**TUBERCULOSIS**

**Tuberculosis** (**TB**) is an [infectious disease](https://en.wikipedia.org/wiki/Infectious_disease) usually caused by [*Mycobacterium tuberculosis*](https://en.wikipedia.org/wiki/Mycobacterium_tuberculosis) (MTB) [bacteria](https://en.wikipedia.org/wiki/Bacteria). Tuberculosis generally affects the [lungs](https://en.wikipedia.org/wiki/Lung), but can also affect other parts of the body. Most infections show no symptoms, in which case it is known as [latent tuberculosis](https://en.wikipedia.org/wiki/Latent_tuberculosis). About 10% of latent infections progress to active disease which, if left untreated, kills about half of those affected. The classic symptoms of active TB are a chronic [cough](https://en.wikipedia.org/wiki/Cough) with [blood-containing](https://en.wikipedia.org/wiki/Hemoptysis) [mucus](https://en.wikipedia.org/wiki/Sputum), [fever](https://en.wikipedia.org/wiki/Fever), [night sweats](https://en.wikipedia.org/wiki/Night_sweats), and [weight loss](https://en.wikipedia.org/wiki/Weight_loss). It was historically called **consumption** due to the weight loss.[]](https://en.wikipedia.org/wiki/Tuberculosis#cite_note-Cha1998-8) [Infection](https://en.wikipedia.org/wiki/Infection) of other organs can cause a wide range of symptoms.

Tuberculosis is [spread from one person to the next](https://en.wikipedia.org/wiki/Human-to-human_transmission) [through the air](https://en.wikipedia.org/wiki/Airborne_disease) when people who have active TB in their lungs cough, spit, speak, or [sneeze](https://en.wikipedia.org/wiki/Sneeze). People with latent TB do not spread the disease. Active infection occurs more often in people with [HIV/AIDS](https://en.wikipedia.org/wiki/HIV/AIDS) and in those who [smoke](https://en.wikipedia.org/wiki/Tobacco_smoking). [Diagnosis](https://en.wikipedia.org/wiki/Diagnosis) of active TB is based on [chest X-rays](https://en.wikipedia.org/wiki/Chest_X-ray), as well as [microscopic](https://en.wikipedia.org/wiki/Microscopic) examination and [culture](https://en.wikipedia.org/wiki/Microbiological_culture) of body fluids. Diagnosis of latent TB relies on the [tuberculin skin test](https://en.wikipedia.org/wiki/Mantoux_test) (TST) or blood tests

Prevention of TB involves screening those at high risk, early detection and treatment of cases, and [vaccination](https://en.wikipedia.org/wiki/Vaccination) with the [bacillus Calmette-Guérin](https://en.wikipedia.org/wiki/Bacillus_Calmette-Gu%C3%A9rin) (BCG) vaccine. Those at high risk include household, workplace, and social contacts of people with active TB. Treatment requires the use of multiple [antibiotics](https://en.wikipedia.org/wiki/Antibiotic) over a long period of time.

**Signs and Symptoms :**

Tuberculosis may infect any part of the body, but most commonly occurs in the lungs (known as pulmonary tuberculosis)]Extrapulmonary TB occurs when tuberculosis develops outside of the lungs, although extrapulmonary TB may coexist with pulmonary TB.

General signs and symptoms include fever, [chills](https://en.wikipedia.org/wiki/Chills), night sweats, [loss of appetite](https://en.wikipedia.org/wiki/Anorexia_(symptom)), weight loss, and [fatigue](https://en.wikipedia.org/wiki/Fatigue_(medical)). Significant [nail clubbing](https://en.wikipedia.org/wiki/Nail_clubbing) may also occur.

**Pulmonary**

If a tuberculosis infection does become active, it most commonly involves the lungs (in about 90% of cases.]Symptoms may include [chest pain](https://en.wikipedia.org/wiki/Chest_pain) and a prolonged cough producing sputum. About 25% of people may not have any symptoms (i.e. they remain "asymptomatic").Occasionally, people may [cough up blood](https://en.wikipedia.org/wiki/Hemoptysis) in small amounts, and in very rare cases, the infection may erode into the [pulmonary artery](https://en.wikipedia.org/wiki/Pulmonary_artery) or a [Rasmussen's aneurysm](https://en.wikipedia.org/wiki/Rasmussen%27s_aneurysm), resulting in massive bleeding. Tuberculosis may become a chronic illness and cause extensive scarring in the upper lobes of the lungs. The upper lung lobes are more frequently affected by tuberculosis than the lower ones.The reason for this difference is not clear.It may be due to either better air flow,or poor [lymph](https://en.wikipedia.org/wiki/Lymph) drainage within the upper lungs.

**Extrapulmonary**

In 15–20% of active cases, the infection spreads outside the lungs, causing other kinds of TB.These are collectively denoted as "extrapulmonary tuberculosis".Extrapulmonary TB occurs more commonly in people with a [weakened immune system](https://en.wikipedia.org/wiki/Immunosuppression) and young children. In those with HIV, this occurs in more than 50% of cases.Notable extrapulmonary infection sites include the [pleura](https://en.wikipedia.org/wiki/Pleural_cavity) (in tuberculous pleurisy), the [central nervous system](https://en.wikipedia.org/wiki/Central_nervous_system) (in [tuberculous meningitis](https://en.wikipedia.org/wiki/Tuberculous_meningitis" \o "Tuberculous meningitis)), the [lymphatic system](https://en.wikipedia.org/wiki/Lymphatic_system) (in [scrofula](https://en.wikipedia.org/wiki/Tuberculous_cervical_lymphadenitis) of the neck), the [genitourinary system](https://en.wikipedia.org/wiki/Genitourinary_system) (in [urogenital tuberculosis](https://en.wikipedia.org/wiki/Urogenital_tuberculosis)), and the [bones](https://en.wikipedia.org/wiki/Bone) and joints (in [Pott disease](https://en.wikipedia.org/wiki/Pott_disease" \o "Pott disease) of the spine), among others. A potentially more serious, widespread form of TB is called "disseminated tuberculosis", it is also known as [miliary tuberculosis](https://en.wikipedia.org/wiki/Miliary_tuberculosis" \o "Miliary tuberculosis).Miliary TB currently makes up about 10% of extrapulmonary cases.

**Causes**

**Mycobacteria**

The main cause of TB is [*Mycobacterium tuberculosis*](https://en.wikipedia.org/wiki/Mycobacterium_tuberculosis) (MTB), a small, [aerobic](https://en.wikipedia.org/wiki/Aerobic_organism), nonmotile [bacillus](https://en.wikipedia.org/wiki/Bacillus). The high [lipid](https://en.wikipedia.org/wiki/Lipid) content of this [pathogen](https://en.wikipedia.org/wiki/Pathogen) accounts for many of its unique clinical characteristics. It [divides](https://en.wikipedia.org/wiki/Cell_division) every 16 to 20 hours, which is an extremely slow rate compared with other bacteria, which usually divide in less than an hour. Mycobacteria have an [outer membrane](https://en.wikipedia.org/wiki/Bacterial_cell_structure) lipid bilayer. If a [Gram stain](https://en.wikipedia.org/wiki/Gram_stain) is performed, MTB either stains very weakly "Gram-positive" or does not retain dye as a result of the high lipid and [mycolic acid](https://en.wikipedia.org/wiki/Mycolic_acid" \o "Mycolic acid) content of its cell wall. MTB can withstand weak [disinfectants](https://en.wikipedia.org/wiki/Disinfectant) and survive in a [dry state](https://en.wikipedia.org/wiki/Endospore) for weeks. In nature, the bacterium can grow only within the cells of a [host](https://en.wikipedia.org/wiki/Host_(biology)) organism, but *M. tuberculosis* can be cultured [in the laboratory](https://en.wikipedia.org/wiki/In_vitro).

Using [histological](https://en.wikipedia.org/wiki/Histology) stains on [expectorated](https://en.wikipedia.org/wiki/Expectorate) samples from [phlegm](https://en.wikipedia.org/wiki/Phlegm) (also called "sputum"), scientists can identify MTB under a microscope. Since MTB retains certain stains even after being treated with acidic solution, it is classified as an [acid-fast bacillus](https://en.wikipedia.org/wiki/Acid-fast_bacillus). The most common acid-fast staining techniques are the [Ziehl–Neelsen stain](https://en.wikipedia.org/wiki/Ziehl%E2%80%93Neelsen_stain" \o "Ziehl–Neelsen stain) and the [Kinyoun stain](https://en.wikipedia.org/wiki/Kinyoun_stain" \o "Kinyoun stain), which dye acid-fast bacilli a bright red that stands out against a blue background. [Auramine-rhodamine staining](https://en.wikipedia.org/wiki/Auramine-rhodamine_stain) and [fluorescence microscopy](https://en.wikipedia.org/wiki/Fluorescence_microscope)are also used.

The [*M. tuberculosis* complex](https://en.wikipedia.org/wiki/Mycobacterium_tuberculosis_complex) (MTBC) includes four other TB-causing [mycobacteria](https://en.wikipedia.org/wiki/Mycobacterium): [*M. bovis*](https://en.wikipedia.org/wiki/Mycobacterium_bovis), [*M. africanum*](https://en.wikipedia.org/wiki/Mycobacterium_africanum), [*M. canetti*](https://en.wikipedia.org/wiki/Mycobacterium_canetti), and [*M. microti*](https://en.wikipedia.org/wiki/Mycobacterium_microti). *M. africanum* is not widespread, but it is a significant cause of tuberculosis in parts of Africa. *M. bovis* was once a common cause of tuberculosis, but the introduction of [pasteurized milk](https://en.wikipedia.org/wiki/Pasteurisation) has almost completely eliminated this as a public health problem in developed countries. *M. canetti* is rare and seems to be limited to the [Horn of Africa](https://en.wikipedia.org/wiki/Horn_of_Africa), although a few cases have been seen in African emigrants. *M. microti* is also rare and is seen almost only in immunodeficient people, although its [prevalence](https://en.wikipedia.org/wiki/Prevalence) may be significantly underestimated.

Other known pathogenic mycobacteria include [*M. leprae*](https://en.wikipedia.org/wiki/Mycobacterium_leprae), [*M. avium*](https://en.wikipedia.org/wiki/Mycobacterium_avium_complex), and [*M. kansasii*](https://en.wikipedia.org/wiki/Mycobacterium_kansasii). The latter two species are classified as "[nontuberculous mycobacteria](https://en.wikipedia.org/wiki/Nontuberculous_mycobacteria" \o "Nontuberculous mycobacteria)" (NTM). NTM cause neither TB nor [leprosy](https://en.wikipedia.org/wiki/Leprosy), but they do cause lung diseases that resemble TB.

### Transmission

When people with active pulmonary TB cough, sneeze, speak, sing, or spit, they expel infectious [aerosol](https://en.wikipedia.org/wiki/Aerosol) droplets 0.5 to 5.0 [µm](https://en.wikipedia.org/wiki/%CE%9Cm) in diameter. A single sneeze can release up to 40,000 droplets. Each one of these droplets may transmit the disease, since the infectious dose of tuberculosis is very small (the inhalation of fewer than 10 bacteria may cause an infection).

#### Risk of transmission

People with prolonged, frequent, or close contact with people with TB are at particularly high risk of becoming infected, with an estimated 22% infection rate.A person with active but untreated tuberculosis may infect 10–15 (or more) other people per year.Transmission should occur from only people with active TB – those with latent infection are not thought to be contagious.The probability of transmission from one person to another depends upon several factors, including the number of infectious droplets expelled by the carrier, the effectiveness of ventilation, the duration of exposure, the [virulence](https://en.wikipedia.org/wiki/Virulence) of the *M. tuberculosis* [strain](https://en.wikipedia.org/wiki/Strain_(biology)), the level of immunity in the uninfected person, and others.The cascade of person-to-person spread can be circumvented by segregating those with active ("overt") TB and putting them on anti-TB drug regimens. After about two weeks of effective treatment, subjects with [nonresistant](https://en.wikipedia.org/wiki/Antibiotic_resistance" \o "Antibiotic resistance) active infections generally do not remain contagious to others. If someone does become infected, it typically takes three to four weeks before the newly infected person becomes infectious enough to transmit the disease to others.

## Tuberculosis Types

A TB infection doesn’t always mean you’ll get sick. There are two forms of the disease:

* **Latent TB.**You have the germs in your body, but your [immune system](https://www.webmd.com/cold-and-flu/10-immune-system-busters-boosters) keeps them from spreading. You don’t have any symptoms, and you’re not contagious. But the infection is still alive and can one day become active. If you’re at high risk for re-activation -- for instance, if you have HIV, you had an infection in the past 2 years, your chest X-ray is unusual, or your immune system is weakened -- your doctor will give you medications to prevent active TB.
* **Active TB.**The germs multiply and make you sick. You can spread the disease to others. Ninety percent of active cases in adults come from a latent TB infection.

**Pathogenesis :**

About 90% of those infected with *M. tuberculosis* have [asymptomatic](https://en.wikipedia.org/wiki/Asymptomatic), latent TB infections (sometimes called LTBI), with only a 10% lifetime chance that the latent infection will progress to overt, active tuberculous disease. In those with HIV, the risk of developing active TB increases to nearly 10% a year. If effective treatment is not given, the death rate for active TB cases is up to 66%.

TB infection begins when the mycobacteria reach the [alveolar air sacs](https://en.wikipedia.org/wiki/Pulmonary_alveolus) of the lungs, where they invade and replicate within [endosomes](https://en.wikipedia.org/wiki/Endosomes) of alveolar [macrophages](https://en.wikipedia.org/wiki/Macrophages). Macrophages identify the bacterium as foreign and attempt to eliminate it by [phagocytosis](https://en.wikipedia.org/wiki/Phagocytosis). During this process, the bacterium is enveloped by the macrophage and stored temporarily in a membrane-bound vesicle called a phagosome. The phagosome then combines with a lysosome to create a phagolysosome. In the phagolysosome, the cell attempts to use [reactive oxygen species](https://en.wikipedia.org/wiki/Reactive_oxygen_species) and acid to kill the bacterium. However, *M. tuberculosis* has a thick, waxy [mycolic acid](https://en.wikipedia.org/wiki/Mycolic_acid" \o "Mycolic acid) capsule that protects it from these toxic substances. *M. tuberculosis* is able to reproduce inside the macrophage and will eventually kill the immune cell.

The primary site of infection in the lungs, known as the "[Ghon focus](https://en.wikipedia.org/wiki/Ghon_focus" \o "Ghon focus)", is generally located in either the upper part of the lower lobe, or the lower part of the [upper lobe](https://en.wikipedia.org/wiki/Lung). Tuberculosis of the lungs may also occur via infection from the blood stream. This is known as a [Simon focus](https://en.wikipedia.org/wiki/Simon_focus) and is typically found in the top of the lung. This hematogenous transmission can also spread infection to more distant sites, such as peripheral lymph nodes, the kidneys, the brain, and the bones. All parts of the body can be affected by the disease, though for unknown reasons it rarely affects the [heart](https://en.wikipedia.org/wiki/Heart), [skeletal muscles](https://en.wikipedia.org/wiki/Skeletal_muscle), [pancreas](https://en.wikipedia.org/wiki/Pancreas), or [thyroid](https://en.wikipedia.org/wiki/Thyroid).

Tuberculosis is classified as one of the [granulomatous](https://en.wikipedia.org/wiki/Granuloma) inflammatory diseases. [Macrophages](https://en.wikipedia.org/wiki/Macrophage), [epithelioid cells](https://en.wikipedia.org/wiki/Epithelioid_cell" \o "Epithelioid cell), [T lymphocytes](https://en.wikipedia.org/wiki/T_cell), [B lymphocytes](https://en.wikipedia.org/wiki/B_cell), and [fibroblasts](https://en.wikipedia.org/wiki/Fibroblast) aggregate to form granulomas, with [lymphocytes](https://en.wikipedia.org/wiki/Lymphocytes) surrounding the infected macrophages. When other macrophages attack the infected macrophage, they fuse together to form a giant multinucleated cell in the alveolar lumen. The granuloma may prevent dissemination of the mycobacteria and provide a local environment for interaction of cells of the immune system. However, more recent evidence suggests that the bacteria use the granulomas to avoid destruction by the host's immune system. Macrophages and [dendritic cells](https://en.wikipedia.org/wiki/Dendritic_cell) in the granulomas are unable to present antigen to lymphocytes; thus the immune response is suppressed. Bacteria inside the granuloma can become dormant, resulting in latent infection. Another feature of the granulomas is the development of abnormal cell death ([necrosis](https://en.wikipedia.org/wiki/Necrosis)) in the center of [tubercles](https://en.wikipedia.org/wiki/Tubercle_(anatomy)). To the naked eye, this has the texture of soft, white cheese and is termed [caseous necrosis](https://en.wikipedia.org/wiki/Caseous_necrosis" \o "Caseous necrosis).

If TB bacteria gain entry to the blood stream from an area of damaged tissue, they can spread throughout the body and set up many foci of infection, all appearing as tiny, white tubercles in the tissues. This severe form of TB disease, most common in young children and those with HIV, is called miliary tuberculosis. People with this disseminated TB have a high fatality rate even with treatment (about 30%).

In many people, the infection waxes and wanes. Tissue destruction and necrosis are often balanced by healing and [fibrosis](https://en.wikipedia.org/wiki/Fibrosis). Affected tissue is replaced by scarring and cavities filled with caseous necrotic material. During active disease, some of these cavities are joined to the air passages ([bronchi](https://en.wikipedia.org/wiki/Bronchi)) and this material can be coughed up. It contains living bacteria, and thus can spread the infection. Treatment with appropriate [antibiotics](https://en.wikipedia.org/wiki/Antibiotic) kills bacteria and allows healing to take place. Upon cure, affected areas are eventually replaced by scar tissue

## Tuberculosis Tests

There are two common tests for tuberculosis:

* **Skin test.** This is also known as the Mantoux tuberculin skin test. A technician injects a small amount of fluid into the skin of your lower arm. After 2 or 3 days, they’ll check for swelling in your arm. If your results are positive, you probably have TB bacteria. But you could also get a false positive. If you’ve gotten a tuberculosis vaccine called bacillus Calmette-Guerin (BCG), the test could say that you have TB when you really don’t. The results can also be false negative, saying that you don’t have TB when you really do, if you have a very new infection. You might get this test more than once.
* **Blood test.** These tests, also called interferon-gamma release assays (IGRAs), measure the response when TB proteins are mixed with a small amount of your blood.

Diagnosis

### Active tuberculosis

Diagnosing active tuberculosis based only on signs and symptoms is difficult, as is diagnosing the disease in those who have a weakened immune system.A diagnosis of TB should, however, be considered in those with signs of lung disease or [constitutional symptoms](https://en.wikipedia.org/wiki/Constitutional_symptoms) lasting longer than two weeks.A [chest X-ray](https://en.wikipedia.org/wiki/Chest_X-ray) and multiple [sputum cultures](https://en.wikipedia.org/wiki/Sputum_culture) for [acid-fast bacilli](https://en.wikipedia.org/wiki/Acid-fast_bacilli) are typically part of the initial evaluation.Interferon-γ release assays and tuberculin skin tests are of little use in most of the developing world.[Interferon gamma release assays](https://en.wikipedia.org/wiki/Interferon_gamma_release_assay) (IGRA) have similar limitations in those with HIV.

A definitive diagnosis of TB is made by identifying *M. tuberculosis* in a clinical sample (e.g., sputum, [pus](https://en.wikipedia.org/wiki/Pus), or a [tissue](https://en.wikipedia.org/wiki/Tissue_(biology)) [biopsy](https://en.wikipedia.org/wiki/Biopsy)). However, the difficult culture process for this slow-growing organism can take two to six weeks for blood or sputum culture. Thus, treatment is often begun before cultures are confirmed.

[Nucleic acid amplification tests](https://en.wikipedia.org/wiki/Nucleic_acid_amplification_test) and [adenosine deaminase](https://en.wikipedia.org/wiki/Adenosine_deaminase) testing may allow rapid diagnosis of TB.These tests, however, are not routinely recommended, as they rarely alter how a person is treated. Blood tests to detect antibodies are not [specific or sensitive](https://en.wikipedia.org/wiki/Sensitivity_and_specificity), so they are not recommende

**Latent tuberculosis**

The [Mantoux tuberculin skin test](https://en.wikipedia.org/wiki/Mantoux_test" \o "Mantoux test) is often used to screen people at high risk for TB. Those who have been previously immunized with the Bacille Calmette-Guerin vaccine may have a false-positive test result. The test may be falsely negative in those with [sarcoidosis](https://en.wikipedia.org/wiki/Sarcoidosis" \o "Sarcoidosis), [Hodgkin's lymphoma](https://en.wikipedia.org/wiki/Hodgkin%27s_lymphoma), [malnutrition](https://en.wikipedia.org/wiki/Malnutrition), and most notably, active tuberculosis. Interferon gamma release assays, on a blood sample, are recommended in those who are positive to the Mantoux test. These are not affected by immunization or most [environmental mycobacteria](https://en.wikipedia.org/wiki/Environmental_mycobacteria), so they generate fewer [false-positive](https://en.wikipedia.org/wiki/False-positive) results. However, they are affected by *M. szulgai*, *M. marinum*, and *M. kansasii*. IGRAs may increase sensitivity when used in addition to the skin test, but may be less sensitive than the skin test when used alone.

The [US Preventive Services Task Force](https://en.wikipedia.org/wiki/US_Preventive_Services_Task_Force) (USPSTF) has recommended screening people who are at high risk for latent tuberculosis with either tuberculin skin tests or interferon-gamma release assays. While some have recommend testing health care workers, evidence of benefit for this is poor as of 2019. The [Centers for Disease Control and Prevention](https://en.wikipedia.org/wiki/Centers_for_Disease_Control_and_Prevention" \o "Centers for Disease Control and Prevention) (CDC) stopped recommending yearly testing of health care workers without known exposure in 2019.

**Prevention :**

Tuberculosis prevention and control efforts rely primarily on the vaccination of infants and the detection and appropriate treatment of active cases. The [World Health Organization](https://en.wikipedia.org/wiki/World_Health_Organization) (WHO) has achieved some success with improved treatment regimens, and a small decrease in case numbers.

### Vaccines

The only available [vaccine](https://en.wikipedia.org/wiki/Vaccine) as of 2011 is [Bacillus Calmette-Guérin](https://en.wikipedia.org/wiki/Bacillus_Calmette-Gu%C3%A9rin) (BCG). In children it decreases the risk of getting the infection by 20% and the risk of infection turning into active disease by nearly 60%.

It is the most widely used vaccine worldwide, with more than 90% of all children being vaccinated. The immunity it induces decreases after about ten years. As tuberculosis is uncommon in most of Canada, Western Europe, and the United States, BCG is administered to only those people at high risk. Part of the reasoning against the use of the vaccine is that it makes the tuberculin skin test falsely positive, reducing the test's usefulness as a screening tool. Several vaccines are being developed.

Intradermal MVA85A Vaccine in addition to BCG injection is not effective in preventing tuberculosis.

### Public health

The World Health Organization (WHO) declared TB a "global health emergency" in 1993, and in 2006, the Stop TB Partnership developed a [Global Plan to Stop Tuberculosis](https://en.wikipedia.org/wiki/Global_Plan_to_Stop_Tuberculosis) that aimed to save 14 million lives between its launch and 2015. A number of targets they set were not achieved by 2015, mostly due to the increase in HIV-associated tuberculosis and the emergence of multiple drug-resistant tuberculosis. A [tuberculosis classification](https://en.wikipedia.org/wiki/Tuberculosis_classification) system developed by the [American Thoracic Society](https://en.wikipedia.org/wiki/American_Thoracic_Society) is used primarily in public health programs.

The benefits and risks of giving anti-tubercular drugs in those exposed to MDR-TB is unclear.[[](https://en.wikipedia.org/wiki/Tuberculosis#cite_note-91)

**Vaccine Development**

NIAID is part of the global research community engaged in finding new ways to prevent tuberculosis (TB) disease in children and adults. In addition to developing new approaches for treatment of people who are infected but have not yet developed disease, researchers are also trying to understand how the TB bacterium interacts with its human host. Scientists are studying how the bacterium evades the immune system to infect people, how it can lay dormant for years and become active at a later stage in life, and why people can have TB disease more than once in their lives. This knowledge will help to find ways to develop vaccines that are able to prime the immune system to recognize *Mycobacterium tuberculosis*, prevent it from infecting people, or prevent latent infections from progressing to active TB disease.

An effective vaccine is considered to be one of the most essential tools needed to reduce this deadly disease worldwide. It is not only one of the most critical but also most challenging areas of science currently being pursued. NIAID is providing support to help identify and evaluate new candidate TB vaccines and immune-boosting vaccine adjuvants to prevent infection or disease and is evaluating the potential of synthetic vaccines to help shorten TB drug treatment regimens.

In addition, NIAID funds vaccine development, including preclinical animal studies and clinical research on those candidate TB vaccines that appear most promising. Several candidates that demonstrated protection against infection with *M. tuberculosis* in small animal models have entered human clinical trials. NIAID collaborates with other government agencies and pharmaceutical companies to assist in moving vaccine candidates towards clinical trials.