

# HOSPITAL PHYSICIAN®

## INFECTIOUS DISEASES BOARD REVIEW MANUAL

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The *Hospital Physician Infectious Diseases Board Review Manual* is a study guide for fellows and practicing physicians preparing for board examinations in infectious diseases. Each manual reviews a topic essential to current practice in the subspecialty of infectious diseases.

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## Diagnosis and Treatment of Latent Tuberculosis Infection

### Contributors:

**Edward D. Chan, MD**

*Department of Medicine*

*National Jewish Medical and Research Center*

*Denver, CO*

**Kathryn Chmura, BA**

*Department of Medicine*

*National Jewish Medical and Research Center*

*Denver, CO*

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Cover Illustration by May Cheney

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## Diagnosis and Treatment of Latent Tuberculosis Infection

Edward D. Chan, MD, and Kathryn Chmura, BA

*“[I]n the treatment of Consumption, . . . in the commencement [it] is easy to cure and difficult to understand; but when it has neither been discovered in due time nor treated upon a proper principle, it becomes easy to understand and difficult to cure.”*

—Niccolo Machiavelli (1469–1527)

### INTRODUCTION

The World Health Organization estimates that one third of the world’s population is latently infected with *Mycobacterium tuberculosis*.<sup>1</sup> From this pool, approximately 9 million active tuberculosis (TB) cases emerge annually, resulting in 2 to 3 million deaths and making TB the second most common cause of death by a single infectious agent in the world.<sup>2</sup> The AIDS epidemic is responsible for the rise in TB cases in many parts of the world (in approximately 1.5 million active TB cases per year there is co-infection with HIV), and co-infection with both agents contributes significantly to TB-related mortality. Ninety-five percent of cases of TB occur in the developing world. Annual incidence rates exceed 300 cases per 100,000 persons in much of sub-Saharan Africa, the Indonesian and Philippine archipelagos, Afghanistan, Bolivia, and Peru.<sup>1,3</sup> Areas with the highest incidence include the most populous nations of India (1.9 million cases/yr) and China (1.4 million cases/yr). In North America, cases occur disproportionately among foreign-born individuals from TB-endemic countries, HIV-infected persons, institutionalized persons, and minorities. The United States saw a decline in TB cases up to the early 1980s due mostly to public health programs, but HIV/AIDS, immigration, and waning TB programs led to a resurgence of TB in the late 1980s and early 1990s.<sup>4</sup> The annual incidence is now declining again, but as TB becomes less frequent in this country, decreased awareness of disease manifestations may lead to delays in diagnosis and treatment.

As indicated by the opening quotation, hundreds of years before the cause of TB was elucidated it was recognized that TB may exist in 2 different forms: infection and disease. Infection occurs by airborne transmission

of tubercle bacilli from person to person. Primary infection is usually asymptomatic but may present with mild nonspecific symptoms, symptoms of acute pneumonia, or severe disseminated disease. After primary infection, *M. tuberculosis* spreads from the lungs to hilar lymph nodes and then throughout the bloodstream, generally resulting in latent TB infection (LTBI) (Figure 1). Most cases of active TB are due to reactivation of latent infection. Reactivation TB is typically a chronic destructive pneumonia with cavitation and fibrosis involving the lung apices and superior segments of lower lobes. This paper focuses on the diagnosis and treatment of LTBI as opposed to management of active disease. Treatment of active TB is discussed in a recent publication and the latest (2003) guidelines from the American Thoracic Society (ATS)/Centers for Disease Control and Prevention/Infectious Diseases Society of America.<sup>5,6</sup>

### CASE STUDY

#### INITIAL PRESENTATION

A 50-year-old woman who works as a nursing assistant at a nursing home receives a tuberculin skin test using 5 units of purified protein derivative (PPD) as part of an annual screening program. After 72 hours, the diameter of the induration is 14 mm, whereas it was 3 mm the previous year. She is asymptomatic, healthy, and does not use tobacco or alcohol. She is not on any medications and is HIV-negative.

- What are the exogenous risk factors for TB infection?
- What are the endogenous risk factors for reactivation TB?

#### RISK FACTORS

Close contact with a person who has pulmonary TB represents the single most important risk factor for TB transmission. Factors associated with a high burden of tubercle bacilli further increase this risk and include