

# Tuberculosis

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## What is tuberculosis?

Tuberculosis (TB) has been with us since ancient times. In the first half of the 20th century, it was generally called “consumption”—an often fatal illness. At that time, when infectious diseases were responsible for the majority of deaths, tuberculosis was a leading cause of death. As special hospitals, called sanatoriums, were used to control the spread of TB along with better nutrition, housing, sanitation and the introduction of antibiotics in the middle of the 20th century, TB and other infectious diseases became curable and less rampant.<sup>1</sup>

Tuberculosis is an airborne infectious disease caused by the bacterium *Mycobacterium tuberculosis* that usually affects the lungs, although other organs and tissues such as the kidney, spine and brain can be affected as well.<sup>2</sup> Fortunately, TB in these parts of the body is usually not infectious.

Want to learn more about tuberculosis? Please view the disease listing at <http://www.lungusa.org/tuberculosis>

Active TB disease of the lungs or throat can be infectious and spread to other people if the infected person coughs, sneezes or spits, releasing the bacteria into the air. People nearby can breathe in these bacteria and become infected if the germs settle in their lungs and begin to multiply.<sup>3</sup> From the lungs, the bacteria can move through the blood to other parts of the body.

Symptoms of active TB disease include prolonged coughing (sometimes including coughing up of blood), repeated night sweats, unexplained weight loss, loss of appetite, fever, chills and general tiredness.<sup>4</sup> Because these signs also may indicate other diseases, a person must consult a healthcare provider to determine their cause.

Not everyone infected with the TB bacteria becomes sick with tuberculosis. If a person’s immune system can successfully fight the infection, they have what is called latent or inactive TB infection. People who have latent TB infection do not feel sick, do not have any symptoms and cannot spread TB to others. The TB

infection may remain inactive for a lifetime, although latent TB infection can become active if the person's immune system becomes weakened (such as with HIV).<sup>5</sup>

People with active TB disease are most likely to spread it to people they spend time with every day. A person with active TB will infect an average of 10 to 15 people each year if they are not properly treated.<sup>6</sup> Repeated exposure to someone with TB disease is generally necessary for infection to take place. Active TB disease can be treated and cured if medical help is sought. TB patients become noninfectious soon after beginning treatment; however, to get rid of TB, therapy must continue for a period of time. People with latent TB infection also can take medicine so they will be less likely to develop active TB disease.

If people with active TB disease do not complete their drug therapy program, they can develop and spread strains of TB that are resistant to available drugs. Multidrug-resistant tuberculosis (MDR-TB) is resistant to two or more of the primary anti-TB drugs, making it very difficult to treat. One MDR-TB case can cost up to \$1 million to treat. Forty-five states and the District of Columbia have reported diagnosing and caring for persons with MDR-TB.<sup>7</sup>

Pockets of drug resistance to TB medications began to appear in the mid-1970s. Drug resistance is troublesome when dealing with any contagious infection, since it indicates the emergence of a strain of “survivor bugs” — bacteria that have developed the ability to withstand antibiotic attack and are passing that ability on to their descendants. In other words, resistance spreads with the infection itself; it therefore tends to concentrate in geographically identifiable areas. The major cause of TB drug resistance is inadequate treatment in terms of drugs used or a patient's failure to complete prescribed treatment.

Extensively drug-resistant tuberculosis (XDR-TB) is an emerging public health threat. This strain is thought to have developed from MDR-TB as they are both resistant to the same primary or first-line anti-TB drugs (isoniazid and rifampin). However, XDR-TB also shows resistance to any fluoroquinolone and at least one of three second-line anti-TB drugs (amikacin, kanamycin or capreomycin).<sup>8</sup> Between 2000 and 2004, there were 17,690 drug-resistant tuberculosis isolates identified worldwide; 20 percent were MDR-TB and 2 percent were XDR-TB.<sup>9</sup>

Want to learn more about XDR-TB? Please view the disease listing at <http://www.lungusa.org/xdrtb>

## Who has tuberculosis?

It is estimated that worldwide nearly one billion people will be newly infected with TB, over 150 million will become sick and 36 million will die from the disease between now and 2020—if TB control is not strengthened.<sup>10</sup> In 2006 there were an estimated 9.2 million new TB cases in the world.<sup>11</sup>

One-third of the increase in global TB cases over the last five years can be attributed to the HIV epidemic.<sup>12</sup> About 10 percent of individuals infected with

latent TB will develop TB disease at some point in their lives. A much higher proportion will develop TB disease if they also are infected with HIV, the virus that causes AIDS. HIV suppresses the immune system, opening the door to new active infection and permitting activation of latent disease. Someone with both latent TB infection and HIV infection has a 7 to 10 percent chance per year of developing active TB disease compared to a 10 percent *lifetime chance* in people without HIV. Between 2005 and 2006, among those TB cases where HIV status was reported, the percentage of TB cases with HIV infection decreased 4.4 percent (from 13.0% to 12.4%). However, the percentage of TB cases with unknown HIV status increased 10.3 percent (from 28.7% to 31.7%). This change in TB cases with HIV infection may be the result of incomplete reporting of HIV test results due to a lack of testing or reporting.<sup>13</sup>

Want to learn more about TB and HIV? Please view the fact sheet at <http://www.lungusa.org/hivtbfactsheet>

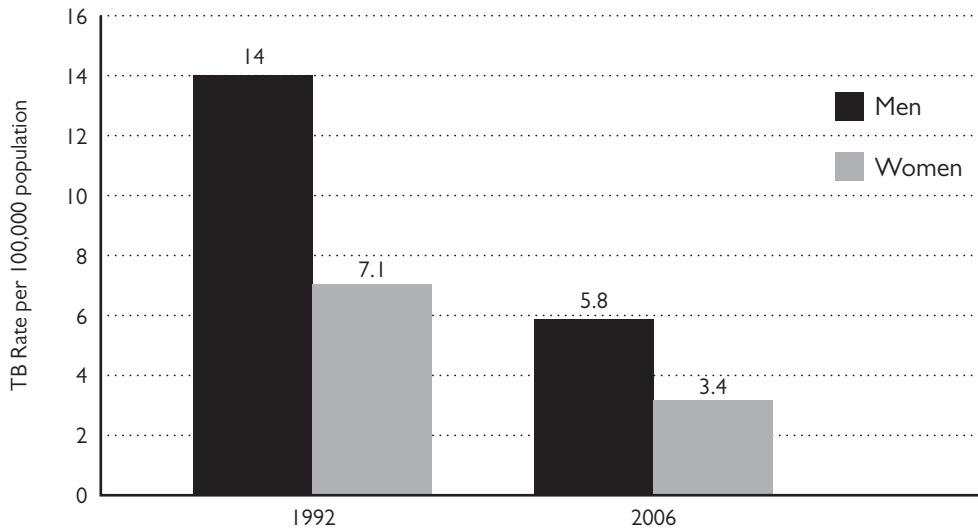
The incidence of TB had been decreasing in the U.S. until 1985 when the number of active TB cases began to rise. It is estimated that approximately 64,000 excess cases of TB occurred in the U.S. between 1985 and 1993.<sup>14</sup> This resurgence was due to a variety of interrelated factors including the HIV epidemic, increased numbers of immigrants, increased poverty, injection drug use and homelessness, poor compliance to drug therapy and an aging population.<sup>15</sup>

During 2007, preliminary data show a total of 13,293 new TB cases in the United States were reported to the Centers for Disease Control and Prevention (CDC)—a 4.2 percent decline from 2006, a 58 percent decline from the 1992 peak of the TB resurgence, and the lowest recorded TB rate (4.4 per 100,000 persons) in the United States since reporting began in 1953.<sup>16</sup> However, the decline is slowing down as noted from an annual average of 7.3 percent decrease between 1993 and 2000 to an average of 3.8 percent decrease between 2000 and 2007.<sup>17</sup>

In part, this decline reflects the impact of federal resources to assist state and local TB-control efforts, wider screening and preventive therapy for those at high risk, and growing support for TB prevention programs among HIV-infected persons.<sup>18</sup>

Want to learn more about tuberculosis trends and data? Please view the *Trend Report on Tuberculosis* at <http://www.lungusa.org/tbtrends>

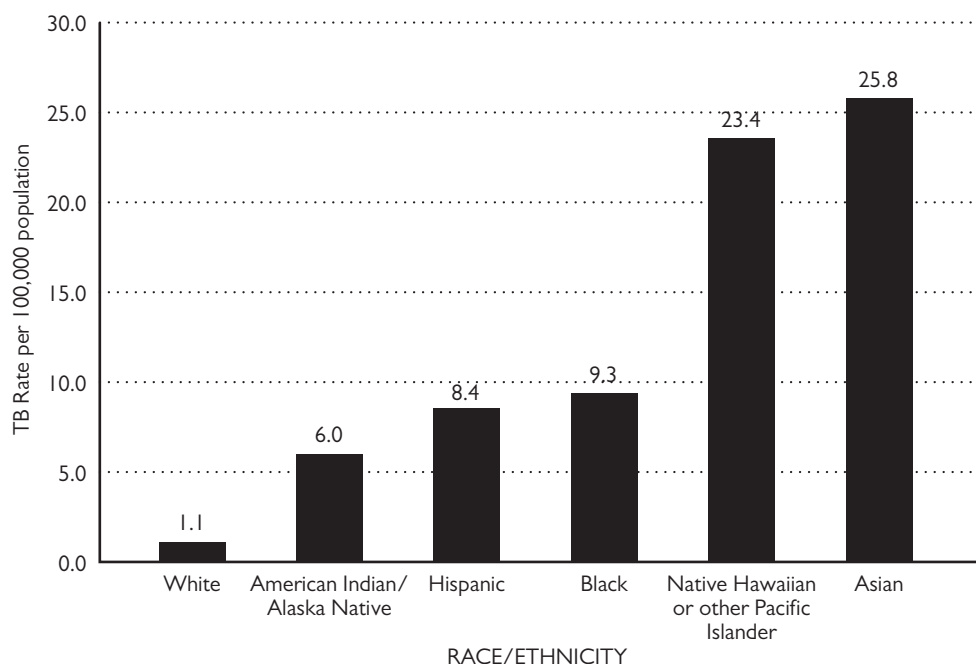
Figure 1 shows that men have a higher TB rate than women; in 2006 it was almost 71 percent higher. The rates of new TB cases in men and women in 2006 were 5.8 and 3.4 per 100,000, respectively. The decrease in the number of cases and the case rate between 1992 and 2006 was notably greater among men than women.<sup>19</sup>

**Figure 1: Tuberculosis Case Rates by Year and Gender, U.S., 1992 and 2006**

Source: Centers for Disease Control and Prevention. Reported Tuberculosis in the United States, 2006. October 2007.

Communities of color and foreign-born persons continued to account for a disproportionate percentage of all reported TB cases in 2007. Based on provisional data, the 2007 TB incidence rate in the United States was almost 23 times greater in non-Hispanic Asians (25.8 per 100,000), over 21 times greater in non-Hispanic Native Hawaiians or other Pacific Islanders (23.4 per 100,000), 8.3 times greater in non-Hispanic Blacks (9.3 per 100,000), over 7 times greater in Hispanics (8.4 per 100,000), and 5.5 times greater in non-Hispanic American Indians/Alaska Natives (6.0 per 100,000) than in non-Hispanic Whites (1.1 per 100,000). Figure 2 shows the tuberculosis rates in 2007 by race/ethnicity in the United States. In 2007, over 71% of TB cases among Blacks were in U.S.-born persons. The TB rate among U.S.-born Blacks was 7.8 times that of Whites born in the United States.<sup>20</sup> Several factors likely contribute to the uneven burden of TB in these communities. Barriers to health care exist among poor and socially excluded communities where TB incidence is 20 times higher compared with higher socioeconomic groups.<sup>21,22</sup> Understanding the role of social determinants of health are key to addressing this disparity.

Want to learn more about TB in diverse communities? Please view the *State of Lung Disease in Diverse Communities 2007* report at <http://www.lungusa.org/solddc-tb>

**Figure 2: Tuberculosis Case Rates by Race/Ethnicity, U.S., 2007\***

Source: Centers for Disease Control and Prevention. Trends in Tuberculosis—United States, 2007. *Morbidity and Mortality Weekly Report*. March 21, 2008; 57(11):281-285.

Note:

\*All categories are non-Hispanic, other than Hispanic.

Preliminary data show that tuberculosis cases among persons born internationally (foreign-born persons) but now living in the United States accounted for 58.5 percent of all reported cases in 2007, compared with 29 percent of reported cases in 1993. The TB case rate among foreign-born persons (20.6 per 100,000) was approximately 9.7 times greater than that for U.S.-born persons (2.1 per 100,000) in 2007.<sup>23</sup> Most cases of active TB disease among foreign-born persons residing in the United States result from initial infection with the tuberculosis germ in the person's country of birth. Four countries of origin (Mexico, the Philippines, India and Vietnam) accounted for over half (51.8%) of all foreign-born cases reported in the United States in 2007.<sup>24</sup>

While the proportion of patients with MDR-TB in the United States has decreased from 2.4 percent in 1993 to approximately 1 percent in 2006, the profile of who has MDR-TB is changing.<sup>25</sup> In 1993, 25.5 percent (103 of 407) of all MDR-TB cases in the United States occurred in foreign-born people. This proportion increased to 80 percent (73 of 91) in 2006. The percentage of U.S.-born patients with MDR-TB has remained less than 0.7 percent since 1998.<sup>26</sup> XDR-TB is still very rare; in 2006 only four cases were reported in the United States and only two had been reported in 2007 as of February 13, 2008. Monitoring of XDR-TB continues in case it shows signs of becoming widespread.<sup>27</sup>

## What is the health impact of tuberculosis?

Tuberculosis is the world's foremost cause of death from a single infectious agent, causing more than 26 percent of avoidable adult deaths in the developing world.<sup>28</sup> The World Health Organization (WHO) estimated that 1.7 million people worldwide died from TB in 2006.<sup>29</sup> In 2005, 646 people died of tuberculosis in the United States, a 1.7 percent decline from 657 deaths in 2004.<sup>30</sup>

While rare, XDR-TB is a serious public health risk. Between 1993 and 2002, XDR-TB patients were 64 percent more likely to die during treatment than MDR-TB patients.<sup>31</sup>

TB takes a heavy toll on the U.S. economy with \$703.1 million in direct health care costs per year. Direct health care costs include \$423.8 million for inpatient care, \$182.3 million for outpatient care, \$72.1 million for screening, \$3.4 million for contact investigations, \$17.9 million for preventive therapy, and \$3.6 million for surveillance and outbreak investigations.<sup>32</sup> The total funding available for TB control worldwide (91% of countries) is estimated at \$2.7 billion in 2008.<sup>33</sup>

Want to learn more about tuberculosis? Please view the fact sheet at <http://www.lungusa.org/tbfactsheet>

## How is tuberculosis diagnosed and managed?

The simplest way to identify a TB infection is by a TB skin test, widely available at health care clinics or providers' offices. One type of skin test, the Mantoux test, is preferred and should be used for screening and diagnosis. In this test, a small amount of testing material is injected under the very top layers of skin on the forearm. In 48 to 72 hours the test is read by a trained health care provider. A significant reaction (redness, swelling) suggests there is TB infection and the health care provider will run more tests, such as a chest x-ray, to determine whether the TB infection is active or latent. In some groups, such as infants under six months of age or those individuals with impaired immunity (such as with HIV infection), the skin test may be negative in the presence of TB infection.<sup>34</sup> People with HIV may need to be retested.

Want to learn more about tuberculosis skin tests? Please view the fact sheet at <http://www.lungusa.org/tbskintestfactsheet>

Tuberculin screening programs should be targeted to each community's high-risk groups. It is extremely important that these screening programs undergo regular evaluation of their usefulness.

Want to learn more about TB skin-testing in high-risk groups and who these groups are? Please visit the Centers for Disease Control and Prevention fact sheet at <http://www.cdc.gov/tb/pubs/tbfactsheets/skintestresults.htm>

Scientists are researching numerous diagnostic tests to replace the time-consuming skin test and sputum analysis (testing matter discharged from the airways) used now. In April 2003, scientists announced the development of a new diagnostic test for TB that is more accurate than the skin test in detecting latent TB infections before people go on to develop active TB.<sup>35</sup>

In 2005, the FDA approved a new blood test (different from above) known as QuantiFERON-TB Gold. It is approved for use in detecting both active TB disease and latent TB infection.<sup>36</sup>

BCG or “bacille Calmette-Guérin” (named for its French developers) is a vaccine used routinely against TB in some countries. BCG is not recommended in the United States for a number of reasons. One is its unsuitability for persons infected with HIV—who, as noted previously, constitute the highest at-risk group for TB.<sup>37</sup> Another is the failure of repeated trials over the years to clearly demonstrate the vaccine’s effectiveness. Results have been inexplicably conflicting, with some studies seemingly showing that it works, others that it is worthless. One recent analysis of those studies suggests that the BCG vaccine may be, at best, 50 percent effective. Generally, vaccines approved for use in the United States are at least 70 percent effective.

In August 1998, the federal Advisory Council for the Elimination of Tuberculosis (ACET) issued a national call for vaccines to combat TB. ACET recommendations include developing a post-infection vaccine for people who already have been exposed to the disease and test positive when given a TB test but have not yet developed active tuberculosis disease.<sup>38</sup> The American Lung Association has urged government health officials to follow the ACET recommendations.

To treat TB infection, the CDC and the American Thoracic Society (ATS) recommend a six- or nine-month treatment schedule consisting of an initial two-month period with the drugs isoniazid, rifampin and pyrazinamide, followed by four or seven months of isoniazid and rifampin for patients with non-drug-resistant TB who follow the treatment plan. Ethambutol (or streptomycin in young children) also should be included in the initial regimen until the results of drug-resistance tests are available.<sup>39</sup>

The CDC and the ATS also have issued treatment guidelines for latent tuberculosis infection. For most individuals with latent TB, these guidelines recommend the nine-month schedule of daily or twice weekly isoniazid as the preferred treatment. The CDC recommends that health care providers use rifampin and pyrazinamide with caution, especially in those patients currently taking other medications that have been associated with liver injury and those with alcoholism, even if alcohol use is discontinued during treatment. However, with careful monitoring, rifampin and pyrazinamide are an option for patients at high risk of developing active TB disease and who are unlikely to complete nine months of isoniazid therapy.<sup>40</sup>

Treatment for MDR-TB is expensive and involves drug therapy over many months or years. Even with the longer course of treatment, the cure rate for MDR-TB is approximately 50 percent, compared to over 90 percent for non-resistant strains of TB. XDR-TB treatment is successful approximately 30 percent of

the time for patients without compromised immune systems; it is even lower for those with compromised immune systems (such as those with HIV/AIDS).<sup>41</sup>

Want to learn more about MDR-TB? Please view the fact sheet at <http://www.lungusa.org/mdr-tbfactsheet>

To counter the increasing problems of MDR-TB and patients who fail to complete the lengthy treatment, the ATS, CDC, and Infectious Diseases Society of America have jointly issued therapy and disease control guidelines for use by health care providers and public health officials. They include recommendations for rapid identification of persons with active disease, relying not only on skin testing (which may give false-negative results) but also on chest x-rays and sputum analysis; and screening of high-risk populations. Other recommendations address the need for comprehensive contact investigation and follow-up; preferred treatment regimens, including management of noncompliance with therapy; environmental control of infection in hospitals and other institutions; and prevention of recurrent infection and protection of health care personnel.<sup>42</sup>

The internationally recommended strategy for TB control by the WHO is directly observed therapy, short-course (DOTS). DOTS aims to decrease TB-related morbidity, deaths and transmission. It combines five elements: political commitment to TB control, access to quality testing methods, directly observed and standardized short-course treatment, adequate supply of drugs, and use of a standardized surveillance and monitoring system. Since DOTS was introduced on a global scale, millions of infectious patients have received effective treatment. DOTS produces cure rates of up to 95 percent even in the poorest of countries. Costing \$11 per patient for a six-month drug supply in some countries, the World Bank has ranked the strategy as one of the most cost-effective of all health interventions.<sup>43</sup> The WHO's new approach to TB control entitled "Stop TB Strategy" goes further than previous efforts to make TB control more comprehensive and effective. DOTS remains at the core of this enhanced approach.<sup>44</sup>

The National Coalition For Elimination of Tuberculosis (NCET) published a report in 2004 warning of a repeat of the neglect that led to the TB resurgence in the United States between 1985 and 1992. It cites the link between the declining rate of decrease in TB cases and the cuts in funding for the CDC's Division of Tuberculosis Elimination. In order to continue to move toward the eradication of TB in the United States and avoid another outbreak, NCET recommended that prevention, detection and treatment efforts should be increased for Blacks in order to eliminate the racial gap in disease rates; the same steps should be taken for foreign-born persons in the United States, especially those who frequently cross the U.S.-Mexico border; DNA fingerprinting efforts should be intensified for all culture-positive TB cases; and more resources should be focused on research of TB diagnosis and treatment.<sup>45</sup>

## What is new in tuberculosis research?

Although TB control programs, like DOTS, have been successful, the decrease

in the TB incidence rate in the United States has slowed down, as mentioned previously. One explanation is that immigrants from high-incidence countries bring TB with them into this country. As immigrants may enter illegally, screening for TB during the immigration process may not be a viable option for reducing TB incidence.

A 2005 study investigated how U.S. investment in tuberculosis control in high-incidence countries could result in a cost savings for the United States by reducing TB among immigrants. The study specifically investigated how U.S. investment in measures like DOTS, tuberculin skin testing and x-ray screening in Haiti, the Dominican Republic and Mexico would impact the tuberculosis-related disease, death, and cost issues in the United States over 20 years. The researchers investigated cost, migration patterns and co-infections (HIV) to predict the impact of U.S. foreign investment. They found that a U.S. investment of \$9.4 million to increase DOTS in Haiti and the Dominican Republic would result in a net savings of \$20 million and in 590 fewer Haitian and Dominican migrant TB infections. However, even more cost effective were the strategies proposed for DOTS implementation in Mexico. The study showed that a \$34.9 million investment in the DOTS strategy there would result in 2,591 fewer TB cases in the United States, 349 fewer deaths and a savings of \$108 million over 20 years. Therefore, it appears that U.S. investment in DOTS control programs in foreign countries has the potential to reduce TB disease and death rates in a very cost-effective manner.<sup>46</sup>

There are also strategies to control the global TB epidemic. While 9.2 million new cases of TB occurred worldwide in 2006, the majority of cases were concentrated in Asia and sub-Saharan Africa.<sup>47</sup> Globally, the number of HIV-positive and MDR-TB co-infected patients continues to increase. While global funding available for TB control has increased greatly since 2002 (reaching \$2 billion), interventions proposed by the Global Plan to Stop TB still require an additional \$1.1 billion in funding. In addition, the national tuberculosis programs of many countries with high incidence fail to conduct TB research, employ skilled staff or have the funding required to carry out the essential operations that would reduce TB rates. To aid in the decline of TB worldwide, the World Health Organization set targets for 2005 of a 70 percent detection rate and an 85 percent cure rate (of all cases). The targets were missed on a global scale as only 60 percent and 84 percent of cases were detected and treated, respectively.<sup>48</sup>

## What is the American Lung Association doing about tuberculosis?

The American Lung Association was founded in 1904 to fight tuberculosis. The National Association for the Study and Prevention of Tuberculosis, as it was known then, was the first nationwide voluntary health organization aimed at conquering a specific disease.

In 1907, Dr. Joseph Wales realized that the small sanatorium on the Brandywine River in Delaware where he worked was down to its last dollar. He wrote

to his cousin, Emily Bissell, asking for help in raising the \$300 needed to keep the sanatorium open. In response, Emily Bissell designed the first American Christmas Seal and borrowed \$40 to have 50,000 of them printed. Before the Christmas season was over, she had raised not \$300, but \$3,000.

The National Association joined the Modern Health Crusade in 1915, taking tuberculosis associations into the nation's schools in a successful master plan for health education.

The National Association embarked on a research program that was to become truly significant in its scope and influence. Representative of the myriad of scientific refinements and improvements were those affecting the x-ray and tuberculin test. The research committee of the National Association began supporting investigations into improved x-ray machines and techniques. The tuberculin skin test and the x-ray became twin tools of diagnosis. The tuberculosis associations, along with health departments and the U.S. Public Health Service, bought and took these tools to locations where people were in order to conduct testing. Examples include screenings at factories in Cleveland and in Harlem as people celebrated the end of World War II.

The National Association launched a medical research and teaching fellowships award program in 1948, targeting young physicians or students in related fields. Some of the country's leading specialists in pulmonary medicine received their start through the National Association's fellowship program.

Currently, the American Lung Association continues to fund research on the basic scientific processes that initiate and control TB infection as well as the molecules and genes in the TB germ that enable it to infect humans and become resistant to drugs. A greater understanding of how the body's immune system protects against TB and why this defense system sometimes fails is being sought. Studies such as these will provide a solid foundation for developing a better TB vaccine.

As more strains of tuberculosis emerge and become resistant to first-line antibiotics, there is an increased reliance on second-line drugs to successfully treat multi-drug-resistant tuberculosis infections. Researchers, funded by the American Lung Association, aim to develop new antibiotic derivatives that regain antibacterial activity against resistant strains with fewer side effects.

Other research is exploring why only some people infected with tuberculosis actually develop the active, infectious disease. Detection and treatment of individuals with latent TB before they become infectious to others could have a huge impact on the incidence of global tuberculosis.

The American Lung Association supports increased U.S. government funding for programs aimed at eliminating TB in the United States as defined by the Institute of Medicine: an incidence rate of less than one TB case per million persons each year. The American Lung Association also supports the Healthy People 2010 goal of less than one new case per 100,000 persons in the United States by 2010.

The American Lung Association also supports increased federal funding to

support the development of the Global Plan to Stop TB and funding for international TB control efforts at the Centers for Disease Control and Prevention, the Fogarty International Center (National Institutes of Health) and the U.S. Agency for International Development.

Thousands of advocates have joined with the American Lung Association to tell Congress that more needs to be done to fight TB. Join the battle against lung disease by visiting <http://lungaction.org>.

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