Advances in Pediatrics 62 (2015) 59–90
ADVANCES IN PEDIATRICS

# Childhood Tuberculosis
## An Overview

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**Keywords**

• Childhood tuberculosis • *Mycobacterium tuberculosis* • Tuberculin skin test • Interferon-γ release assay

**Key points**

- Tuberculosis (TB) is one of the oldest diseases known to mankind and still ranks as the second leading cause of death from infection worldwide.
- Transmission of *Mycobacterium tuberculosis* occurs person to person via inhalation of mucous droplets that become airborne when an individual with pulmonary or laryngeal TB coughs, sneezes, speaks, laughs, or sings.
- Even though TB incidence in the United States is low, pediatricians in this country should always consider TB as cause of a child's symptoms, especially those who traveled to endemic areas.
- The Centers for Disease Control and Prevention guidelines indicate that a tuberculin skin test (TST) or an interferon-γ release assay (IGRA) may be used to test for latent TB infection. An IGRA is preferred over the TST when testing people who are Bacille-Calmette-Guérin (BCG) vaccinated or are unlikely to return for TST reading.
- Multidrug-resistant TB strains are resistant to isoniazid and rifampin, while extensively drug-resistant TB is also resistant to fluoroquinolones and at least one of the second-line injectable drugs (amikacin, kanamycin, and capreomycin).
- BCG vaccine protects young children against severe forms of the disease (eg, TB meningitis) and disseminated TB. It has variable efficacy against pulmonary TB.

## INTRODUCTION

Is it tuberculosis (TB) or another pulmonary process? Is it latent or active TB? If it is active TB, is it due to a susceptible or resistant strain? Will my pediatric patient tolerate the drug regimen that was prescribed without having side effects? How did this bacillus manage to survive millions of years in nature and thousands of years in our bodies and make best use of our immune

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0065-3101/15/$ – see front matter
http://dx.doi.org/10.1016/j.yapd.2015.04.001 © 2015 Elsevier Inc. All rights reserved.

system? Will there ever be a vaccine as good as the polio vaccine to eradicate TB? All these and more questions are addressed in this article, starting with a brief historical overview, then moving to the most recent World Health Organization (WHO) report that was released in 2014. Next is the pathogenesis section, with reference to Tobin's work and the utilization of the zebrafish model in trying to elucidate how this organism takes over our immune system in the smartest of ways to survive. This article then addresses the challenges that clinicians face in trying to make the correct diagnosis and choosing the right drug regimen in light of the finding that techniques to diagnose and check drug susceptibilities have been lacking in sensitivity. The emerging concern of multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB is discussed as well. Finally, this article addresses what the future holds in regards to new vaccines in clinical trials.

## HISTORY

TB is one of the oldest diseases known to mankind [1]. It is possible that the genus Mycobacterium originated more than 150 million years ago and that a progenitor of *Mycobacterium tuberculosis* (Mtb) was present in East Africa as early as 3 million years ago. It is likely that all modern members of the *Mycobacterium tuberculosis* complex (MTBC), including not only Mtb but also its African variants *M africanum* and *M canettii* as well as *M bovis* had a common African ancestor about 35,000 to 15,000 years ago [2]. Recent work based on phylogenetic analysis of Mtb strains goes further to suggest that Mtb has been infecting humans for more than 70,000 years [3].

Given the long historical relationship between TB and humans, it may seem surprising that TB still ranks as the second leading cause of death from infection worldwide. However, the long coevolution of the human immune system with Mtb may also explain the remarkable ability of this bacterium to evade the immune response.

In Egypt, TB was documented more than 5000 years ago with evidence of Pott deformities in Egyptian mummies in early Egyptian art. There are written texts as well describing TB in India and China 3300 and 2300 years ago, respectively [2]. In Greece, it was called phthisis, and Hippocrates wrote in his *Book I, Of the Epidemics*: "Consumption was the most considerable of the diseases which then prevailed, and the only one which proved fatal to many persons" [2]. In the middle ages, scrofula was treated with the "royal touch" by monarchs in Europe [2,4]. TB has claimed its victims throughout much of known human history. It reached epidemic proportions in Europe and North America during the eighteenth and nineteenth centuries.

It was René Théophile Hyacinthe Laennec who clearly elucidated the pathogenesis of TB early in the nineteenth century. Jean-Antoine Villemin demonstrated the infectious nature of TB in 1865 after inoculating a rabbit with pus taken from a tuberculous cavity [2]. On March 24, 1882, Hermann Heinrich Robert Koch made his famous presentation, *Die Aetiologie der Tuberculose*, demonstrating that the tubercle bacillus was the causative agent of TB [5].

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