allergy and Infectious Diseases
- (https://www.niaid.nih.gov/diseases-conditions/tuberculosis)

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