[Template:Pp-semi-indef](/wiki/Template:Pp-semi-indef" \o "Template:Pp-semi-indef) [Template:Pp-move-indef](/wiki/Template:Pp-move-indef) [Template:Good article](/wiki/Template:Good_article) [Template:Use dmy dates](/wiki/Template:Use_dmy_dates) [Template:Infobox medical condition](/wiki/Template:Infobox_medical_condition) **Tuberculosis** (**TB**) is an [infectious disease](/wiki/Infectious_disease) caused by the bacterium [*Mycobacterium tuberculosis*](/wiki/Mycobacterium_tuberculosis) (MTB).<ref name=WHO2015Fact/> Tuberculosis generally affects the [lungs](/wiki/Lung), but can also affect other parts of the body. Most infections do not have symptoms, known as [latent tuberculosis](/wiki/Latent_tuberculosis). About 10% of latent infections progress to active disease which, if left untreated, kills about half of those infected. The classic symptoms of active TB are a chronic [cough](/wiki/Cough) with [blood-containing](/wiki/Hemoptysis) [sputum](/wiki/Sputum), [fever](/wiki/Fever), [night sweats](/wiki/Night_sweats), and [weight loss](/wiki/Weight_loss).<ref name=WHO2015Fact/> The historical term "**consumption**" came about due to the weight loss.<ref name=Cha1998>[Template:Cite book](/wiki/Template:Cite_book)</ref> Infection of other organs can cause a wide range of symptoms.<ref name=ID10>[Template:Cite book](/wiki/Template:Cite_book)</ref>

Tuberculosis is [spread through the air](/wiki/Airborne_disease) when people who have active TB in their lungs cough, spit, speak, or sneeze.<ref name=WHO2015Fact/><ref name=CDC2012B>[Template:Cite web](/wiki/Template:Cite_web)</ref> People with latent TB do not spread the disease. Active infection occurs more often in people with [HIV/AIDS](/wiki/HIV/AIDS) and in those who [smoke](/wiki/Tobacco_smoking).<ref name=WHO2015Fact/> Diagnosis of active TB is based on [chest X-rays](/wiki/Chest_X-ray), as well as [microscopic](/wiki/Microscopic) examination and [culture](/wiki/Microbiological_culture) of body fluids. Diagnosis of latent TB relies on the [tuberculin skin test](/wiki/Mantoux_test) (TST) or blood tests.<ref name=AP>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

Prevention of TB involves screening those at high risk, early detection and treatment of cases, and [vaccination](/wiki/Vaccination) with the [bacillus Calmette-Guérin](/wiki/Bacillus_Calmette-Guérin) vaccine.[[1]](#cite_note-1)[[2]](#cite_note-2)<ref name=TBCon2008>[Template:Cite book](/wiki/Template:Cite_book)</ref> Those at high risk include household, workplace, and social contacts of people with active TB.<ref name=TBCon2008/> Treatment requires the use of multiple [antibiotics](/wiki/Antibiotic) over a long period of time.<ref name=WHO2015Fact/> [Antibiotic resistance](/wiki/Antibiotic_resistance) is a growing problem with increasing rates of [multiple drug-resistant tuberculosis](/wiki/Multi-drug-resistant_tuberculosis) (MDR-TB).<ref name=WHO2015Fact/>

One-third of the world's population is thought to be infected with TB.<ref name=WHO2015Fact/> New infections occur in about 1% of the population each year.<ref name=WHO2002>[Template:Cite web](/wiki/Template:Cite_web)</ref> In 2014, there were 9.6 million cases of active TB which resulted in 1.5 million deaths. More than 95% of deaths occurred in [developing countries](/wiki/Developing_countries). The number of new cases each year has decreased since 2000.<ref name=WHO2015Fact>[Template:Cite web](/wiki/Template:Cite_web)</ref> About 80% of people in many Asian and African countries test positive while 5–10% of people in the United States population tests positive by the tuberculin test.<ref name=Robbins>[Template:Cite book](/wiki/Template:Cite_book)</ref> Tuberculosis has been present in humans since [ancient times](/wiki/Ancient_history).<ref name=Lancet11>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> [thumb|upright=1.4|Video explanation](/wiki/File:Tuberculosis_video.webm) [Template:TOC limit](/wiki/Template:TOC_limit)

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## Signs and symptoms[[edit](/index.php?title=(none)&action=edit&section=1)]

[thumb|upright=1.5|The main symptoms of variants and stages of tuberculosis are given,](/wiki/File:Tuberculosis_symptoms.svg)[[3]](#cite_note-3) with many symptoms overlapping with other variants, while others are more (but not entirely) specific for certain variants. Multiple variants may be present simultaneously. Tuberculosis may infect any part of the body, but most commonly occurs in the lungs (known as pulmonary tuberculosis).<ref name=ID10/> Extrapulmonary TB occurs when tuberculosis develops outside of the lungs, although extrapulmonary TB may coexist with pulmonary TB.<ref name=ID10/>

General signs and symptoms include [fever](/wiki/Fever), [chills](/wiki/Chills), [night sweats](/wiki/Night_sweats), [loss of appetite](/wiki/Anorexia_(symptom)), [weight loss](/wiki/Weight_loss), and [fatigue](/wiki/Fatigue_(medical)).<ref name=ID10/> Significant [nail clubbing](/wiki/Nail_clubbing) may also occur.<ref name=Pet2005/>

### Pulmonary[[edit](/index.php?title=(none)&action=edit&section=2)]

If a tuberculosis infection does become active, it most commonly involves the lungs (in about 90% of cases).<ref name=Lancet11/>[[4]](#cite_note-4) Symptoms may include [chest pain](/wiki/Chest_pain) and a prolonged cough producing sputum. About 25% of people may not have any symptoms (i.e. they remain "asymptomatic").<ref name=Lancet11/> Occasionally, people may [cough up blood](/wiki/Hemoptysis) in small amounts, and in very rare cases, the infection may erode into the [pulmonary artery](/wiki/Pulmonary_artery) or a [Rasmussen's aneurysm](/wiki/Rasmussen's_aneurysm), resulting in massive bleeding.<ref name=ID10/>[[5]](#cite_note-5) 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.<ref name=ID10/> The reason for this difference is not clear.[[6]](#cite_note-6) It may be due either to better air flow,[[6]](#cite_note-6) or to poor [lymph](/wiki/Lymph) drainage within the upper lungs.<ref name=ID10/>

### Extrapulmonary[[edit](/index.php?title=(none)&action=edit&section=3)]

In 15–20% of active cases, the infection spreads outside the lungs, causing other kinds of TB.[[7]](#cite_note-7) These are collectively denoted as "extrapulmonary tuberculosis".<ref name=Extra2005>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Extrapulmonary TB occurs more commonly in [immunosuppressed](/wiki/Immunosuppression) persons and young children. In those with HIV, this occurs in more than 50% of cases.<ref name=Extra2005/> Notable extrapulmonary infection sites include the [pleura](/wiki/Pleural_cavity) (in tuberculous pleurisy), the [central nervous system](/wiki/Central_nervous_system) (in tuberculous [meningitis](/wiki/Meningitis)), the [lymphatic system](/wiki/Lymphatic_system) (in [scrofula](/wiki/Tuberculous_cervical_lymphadenitis) of the neck), the [genitourinary system](/wiki/Genitourinary_system) (in [urogenital tuberculosis](/wiki/Urogenital_tuberculosis)), and the bones and joints (in [Pott disease](/wiki/Pott_disease) of the spine), among others. When it spreads to the bones, it is also known as "osseous tuberculosis",[[8]](#cite_note-8) a form of [osteomyelitis](/wiki/Osteomyelitis).[[6]](#cite_note-6) Sometimes, bursting of a tubercular abscess through skin results in tuberculous ulcer.[[9]](#cite_note-9) An ulcer originating from nearby infected lymph nodes is painless, slowly enlarging and has an appearance of "wash leather".[[10]](#cite_note-10) A potentially more serious, widespread form of TB is called "disseminated tuberculosis", also known as [miliary tuberculosis](/wiki/Miliary_tuberculosis).<ref name=ID10/> Miliary TB makes up about 10% of extrapulmonary cases.<ref name=Gho2008/>

## Causes[[edit](/index.php?title=(none)&action=edit&section=4)]

### Mycobacteria[[edit](/index.php?title=(none)&action=edit&section=5)]

[Template:Main article](/wiki/Template:Main_article) [thumb|](/wiki/File:Mycobacterium_tuberculosis.jpg)[Scanning electron micrograph](/wiki/Scanning_electron_micrograph) of *M. tuberculosis* The main cause of TB is [*Mycobacterium tuberculosis*](/wiki/Mycobacterium_tuberculosis), a small, [aerobic](/wiki/Aerobic_organism), nonmotile [bacillus](/wiki/Bacillus).<ref name=ID10/> The high [lipid](/wiki/Lipid) content of this pathogen accounts for many of its unique clinical characteristics.[[11]](#cite_note-11) It [divides](/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.[[12]](#cite_note-12) Mycobacteria have an [outer membrane](/wiki/Bacterial_cell_structure) lipid bilayer.<ref name=Niederweis2010>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> If a [Gram stain](/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](/wiki/Mycolic_acid) content of its cell wall.<ref name=Madison\_2001>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> MTB can withstand weak [disinfectants](/wiki/Disinfectant) and survive in a [dry state](/wiki/Endospore) for weeks. In nature, the bacterium can grow only within the cells of a [host](/wiki/Host_(biology)) organism, but *M. tuberculosis* can be cultured [in the laboratory](/wiki/In_vitro).<ref name=Parish\_1999>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

Using [histological](/wiki/Histology) stains on [expectorated](/wiki/Expectorate) samples from [phlegm](/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](/wiki/Acid-fast_bacillus).[[13]](#cite_note-13) The most common acid-fast staining techniques are the [Ziehl–Neelsen stain](/wiki/Ziehl–Neelsen_stain)<ref name=Stain2000>[Template:Cite book](/wiki/Template:Cite_book)</ref> and the [Kinyoun stain](/wiki/Kinyoun_stain), which dye acid-fast bacilli a bright red that stands out against a blue background.[[14]](#cite_note-14) [Auramine-rhodamine staining](/wiki/Auramine-rhodamine_stain)<ref name=Kommareddi\_1984>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> and [fluorescence microscopy](/wiki/Fluorescence_microscope)[[15]](#cite_note-15) are also used.

The *M. tuberculosis* complex (MTBC) includes four other TB-causing [mycobacteria](/wiki/Mycobacterium): [*M. bovis*](/wiki/Mycobacterium_bovis), [*M. africanum*](/wiki/Mycobacterium_africanum), [*M. canetti*](/wiki/Mycobacterium_canetti), and [*M. microti*](/wiki/Mycobacterium_microti).[[16]](#cite_note-16) *M. africanum* is not widespread, but it is a significant cause of tuberculosis in parts of Africa.[[17]](#cite_note-17)[[18]](#cite_note-18) *M. bovis* was once a common cause of tuberculosis, but the introduction of [pasteurized milk](/wiki/Pasteurisation) has almost completely eliminated this as a public health problem in developed countries.<ref name=Robbins/>[[19]](#cite_note-19) *M. canetti* is rare and seems to be limited to the [Horn of Africa](/wiki/Horn_of_Africa), although a few cases have been seen in African emigrants.[[20]](#cite_note-20)[[21]](#cite_note-21) *M. microti* is also rare and is seen almost only in immunodeficient people, although its [prevalence](/wiki/Prevalence) may be significantly underestimated.[[22]](#cite_note-22) Other known pathogenic mycobacteria include [*M. leprae*](/wiki/Mycobacterium_leprae), [*M. avium*](/wiki/Mycobacterium_avium_complex), and [*M. kansasii*](/wiki/Mycobacterium_kansasii). The latter two species are classified as "[nontuberculous mycobacteria](/wiki/Nontuberculous_mycobacteria)" (NTM). NTM cause neither TB nor [leprosy](/wiki/Leprosy), but they do cause pulmonary diseases that resemble TB.<ref name=ALA\_1997>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

### Risk factors[[edit](/index.php?title=(none)&action=edit&section=6)]

[Template:Main article](/wiki/Template:Main_article) A number of factors make people more susceptible to TB infections. The most important risk factor globally is HIV; 13% of all people with TB are infected by the virus.<ref name=WHO2011>[Template:Cite web](/wiki/Template:Cite_web)</ref> This is a particular problem in [sub-Saharan Africa](/wiki/Sub-Saharan_Africa), where rates of HIV are high.[[23]](#cite_note-23)[[24]](#cite_note-24) Of people without HIV who are infected with tuberculosis, about 5–10% develop active disease during their lifetimes;<ref name=Pet2005>[Template:Cite book](/wiki/Template:Cite_book)</ref> in contrast, 30% of those coinfected with HIV develop the active disease.<ref name=Pet2005/>

Tuberculosis is closely linked to both overcrowding and [malnutrition](/wiki/Malnutrition), making it one of the principal [diseases of poverty](/wiki/Diseases_of_poverty).<ref name=Lancet11/> Those at high risk thus include: people who inject illicit drugs, inhabitants and employees of locales where vulnerable people gather (e.g. prisons and homeless shelters), medically underprivileged and resource-poor communities, high-risk ethnic minorities, children in close contact with high-risk category patients, and health-care providers serving these patients.<ref name=Griffith\_1996>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

Chronic lung disease is another significant risk factor. [Silicosis](/wiki/Silicosis) increases the risk about 30-fold.<ref name=table3>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Those who smoke [cigarettes](/wiki/Cigarette) have nearly twice the risk of TB compared to nonsmokers.[[25]](#cite_note-25) Other disease states can also increase the risk of developing tuberculosis. These include [alcoholism](/wiki/Alcoholism)<ref name=Lancet11/> and [diabetes mellitus](/wiki/Diabetes_mellitus) (three-fold increase).[[26]](#cite_note-26) Certain medications, such as [corticosteroids](/wiki/Corticosteroids) and [infliximab](/wiki/Infliximab) (an anti-αTNF monoclonal antibody), are becoming increasingly important risk factors, especially in the [developed world](/wiki/Developed_world).<ref name=Lancet11/>

[Genetic susceptibility](/wiki/Genetic_susceptibility) also exists,[[27]](#cite_note-27) for which the overall importance remains undefined.<ref name=Lancet11/>

## Mechanism[[edit](/index.php?title=(none)&action=edit&section=7)]

[thumb|upright|Public health campaigns in the 1920s tried to halt the spread of TB.](/wiki/File:TB_poster.jpg)

### Transmission[[edit](/index.php?title=(none)&action=edit&section=8)]

When people with active pulmonary TB cough, sneeze, speak, sing, or spit, they expel infectious [aerosol](/wiki/Aerosol) droplets 0.5 to 5.0 [µm](/wiki/Μm) in diameter. A single sneeze can release up to 40,000 droplets.<ref name=Cole\_1998>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> 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).[[28]](#cite_note-28) 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.<ref name=Ahmed\_2011>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> A person with active but untreated tuberculosis may infect 10–15 (or more) other people per year.[[29]](#cite_note-29) Transmission should occur from only people with active TB – those with latent infection are not thought to be contagious.<ref name=Robbins/> 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](/wiki/Virulence) of the *M. tuberculosis* [strain](/wiki/Strain_(biology)), the level of immunity in the uninfected person, and others.<ref name=CDCcourse>[Template:Cite web](/wiki/Template:Cite_web)</ref> 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](/wiki/Antibiotic_resistance) active infections generally do not remain contagious to others.[[30]](#cite_note-30) 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.[[31]](#cite_note-31)

### Pathogenesis[[edit](/index.php?title=(none)&action=edit&section=9)]

[thumbnail|Microscopy of tuberculous epididymitis.](/wiki/File:Tuberculous_epididymitis_Low_Power.jpg) [H&E](/wiki/H&E) stain About 90% of those infected with *M. tuberculosis* have [asymptomatic](/wiki/Asymptomatic), latent TB infections (sometimes called LTBI),<ref name=Book90>[Template:Cite book](/wiki/Template:Cite_book)</ref> with only a 10% lifetime chance that the latent infection will progress to overt, active tuberculous disease.<ref name=Arch2009>[Template:Cite book](/wiki/Template:Cite_book)</ref> In those with HIV, the risk of developing active TB increases to nearly 10% a year.<ref name=Arch2009/> If effective treatment is not given, the death rate for active TB cases is up to 66%.<ref name=WHO2012data>[Template:Cite web](/wiki/Template:Cite_web)</ref>

TB infection begins when the mycobacteria reach the [pulmonary alveoli](/wiki/Pulmonary_alveolus), where they invade and replicate within [endosomes](/wiki/Endosomes) of alveolar [macrophages](/wiki/Macrophages).<ref name=Robbins/><ref name=Houben>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Macrophages identify the bacterium as foreign and attempt to eliminate it by [phagocytosis](/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](/wiki/Reactive_oxygen_species) and acid to kill the bacterium. However, *M. tuberculosis* has a thick, waxy [mycolic acid](/wiki/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](/wiki/Ghon_focus)", is generally located in either the upper part of the lower lobe, or the lower part of the [upper lobe](/wiki/Lung).<ref name=Robbins/> Tuberculosis of the lungs may also occur via infection from the blood stream. This is known as a [Simon focus](/wiki/Simon_focus) and is typically found in the top of the lung.[[32]](#cite_note-32) This hematogenous transmission can also spread infection to more distant sites, such as peripheral lymph nodes, the kidneys, the brain, and the bones.<ref name=Robbins/><ref name=Herrmann\_2005>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> All parts of the body can be affected by the disease, though for unknown reasons it rarely affects the [heart](/wiki/Heart), [skeletal muscles](/wiki/Skeletal_muscle), [pancreas](/wiki/Pancreas), or [thyroid](/wiki/Thyroid).[[33]](#cite_note-33) [thumb|left|upright=90%|](/wiki/File:Carswell-Tubercle.jpg)[Robert Carswell's](/wiki/Robert_Carswell_(pathologist)) illustration of tubercle[[34]](#cite_note-34)

Tuberculosis is classified as one of the [granulomatous](/wiki/Granuloma) inflammatory diseases. [Macrophages](/wiki/Macrophage), [T lymphocytes](/wiki/T_cell), [B lymphocytes](/wiki/B_cell), and [fibroblasts](/wiki/Fibroblast) aggregate to form [granulomas](/wiki/Granuloma), with [lymphocytes](/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.[[35]](#cite_note-35) However, more recent evidence suggests that the bacteria use the granulomas to avoid destruction by the host's immune system. Macrophages and [dendritic cells](/wiki/Dendritic_cell) in the granulomas are unable to present antigen to lymphocytes; thus the immune response is suppressed.[[36]](#cite_note-36) Bacteria inside the granuloma can become dormant, resulting in latent infection. Another feature of the granulomas is the development of abnormal cell death ([necrosis](/wiki/Necrosis)) in the center of [tubercles](/wiki/Tubercle_(anatomy)). To the naked eye, this has the texture of soft, white cheese and is termed [caseous necrosis](/wiki/Caseous_necrosis).<ref name=Grosset>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

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.[[37]](#cite_note-37) This severe form of TB disease, most common in young children and those with HIV, is called miliary tuberculosis.[[38]](#cite_note-38) People with this disseminated TB have a high fatality rate even with treatment (about 30%).<ref name=Gho2008>[Template:Cite book](/wiki/Template:Cite_book)</ref>[[39]](#cite_note-39) In many people, the infection waxes and wanes. Tissue destruction and necrosis are often balanced by healing and [fibrosis](/wiki/Fibrosis).<ref name=Grosset/> 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](/wiki/Bronchi) and this material can be coughed up. It contains living bacteria, so can spread the infection. Treatment with appropriate [antibiotics](/wiki/Antibiotic) kills bacteria and allows healing to take place. Upon cure, affected areas are eventually replaced by scar tissue.<ref name=Grosset/> [Template:Clear](/wiki/Template:Clear)

## Diagnosis[[edit](/index.php?title=(none)&action=edit&section=10)]

[Template:Main article](/wiki/Template:Main_article) [thumb|*M. tuberculosis* (](/wiki/File:TB_in_sputum.png)[stained red](/wiki/Ziehl-Neelsen_stain)) in [sputum](/wiki/Sputum)

### Active tuberculosis[[edit](/index.php?title=(none)&action=edit&section=11)]

Diagnosing active tuberculosis based only on signs and symptoms is difficult,<ref name=DiagP2011>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> as is diagnosing the disease in those who are immunosuppressed.<ref name=Clinic2009>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> A diagnosis of TB should, however, be considered in those with signs of lung disease or [constitutional symptoms](/wiki/Constitutional_symptoms) lasting longer than two weeks.<ref name=Clinic2009/> A [chest X-ray](/wiki/Chest_X-ray) and multiple [sputum cultures](/wiki/Sputum_culture) for [acid-fast bacilli](/wiki/Acid-fast_bacilli) are typically part of the initial evaluation.<ref name=Clinic2009/> Interferon-γ release assays and tuberculin skin tests are of little use in the developing world.[[40]](#cite_note-40)[[41]](#cite_note-41) IGRA have similar limitations in those with HIV.[[41]](#cite_note-41)[[42]](#cite_note-42) A definitive diagnosis of TB is made by identifying *M. tuberculosis* in a clinical sample (e.g., sputum, [pus](/wiki/Pus), or a [tissue](/wiki/Tissue_(biology)) [biopsy](/wiki/Biopsy)). However, the difficult culture process for this slow-growing organism can take two to six weeks for blood or sputum culture.[[43]](#cite_note-43) Thus, treatment is often begun before cultures are confirmed.<ref name=NICE2011/>

[Nucleic acid amplification tests](/wiki/Nucleic_acid_amplification_test) and [adenosine deaminase](/wiki/Adenosine_deaminase) testing may allow rapid diagnosis of TB.<ref name=DiagP2011/> These tests, however, are not routinely recommended, as they rarely alter how a person is treated.<ref name=NICE2011/> Blood tests to detect antibodies are not [specific or sensitive](/wiki/Sensitivity_and_specificity), so they are not recommended.[[44]](#cite_note-44)

### Latent tuberculosis[[edit](/index.php?title=(none)&action=edit&section=12)]

[Template:Main article](/wiki/Template:Main_article) [thumb|](/wiki/File:Mantoux_tuberculin_skin_test.jpg)[Mantoux tuberculin skin test](/wiki/Mantoux_test) The [Mantoux tuberculin skin test](/wiki/Mantoux_test) is often used to screen people at high risk for TB.<ref name=Clinic2009/> Those who have been previously immunized may have a false-positive test result.<ref name=Rothel\_2005>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> The test may be falsely negative in those with [sarcoidosis](/wiki/Sarcoidosis), [Hodgkin's lymphoma](/wiki/Hodgkin's_lymphoma), [malnutrition](/wiki/Malnutrition), and most notably, active tuberculosis.<ref name=Robbins/> [Interferon gamma release assays](/wiki/Interferon_gamma_release_assays) (IGRAs), on a blood sample, are recommended in those who are positive to the Mantoux test.<ref name=NICE2011>[Template:NICE](/wiki/Template:NICE)</ref> These are not affected by immunization or most [environmental mycobacteria](/wiki/Environmental_mycobacteria), so they generate fewer [false-positive](/wiki/False-positive) results.[[45]](#cite_note-45) However, they are affected by *M. szulgai*, *M. marinum*, and *M. kansasii*.[[46]](#cite_note-46) IGRAs may increase sensitivity when used in addition to the skin test, but may be less sensitive than the skin test when used alone.[[47]](#cite_note-47)

## Prevention[[edit](/index.php?title=(none)&action=edit&section=13)]

Tuberculosis prevention and control efforts rely primarily on the vaccination of infants and the detection and appropriate treatment of active cases.<ref name=Lancet11/> The [World Health Organization](/wiki/World_Health_Organization) has achieved some success with improved treatment regimens, and a small decrease in case numbers.<ref name=Lancet11/>

### Vaccines[[edit](/index.php?title=(none)&action=edit&section=14)]

[Template:Main article](/wiki/Template:Main_article) The only available [vaccine](/wiki/Vaccine) as of 2011 is [Bacillus Calmette-Guérin](/wiki/Bacillus_Calmette-Guérin) (BCG).<ref name=McS2011>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> In children it decreases the risk of getting the infection by 20% and the risk of infection turning into disease by nearly 60%.[[48]](#cite_note-48) It is the most widely used vaccine worldwide, with more than 90% of all children being [vaccinated](/wiki/Vaccinated).<ref name=Lancet11/> The immunity it induces decreases after about ten years.<ref name=Lancet11/> As tuberculosis is uncommon in most of Canada, the United Kingdom, and the United States, BCG is administered only to those people at high risk.[[49]](#cite_note-49)[[50]](#cite_note-50)<ref name=UK06>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Part of the reasoning against the use of the vaccine is that it makes the [tuberculin skin test](/wiki/Tuberculin_skin_test) falsely positive, reducing the test's use in screening.<ref name=UK06/> A number of new vaccines are currently in development.<ref name=Lancet11/>

### Public health[[edit](/index.php?title=(none)&action=edit&section=15)]

The World Health Organization declared TB a "global health emergency" in 1993,<ref name=Lancet11/> and in 2006, the Stop TB Partnership developed a [Global Plan to Stop Tuberculosis](/wiki/Global_Plan_to_Stop_Tuberculosis) that aims to save 14 million lives between its launch and 2015.[[51]](#cite_note-51) A number of targets they have set are not likely to be achieved by 2015, mostly due to the increase in HIV-associated tuberculosis and the emergence of multiple drug-resistant tuberculosis.<ref name=Lancet11/> A [tuberculosis classification](/wiki/Tuberculosis_classification) system developed by the [American Thoracic Society](/wiki/American_Thoracic_Society) is used primarily in public health programs.[[52]](#cite_note-52)

## Management[[edit](/index.php?title=(none)&action=edit&section=16)]

[Template:Main article](/wiki/Template:Main_article) Treatment of TB uses antibiotics to kill the bacteria. Effective TB treatment is difficult, due to the unusual structure and chemical composition of the mycobacterial cell wall, which hinders the entry of drugs and makes many antibiotics ineffective.[[53]](#cite_note-53) The two antibiotics most commonly used are [isoniazid](/wiki/Isoniazid) and [rifampicin](/wiki/Rifampicin), and treatments can be prolonged, taking several months.<ref name=CDCcourse/> Latent TB treatment usually employs a single antibiotic,<ref name=Latent2011/> while active TB disease is best treated with combinations of several antibiotics to reduce the risk of the bacteria developing [antibiotic resistance](/wiki/Antibiotic_resistance).<ref name=Lancet11/> People with latent infections are also treated to prevent them from progressing to active TB disease later in life.<ref name=Latent2011>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> [Directly observed therapy](/wiki/Directly_observed_therapy), i.e., having a health care provider watch the person take their medications, is recommended by the WHO in an effort to reduce the number of people not appropriately taking antibiotics.[[54]](#cite_note-54) The evidence to support this practice over people simply taking their medications independently is poor.[[55]](#cite_note-55) Methods to remind people of the importance of treatment do, however, appear effective.[[56]](#cite_note-56)

### New onset[[edit](/index.php?title=(none)&action=edit&section=17)]

The recommended treatment of new-onset pulmonary tuberculosis, as of 2010, is six months of a combination of antibiotics containing rifampicin, isoniazid, [pyrazinamide](/wiki/Pyrazinamide), and [ethambutol](/wiki/Ethambutol) for the first two months, and only rifampicin and isoniazid for the last four months.<ref name=Lancet11/> Where resistance to isoniazid is high, ethambutol may be added for the last four months as an alternative.<ref name=Lancet11/>

### Recurrent disease[[edit](/index.php?title=(none)&action=edit&section=18)]

If tuberculosis recurs, testing to determine to which antibiotics it is sensitive is important before determining treatment.<ref name=Lancet11/> If multiple drug-resistant TB is detected, treatment with at least four effective antibiotics for 18 to 24 months is recommended.<ref name=Lancet11/>

### Medication resistance[[edit](/index.php?title=(none)&action=edit&section=19)]

Primary resistance occurs when a person becomes infected with a resistant strain of TB. A person with fully susceptible MTB may develop secondary (acquired) resistance during therapy because of inadequate treatment, not taking the prescribed regimen appropriately (lack of compliance), or using low-quality medication.<ref name=OBrien>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Drug-resistant TB is a serious public health issue in many developing countries, as its treatment is longer and requires more expensive drugs. MDR-TB is defined as resistance to the two most effective first-line TB drugs: rifampicin and isoniazid. [Extensively drug-resistant TB](/wiki/Extensively_drug-resistant_tuberculosis) is also resistant to three or more of the six classes of second-line drugs.[[57]](#cite_note-57) [Totally drug-resistant TB](/wiki/Totally_drug-resistant_tuberculosis) is resistant to all currently used drugs.<ref name=TR2012>[Template:Cite web](/wiki/Template:Cite_web)</ref> It was first observed in 2003 in Italy,[[58]](#cite_note-58) but not widely reported until 2012,<ref name=TR2012/>[[59]](#cite_note-59) and has also been found in Iran and India.[[60]](#cite_note-60)[[61]](#cite_note-61) [Bedaquiline](/wiki/Bedaquiline) is tentatively supported for use in multiple drug-resistant TB.[[62]](#cite_note-62) XDR-TB is a term sometimes used to define *extensively resistant* TB, and constitutes one in ten cases of MDR-TB. Cases of XDR TB have been identified in more than 90% of countries.[[60]](#cite_note-60)

## Prognosis[[edit](/index.php?title=(none)&action=edit&section=20)]

[thumb|upright=1.6|](/wiki/File:Tuberculosis_world_map_-_DALY_-_WHO2004.svg)[Age-standardized](/wiki/Age_adjustment) [disability-adjusted life years](/wiki/Disability-adjusted_life_year) caused by tuberculosis per 100,000 inhabitants in 2004.[[63]](#cite_note-63)[Template:Multicol](/wiki/Template:Multicol) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Multicol-break](/wiki/Template:Multicol-break) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Multicol-break](/wiki/Template:Multicol-break) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Legend](/wiki/Template:Legend) [Template:Multicol-end](/wiki/Template:Multicol-end) Progression from TB infection to overt TB disease occurs when the bacilli overcome the immune system defenses and begin to multiply. In primary TB disease (some 1–5% of cases), this occurs soon after the initial infection.<ref name=Robbins/> However, in the majority of cases, a [latent infection](/wiki/Latent_tuberculosis) occurs with no obvious symptoms.<ref name=Robbins/> These dormant bacilli produce active tuberculosis in 5–10% of these latent cases, often many years after infection.<ref name=Pet2005/>

The risk of reactivation increases with immunosuppression, such as that caused by infection with HIV. In people coinfected with *M. tuberculosis* and HIV, the risk of reactivation increases to 10% per year.<ref name=Robbins/> Studies using DNA fingerprinting of *M. tuberculosis* strains have shown reinfection contributes more substantially to recurrent TB than previously thought,[[64]](#cite_note-64) with estimates that it might account for more than 50% of reactivated cases in areas where TB is common.[[65]](#cite_note-65) The chance of death from a case of tuberculosis is about 4% as of 2008, down from 8% in 1995.<ref name=Lancet11/>

## Epidemiology[[edit](/index.php?title=(none)&action=edit&section=21)]

[Template:Main article](/wiki/Template:Main_article) [thumb|left|upright=1.6|alt=World map with](/wiki/File:Tuberculosis-prevalence-WHO-2009.svg) [sub-Saharan Africa](/wiki/Sub-Saharan_Africa) in various shades of yellow, marking prevalences above 300 per 100,000, and with the U.S., Canada, Australia, and northern Europe in shades of deep blue, marking prevalences around 10 per 100,000. Asia is yellow but not quite so bright, marking prevalences around 200 per 100,000 range. South America is a darker yellow.|In 2007, the prevalence of TB per 100,000 people was highest in sub-Saharan Africa, and was also relatively high in Asia.<ref name=WHO2009-Burden>[Template:Cite book](/wiki/Template:Cite_book)</ref> Roughly one-third of the world's population has been infected with *M. tuberculosis*,<ref name=WHO2012data/> with new infections occurring in about 1% of the population each year.<ref name=WHO2002/> However, most infections with *M. tuberculosis* do not cause TB disease,<ref name=CDC>[Template:Cite web](/wiki/Template:Cite_web)</ref> and 90–95% of infections remain asymptomatic.<ref name=Book90/> In 2012, an estimated 8.6 million chronic cases were active.[[66]](#cite_note-66) In 2010, 8.8 million new cases of TB were diagnosed, and 1.20–1.45 million deaths occurred, most of these occurring in [developing countries](/wiki/Developing_nation).<ref name=WHO2011/><ref name=Loz2012>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Of these 1.45 million deaths, about 0.35 million occur in those also infected with HIV.<ref name=WHO2011Control>[Template:Cite web](/wiki/Template:Cite_web)</ref>

Tuberculosis is the second-most common cause of death from infectious disease (after those due to HIV/AIDS).<ref name=ID10/> The total number of tuberculosis cases has been decreasing since 2005, while new cases have decreased since 2002.<ref name=WHO2011/> China has achieved particularly dramatic progress, with about an 80% reduction in its TB mortality rate between 1990 and 2010.<ref name=WHO2011Control/> The number of new cases has declined by 17% between 2004–2014.[[60]](#cite_note-60) Tuberculosis is more common in developing countries; about 80% of the population in many Asian and African countries test positive in tuberculin tests, while only 5–10% of the US population test positive.<ref name=Robbins/> Hopes of totally controlling the disease have been dramatically dampened because of a number of factors, including the difficulty of developing an effective vaccine, the expensive and time-consuming diagnostic process, the necessity of many months of treatment, the increase in HIV-associated tuberculosis, and the emergence of drug-resistant cases in the 1980s.<ref name=Lancet11/>

In 2007, the country with the highest estimated incidence rate of TB was [Swaziland](/wiki/Swaziland), with 1,200 cases per 100,000 people. India had the largest total incidence, with an estimated 2.0 million new cases.<ref name=WHO2009-Epidemiology>[Template:Cite book](/wiki/Template:Cite_book)</ref> In developed countries, tuberculosis is less common and is found mainly in urban areas. Rates per 100,000 people in different areas of the world were: globally 178, Africa 332, the Americas 36, Eastern Mediterranean 173, Europe 63, Southeast Asia 278, and Western Pacific 139 in 2010.<ref name=WHO2011Control/> In Canada and Australia, tuberculosis is many times more common among the [aboriginal peoples](/wiki/Aboriginal_peoples), especially in remote areas.[[67]](#cite_note-67)[[68]](#cite_note-68) In the United States [Native Americans](/wiki/Native_Americans_in_the_United_States) have a fivefold greater mortality from TB,[[69]](#cite_note-69) and racial and ethnic minorities accounted for 84% of all reported TB cases.[[70]](#cite_note-70) The rates of TB varies with age. In Africa, it primarily affects adolescents and young adults.[[71]](#cite_note-71) However, in countries where incidence rates have declined dramatically (such as the United States), TB is mainly a disease of older people and the immunocompromised (risk factors are listed above).<ref name=Robbins/>[[72]](#cite_note-72)Worldwide, 22 "high-burden" states or countries together experience 80% of cases as well as 83% of deaths.[[60]](#cite_note-60)

## History[[edit](/index.php?title=(none)&action=edit&section=22)]

[Template:Main article](/wiki/Template:Main_article) [thumb|Egyptian](/wiki/File:Mummy_at_British_Museum.jpg) [mummy](/wiki/Mummy) in the [British Museum](/wiki/British_Museum) – tubercular decay has been found in the spines of [Egyptian](/wiki/Egypt) [mummies](/wiki/Mummy).

Tuberculosis has been present in humans since [antiquity](/wiki/Ancient_history).<ref name=Lancet11/> The earliest unambiguous detection of *M. tuberculosis* involves evidence of the disease in the remains of bison in Wyoming dated to around 17,000 years ago.[[73]](#cite_note-73) However, whether tuberculosis originated in bovines, then was transferred to humans, or whether it diverged from a common ancestor, is currently unclear.[[74]](#cite_note-74) A comparison of the [genes](/wiki/Gene) of *M. tuberculosis* complex (MTBC) in humans to MTBC in animals suggests humans did not acquire MTBC from animals during animal domestication, as was previously believed. Both strains of the tuberculosis bacteria share a common ancestor, which could have infected humans even before the [Neolithic Revolution](/wiki/Neolithic_Revolution).[[75]](#cite_note-75) Skeletal remains show prehistoric humans (4000 [BC](/wiki/Common_Era)) had TB, and researchers have found tubercular decay in the spines of [Egyptian](/wiki/Egypt) [mummies](/wiki/Mummy) dating from 3000–2400 BC.[[76]](#cite_note-76) Genetic studies suggest TB was present in [the Americas](/wiki/The_Americas) from about 100 AD.[[77]](#cite_note-77) Before the [Industrial Revolution](/wiki/Industrial_Revolution), folklore often associated tuberculosis with [vampires](/wiki/Vampire). When one member of a family died from it, the other infected members would lose their health slowly. People believed this was caused by the original person with TB draining the life from the other family members.<ref name=sledzik>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

Although the pulmonary form associated with [tubercles](/wiki/Tubercle_(anatomy)) was established as a pathology by [Dr Richard Morton](/wiki/Dr_Richard_Morton) in 1689,[[78]](#cite_note-78)[[79]](#cite_note-79) due to the variety of its symptoms, TB was not identified as a single disease until the 1820s. It was not named "tuberculosis" until 1839, by [J. L. Schönlein](/wiki/Johann_Lukas_Schönlein).[[80]](#cite_note-80) During 1838–1845, Dr. John Croghan, the owner of [Mammoth Cave](/wiki/Mammoth_Cave), brought a number of people with tuberculosis into the cave in the hope of curing the disease with the constant temperature and purity of the cave air; they died within a year.[[81]](#cite_note-81) Hermann Brehmer opened the first TB [sanatorium](/wiki/Sanatorium) in 1859 in Görbersdorf (now [Sokołowsko](/wiki/Sokołowsko)), [Silesia](/wiki/Silesia).<ref name =sanatoria>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

[upright|thumb|left|Dr. Robert Koch discovered the tuberculosis bacillus.](/wiki/File:RobertKoch.jpg)

The bacillus causing tuberculosis, *M. tuberculosis*, was identified and described on 24 March 1882 by [Robert Koch](/wiki/Robert_Koch). He received the [Nobel Prize in physiology or medicine](/wiki/Nobel_Prize_in_physiology_or_medicine) in 1905 for this discovery.[[82]](#cite_note-82) Koch did not believe the bovine (cattle) and human tuberculosis diseases were similar, which delayed the recognition of infected milk as a source of infection. Later, the risk of transmission from this source was dramatically reduced by the invention of the [pasteurization](/wiki/Pasteurization) process. Koch announced a [glycerine](/wiki/Glycerine) extract of the tubercle bacilli as a "remedy" for tuberculosis in 1890, calling it "tuberculin". While it was not effective, it was later successfully adapted as a screening test for the presence of pre-symptomatic tuberculosis.[[83]](#cite_note-83) The [World Tuberculosis Day](/wiki/World_Tuberculosis_Day) was established on 24 March for this reason.

[Albert Calmette](/wiki/Albert_Calmette) and [Camille Guérin](/wiki/Camille_Guérin) achieved the first genuine success in immunization against tuberculosis in 1906, using attenuated bovine-strain tuberculosis. It was called [bacille Calmette–Guérin](/wiki/BCG_vaccine) (BCG). The BCG vaccine was first used on humans in 1921 in France,<ref name=Bonah>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> but received widespread acceptance in the US, Great Britain, and Germany only after World War II.<ref name=Comstock>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

Tuberculosis caused the most widespread public concern in the 19th and early 20th centuries as an [endemic](/wiki/Endemic_(epidemiology)) disease of the urban poor. In 1815, one in four deaths in England was due to "consumption". By 1918, one in six deaths in France was still caused by TB. After TB was determined to be contagious, in the 1880s, it was put on a [notifiable disease](/wiki/List_of_notifiable_diseases) list in Britain; campaigns were started to stop people from spitting in public places, and the infected poor were "encouraged" to enter [sanatoria](/wiki/Sanatorium) that resembled prisons (the sanatoria for the middle and upper classes offered excellent care and constant medical attention).<ref name =sanatoria/> Whatever the (purported) benefits of the "fresh air" and labor in the sanatoria, even under the best conditions, 50% of those who entered died within five years (*circa* 1916).<ref name =sanatoria/>

In Europe, rates of tuberculosis began to rise in the early 1600s to a peak level in the 1800s, when it caused nearly 25% of all deaths.[[84]](#cite_note-84) By the 1950s, mortality had decreased nearly 90%.[[85]](#cite_note-85) Improvements in public health began significantly reducing rates of tuberculosis even before the arrival of [streptomycin](/wiki/Streptomycin) and other antibiotics, although the disease remained a significant threat to public health such that when the [Medical Research Council](/wiki/Medical_Research_Council_(UK)) was formed in Britain in 1913, its initial focus was tuberculosis research.[[86]](#cite_note-86) In 1946, the development of the antibiotic [streptomycin](/wiki/Streptomycin) made effective treatment and cure of TB a reality. Prior to the introduction of this drug, the only treatment (except sanatoria) was surgical intervention, including the "[pneumothorax](/wiki/Pneumothorax) technique", which involved collapsing an infected lung to "rest" it and allow tuberculous lesions to heal.[[87]](#cite_note-87) Because of the emergence of MDR-TB, surgery has been re-introduced as an option within the generally accepted standard of care in treating TB infections. Current surgical interventions involve removal of pathological chest cavities ("bullae") in the lungs to reduce the number of bacteria and to increase the exposure of the remaining bacteria to drugs in the bloodstream, thereby simultaneously reducing the total bacterial load and increasing the effectiveness of systemic antibiotic therapy.[[88]](#cite_note-88) Hopes of completely eliminating TB (*cf.* [smallpox](/wiki/Smallpox)) from the population were dashed after the rise of [drug-resistant](/wiki/Antibiotic_resistant) strains in the 1980s. The subsequent resurgence of tuberculosis resulted in the declaration of a global health emergency by the World Health Organization in 1993.[[89]](#cite_note-89)

## Society and culture[[edit](/index.php?title=(none)&action=edit&section=23)]

### Names[[edit](/index.php?title=(none)&action=edit&section=24)]

*Phthisis* is a Greek word for consumption, an old term for pulmonary tuberculosis;<ref name=Cha1998/> around 460 BC, [Hippocrates](/wiki/Hippocrates) described phthisis as a disease of dry seasons.[[90]](#cite_note-90) The abbreviation "TB" is short for *tubercle* [*bacillus*](/wiki/Bacillus_(shape)).

### Public health efforts[[edit](/index.php?title=(none)&action=edit&section=25)]

The [World Health Organization](/wiki/World_Health_Organization), [Bill and Melinda Gates Foundation](/wiki/Bill_and_Melinda_Gates_Foundation), and US government are subsidizing a fast-acting diagnostic tuberculosis test for use in low- and middle-income countries.<ref name=PressRelease2012/><ref name=Xpert2011>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>[[91]](#cite_note-91) In addition to being fast-acting, the test can determine if there is resistance to the antibiotic rifampicin which may indicate multi-drug resistant tuberculosis and is accurate in those who are also infected with HIV.<ref name=PressRelease2012>[Template:Cite web](/wiki/Template:Cite_web)</ref>[[92]](#cite_note-92) Many resource-poor places as of 2011 have access to only sputum microscopy.[[93]](#cite_note-93) India had the highest total number of TB cases worldwide in 2010, in part due to poor disease management within the private and public health care sector.[[94]](#cite_note-94) Programs such as the [Revised National Tuberculosis Control Program](/wiki/Revised_National_Tuberculosis_Control_Program) are working to reduce TB levels amongst people receiving public health care.[[95]](#cite_note-95)[[96]](#cite_note-96) A 2014 the [EIU](/wiki/Economist_Intelligence_Unit)-healthcare report that the need to address apathy and urging for increased funding. The report cites among others Lucica Ditui "[TB] is like an orphan. It has been neglected even in countries with a high burden and often forgotten by donors and those investing in health interventions."[[60]](#cite_note-60) Slow progress has led to frustration, expressed by executive director of the [Global Fund to Fight AIDS, Tuberculosis and Malaria](/wiki/Global_Fund_to_Fight_AIDS,_Tuberculosis_and_Malaria) – Mark Dybul: "we have the tools to end TB as a pandemic and public health threat on the planet, but we are not doing it."[[60]](#cite_note-60) Several international organizations are pushing for more transparency in treatment, and more countries are implementing mandatory reporting of cases to the government, although adherence is often sketchy. Commercial treatment-providers may at times overprescribe second-line drugs as well as supplementary treatment, promoting demands for further regulations.[[60]](#cite_note-60) The government of Brazil provides universal TB-care, which reduces this problem.[[60]](#cite_note-60) Conversely, falling rates of TB-infection may not relate to the number of programs directed at reducing infection rates, but may be tied to increased level of education, income and health of the population.[[60]](#cite_note-60) Costs of the disease, as calculated by the World Bank in 2009 may exceed 150 billion USD per year in "high burden" countries.[[60]](#cite_note-60) Lack of progress eradicating the disease may also be due to lack of patient follow-up – as among the 250M [rural migrants in China](/wiki/Migration_in_China).[[60]](#cite_note-60)

### Stigma[[edit](/index.php?title=(none)&action=edit&section=26)]

Slow progress in preventing the disease may in part be due to [stigma](/wiki/Social_stigma) associated with TB.[[60]](#cite_note-60) Stigma may be due to the fear of transmission from affected individuals. This stigma may additionally arise due to links between TB and poverty, and in [Africa, AIDS](/wiki/AIDS_in_Africa).[[60]](#cite_note-60) Such stigmatization may be both real and perceived, for example; in Ghana individuals with TB are banned from attending public gatherings.[[97]](#cite_note-97) Stigma towards TB may result in delays in seeking treatment,[[60]](#cite_note-60) lower treatment compliance, and family members keeping cause of death secret[[97]](#cite_note-97) – allowing the disease to spread further.[[60]](#cite_note-60) At odds is Russia, where stigma was associated with increased treatment compliance.[[97]](#cite_note-97) TB stigma also affects socially marginalized individuals to a greater degree and varies between regions.[[97]](#cite_note-97) One way to decrease stigma may be through the promotion of "TB clubs", where those infected may share experiences and offer support, or through counseling.[[97]](#cite_note-97) Some studies have shown TB education programs to be effective in decreasing stigma, and may thus be effective in increasing treatment adherence.[[97]](#cite_note-97) Despite this, studies on relationship between reduced stigma and mortality are lacking as of 2010, and similar efforts to decrease stigma surrounding AIDS have been minimally effective.[[97]](#cite_note-97) Some have claimed the stigma to be worse than the disease, and healthcare providers may unintentionally reinforce stigma, as those with TB are often perceived as difficult or otherwise undesirable.[[60]](#cite_note-60) A greater understanding of the social and cultural dimensions of tuberculosis may also help with stigma reduction.[[98]](#cite_note-98)

## Research[[edit](/index.php?title=(none)&action=edit&section=27)]

The BCG vaccine has limitations, and research to develop new TB vaccines is ongoing.<ref name=VacRes2011>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> A number of potential candidates are currently in [phase I and II clinical trials](/wiki/Clinical_trial).<ref name=VacRes2011/> Two main approaches are being used to attempt to improve the efficacy of available vaccines. One approach involves adding a subunit vaccine to BCG, while the other strategy is attempting to create new and better live vaccines.<ref name=VacRes2011/> [MVA85A](/wiki/MVA85A), an example of a subunit vaccine, currently in trials in South Africa, is based on a genetically modified [vaccinia](/wiki/Vaccinia) virus.<ref name=Ibanga\_2006>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Vaccines are hoped to play a significant role in treatment of both latent and active disease.[[99]](#cite_note-99) To encourage further discovery, researchers and policymakers are promoting new economic models of vaccine development, including prizes, tax incentives, and [advance market commitments](/wiki/Advance_market_commitments).[[100]](#cite_note-100)[[101]](#cite_note-101) A number of groups, including the [Stop TB Partnership](/wiki/Stop_TB_Partnership),[[102]](#cite_note-102) the South African Tuberculosis Vaccine Initiative, and the [Aeras Global TB Vaccine Foundation](/wiki/Aeras_Global_TB_Vaccine_Foundation), are involved with research.[[103]](#cite_note-103) Among these, the Aeras Global TB Vaccine Foundation received a gift of more than $280 million (US) from the [Bill and Melinda Gates Foundation](/wiki/Bill_and_Melinda_Gates_Foundation) to develop and license an improved vaccine against tuberculosis for use in high burden countries.[[104]](#cite_note-104)[[105]](#cite_note-105) A number of medications are being studied for multi drug resistant tuberculosis including: [bedaquiline](/wiki/Bedaquiline) and [delamanid](/wiki/Delamanid).<ref name=Zumla2012>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Bedaquiline received U.S. [Food and Drug Administration](/wiki/Food_and_Drug_Administration) (FDA) approval in late 2012.[[106]](#cite_note-106) The safety and effectiveness of these new agents are still uncertain, because they are based on the results of a relatively small studies.[[107]](#cite_note-107) However, existing data suggest that patients taking bedaquiline in addition to standard TB therapy are five times more likely to die than those without the new drug,[[108]](#cite_note-108) which has resulted in medical journal articles raising health policy questions about why the FDA approved the drug and whether financial ties to the company making bedaquiline influenced physicians' support for its use [[107]](#cite_note-107)[[109]](#cite_note-109)

## Other animals[[edit](/index.php?title=(none)&action=edit&section=28)]

Mycobacteria infect many different animals, including birds,[[110]](#cite_note-110) rodents,[[111]](#cite_note-111) and reptiles.[[112]](#cite_note-112) The subspecies *Mycobacterium tuberculosis*, though, is rarely present in wild animals.[[113]](#cite_note-113) An effort to eradicate bovine tuberculosis caused by [*Mycobacterium bovis*](/wiki/Mycobacterium_bovis) from the cattle and deer herds of [New Zealand](/wiki/New_Zealand) has been relatively successful.[[114]](#cite_note-114) Efforts in Great Britain have been less successful.[[115]](#cite_note-115)[[116]](#cite_note-116) [Template:As of](/wiki/Template:As_of), tuberculosis appears to be widespread among captive [elephants](/wiki/Elephant) in the US. It is believed that the animals originally acquired the disease from humans, a process called [reverse zoonosis](/wiki/Reverse_zoonosis). Because the disease can spread through the air to infect both humans and other animals, it is a public health concern affecting [circuses](/wiki/Circus) and [zoos](/wiki/Zoo).[[117]](#cite_note-117)[[118]](#cite_note-118)

## References[[edit](/index.php?title=(none)&action=edit&section=29)]

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## External links[[edit](/index.php?title=(none)&action=edit&section=30)]

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