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## HIV and Tuberculosis

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### INTRODUCTION

In 2015, the World Health Organization (WHO) announced that tuberculosis (TB), an infection caused by *Mycobacterium tuberculosis* (MTb), is now the leading cause of death worldwide due to an infectious disease, surpassing human immunodeficiency virus (HIV).<sup>1</sup> Among HIV-infected patients, TB is the most common opportunistic infection and the most deadly, accounting for one in every three HIV-related deaths in 2015.

The Centers for Disease Control and Prevention (CDC) guidelines recommend treating TB and HIV concurrently to reduce mortality.<sup>2</sup> However, managing these two disease states simultaneously is challenging due to the possibility of drug interactions, overlapping toxicities, immune reconstitution inflammatory syndrome (IRIS), and poor patient adherence to complex drug regimens. Pharmacists can play an active role in managing drug interactions, treatment of IRIS, and finding innovative ways to increase patient adherence.

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### EPIDEMIOLOGY

Approximately one-third of the world's population is believed to be infected with TB. Worldwide, WHO estimated 9.6 million new cases of active TB in 2014.<sup>1</sup> Of those new cases, 12% (1.1 million) were HIV-positive. An estimated 1.5 million people died from TB in 2014; one-fourth of those were HIV-positive. The vast majority of TB and HIV/TB cases occur in developing nations. Three-fourths of cases of new persons co-infected with HIV/TB occurred in Africa, and there were an estimated 480,000 cases of multidrug-resistant (MDR) TB. The WHO reports that an estimated 43 million lives have been saved in the last 15 years due to effective diagnosis and treatment but emphasizes that TB remains a deadly worldwide problem, especially in HIV patients.

In 2014, 9,421 cases of TB were reported in the United States.<sup>3</sup> Foreign-born persons accounted for 66% of those cases. Approximately 500 people die each year due to TB. In the United States, 8.6% of HIV-infected patients are co-infected with TB, the majority of cases also occurring in foreign-born persons. Ninety-one cases of TB were MDR-TB. Since the early 1990s, an overall decline in TB, MDR-TB, and patients co-infected with HIV and TB has continued; however, the rate of decline has slowed in recent years. Additionally, an increase in the number of foreign-born persons with TB and HIV/TB has increased each year since 1993.

## MICROBIOLOGY

MTb is an acid-fast, rod-shaped, obligate aerobe.<sup>4</sup> Tissues with high oxygen concentrations, such as lung tissue, are ideal environments for the survival of MTb. Especially in immunocompromised hosts, MTb can spread to other organs. The cell wall of MTb consists of a thick waxy coating, rich in lipids (primarily mycolic acids) and peptidoglycan. The thick cell wall prevents destruction from lysosomal enzymes and facilitates survival within macrophages. The cell wall structure also prevents the penetration of many antibiotics. The waxy coating resists Gram staining; Ziehl-Neelsen staining must be used to identify the bacteria. Two media are used to grow MTb: *Middlebrook's medium*, an agar-based medium, and *Lowen-Jensen medium*, an egg-based medium. MTb replicates slowly (15 to 20 hours), and inhibitors to faster-growing bacteria must be added to the media to prevent contamination. The time for visual growth of colonies is 4 to 6 weeks for both media.

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## TRANSMISSION AND INFECTION CONTROL

MTb is transmitted via droplets that are expelled through the air by coughing (sneezing, shouting, etc).<sup>2</sup> Infection is related to the amount of bacilli within these droplets. Infection occurs following the inhalation of droplets and their movement through the respiratory tract to the alveoli. In most immunocompetent individuals, the immune system prevents any further replication of MTb. Despite the presence of tubercle bacilli in the body, these individuals are asymptomatic and are not infectious. Immunologic test results, however, will be positive. These individuals are considered to have *latent TB infection* (LTBI). Individuals unable to prevent replication of MTb develop symptoms and can spread the disease to others. They are said to have *active TB*.

Transmission of active TB is possible between patients with TB and healthcare workers in the healthcare setting; therefore, control measures should be in place to mitigate transmission. The CDC recommends that a TB infection control program consist of a three-tiered hierarchy of control measures: (1) administrative measures, (2) environmental controls, and (3) the use of protective respiratory equipment.<sup>2</sup> Administrative measures refer to having procedures and personnel in place to reduce exposure to TB patients. Such measures include not only managing patients with TB but having a control plan, educating and training healthcare workers on TB, and assigning persons to be in charge of TB infection control. Environmental controls refer to the physical containment of the infection source through the use of proper ventilation and airflow. Finally, the use of protective respiratory equipment (e.g., masks) should be employed to reduce exposure to infective droplet nuclei.

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## DIAGNOSIS OF ACTIVE TB

The classical signs of active TB typically include fatigue, night sweats, loss of appetite, fever, and unexplained weight loss.<sup>2</sup> *Pulmonary TB* is the most common form