



## Yesterday

- Tuberculosis (TB) is one of the oldest human diseases. Mummies from ancient Egypt show signs of tubercular decay, and TB was common in both ancient Greece and Imperial Rome.
- Physicians identified TB by its hallmark symptoms: dry, persistent cough, bloody sputum, intermittent fevers, and flushed complexion. Emaciation often preceded a difficult death, giving TB the name “consumption”.
- In 1882, the German physician Robert Koch announced his discovery that a microbe he called *Mycobacterium tuberculosis (Mtb)* causes TB. He also demonstrated that TB can be spread from person to person, carried by droplets expelled when an infected person coughs, sneezes, speaks, or laughs.
- A century ago, TB was a leading cause of death in the United States and in many European countries. TB disease and deaths have declined steadily from the early 1900s due largely to the introduction of effective antibiotics and improvements in living conditions.
- There is an inexpensive TB vaccine available known as Bacille Calmette Guerin, but its effectiveness is limited. More than one billion people have been inoculated since the vaccine was introduced in 1921. It can prevent severe forms of TB in young children but it is not reliable in preventing adult pulmonary TB.
- Before antibiotics became an effective treatment for TB in the 1940s, patients were treated in sanatoria, where therapy included plenty of fresh air, sleep, wholesome food, and exercise.

## Today

- In 1993, the World Health Organization (WHO) declared TB a “global health emergency”. While improvements in global control have been implemented, TB continues to be a leading cause of death from an infectious disease in many countries of the world.
- It is estimated that one-third of the world’s population is infected with the TB bacterium, and that 16.2 million people currently have TB.
- TB remains one of the leading causes of death and illness in the world. Approximately 9.4 million new cases were reported in 2008 by the WHO. For 2008, the WHO reported an estimated 1.8 million deaths from TB, including 500,000 people who were also infected with HIV.
- The greatest number of deaths from TB per capita occurs in Africa, where HIV has led to rapid growth of the TB epidemic, and increases the likelihood of dying from TB.
- From 1985-1992, rates of TB in the United States increased, due largely to the HIV epidemic, cutbacks in public health infrastructure and treatment programs, increasing poverty, homelessness, and drug abuse.
- Since 1992, a large influx of Federal funds and renewed emphasis on TB therapy, prevention, and control again led to TB to decline in the United States. The Centers for Disease Control and Prevention reported nearly 13,000 cases of TB, a reduction of 3.8% from the previous year.
- The TB crisis is intensified by the emergence of drug-resistant forms of the pathogen.
- Because of the long duration and associated side effects of standard TB drug treatment, patients often do not complete the full course of therapy. This fosters emergence of single- and multi-drug resistant TB (MDR-TB) strains. The treatment course for drug-resistant TB is even longer, sometimes more than two years. This therapy usually includes the use of costly second-line drugs that are often less effective and more toxic. In addition, patients with drug-resistant TB may remain infectious for long periods, thereby increasing the chance for transmission of resistant strains.
- A virtually untreatable form of MDR-TB, called extensively drug resistant TB (XDR-TB), was first defined in 2006. Global incidence of XDR-TB is difficult to determine. However, in 2008, it was estimated that out of 10,000 TB patients, between 300 and 400 have drug-resistant TB and of those, 5-6 patients have the more resistant form, XDR-TB.

- The devastating global impact of TB makes it a high priority research area. NIH is supporting research to develop novel TB vaccines, drugs, and diagnostics through studies to characterize how the bacterium and host interact and to better understand how drug resistance develops and can be avoided in the future.
- NIH is expanding its existing HIV/AIDS clinical trial networks for TB studies, which may result in novel collaborations and critical data to improve TB control and care strategies.
- Recent advances in NIH supported TB research that may improve control of TB worldwide:

#### *Diagnostics*

- A new diagnostic test that can identify TB and drug resistance directly from patient samples within 2 hours is being evaluated in late stage clinical testing. Currently available diagnostics take several months to diagnose drug resistant TB.
- Characterization of antibodies and other components of the immune response may help identify people who are infected with *Mtb* and are at the highest risk of developing active disease.
- The NIAID Tuberculosis Clinical Diagnostics Research Consortium (<https://www.tbcdrc.org/home.aspx>) provides expertise and infrastructure to help evaluate early stage diagnostics for their potential to make significant contributions to TB diagnosis in high burden countries.

#### *Treatment*

- Several promising new drug candidates have entered clinical trials and other drug candidates are being tested in the laboratory and in animals.
- Researchers are evaluating shorter treatment regimens that may make it easier for people to complete drug therapy.
- Several antibiotics that are already approved by the FDA for other infections are being evaluated as additions to current TB drug regimens to improve treatment of drug-resistant TB.
- NIAID researchers are conducting two new clinical trials in South Korea that will address how drugs penetrate into lesions of TB patients undergoing lung surgery. The researchers also will evaluate new drugs for XDR-TB.

#### *Vaccines*

- Several new vaccine candidates are in advanced clinical trials, and additional candidates are being analyzed in animal studies.
- Research is underway to better understand how the Bacille Calmette Guerin vaccine provides protection against TB in children to help improve the effectiveness of this vaccine.

### **Tomorrow**

- These and future priority research areas will improve our understanding of TB and its various manifestations and improve our ability to prevent and treat this deadly disease. Areas of interest include:
  - the basic biology of TB in humans and the development and spread of MDR- and XDR-TB;
  - technologies to rapidly diagnose drug resistance in TB patients;
  - the interplay between TB, HIV, and other co-infections; and
  - the development of effective strategies to prevent infection with *Mtb* or the development of active TB disease.

***Additional information about TB and NIH-supported TB research can be found at:***

<http://www.niaid.nih.gov/topics/tuberculosis/Pages/Default.aspx>

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