Chapter 2
Transmission and Pathogenesis of Tuberculosis

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Chapter Objectives

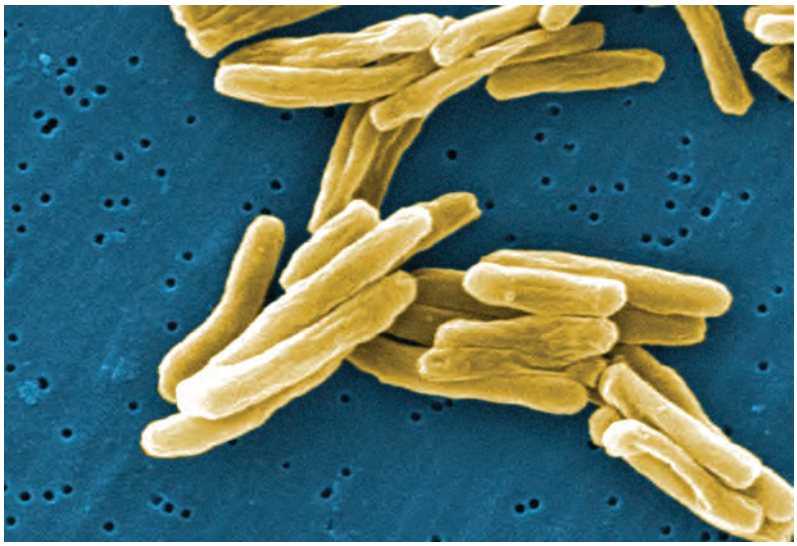
After working through this chapter, you should be able to

- Identify ways in which tuberculosis (TB) is spread;
- Describe the pathogenesis of TB;
- Identify conditions that increase the risk of TB infection progressing to TB disease;
- Define drug resistance; and
- Describe the TB classification system.

Introduction

TB is an airborne disease caused by the bacterium *Mycobacterium tuberculosis* (*M. tuberculosis*) (Figure 2.1). *M. tuberculosis* and seven very closely related mycobacterial species (*M. bovis, M. africanum, M. microti, M. caprae, M. pinnipedii, M. canetti* and *M. mungi*) together comprise what is known as the *M. tuberculosis* complex. Most, but not all, of these species have been found to cause disease in humans. In the United States, the majority of TB cases are caused by *M. tuberculosis*. *M. tuberculosis* organisms are also called tubercle bacilli.

Figure 2.1
Mycobacterium tuberculosis

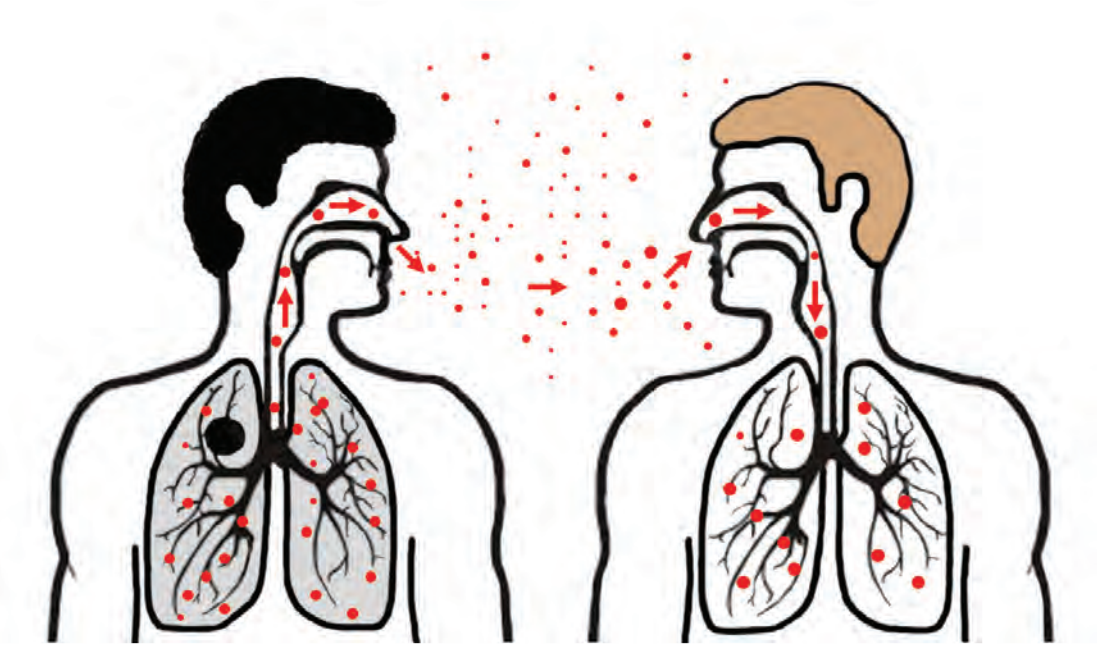


Transmission of TB

M. tuberculosis is carried in airborne particles, called droplet nuclei, of 1–5 microns in diameter. Infectious droplet nuclei are generated when persons who have pulmonary or laryngeal TB disease cough, sneeze, shout, or sing. Depending on the environment, these tiny particles can remain suspended in the air for several hours. *M. tuberculosis* is transmitted through the air, **not** by surface contact. Transmission occurs when a person inhales droplet nuclei containing *M. tuberculosis*, and the droplet nuclei traverse the mouth or nasal passages, upper respiratory tract, and bronchi to reach the alveoli of the lungs (Figure 2.2).

***M. tuberculosis* is carried in airborne particles, called droplet nuclei, of 1–5 microns in diameter. Infectious droplet nuclei are generated when persons who have pulmonary or laryngeal TB disease cough, sneeze, shout, or sing.**

Figure 2.2
Transmission of TB
TB is spread from person to person through the air. The dots in the air represent droplet nuclei containing tubercle bacilli.



Factors that Determine the Probability of *M. tuberculosis* Transmission

There are four factors that determine the probability of transmission of *M. tuberculosis* (Table 2.1).

Table 2.1
Factors that Determine the Probability of Transmission of *M. tuberculosis*

Factor	Description
Susceptibility	Susceptibility (immune status) of the exposed individual
Infectiousness	Infectiousness of the person with TB disease is directly related to the number of tubercle bacilli that he or she expels into the air. Persons who expel many tubercle bacilli are more infectious than patients who expel few or no bacilli (Table 2.2) (see Chapter 7, TB Infection Control)
Environment	Environmental factors that affect the concentration of *M. tuberculosis* organisms (Table 2.3)
Exposure	Proximity, frequency, and duration of exposure (Table 2.4)

Table 2.2
Characteristics of a Patient with TB Disease that Are Associated with Infectiousness

Factor	Description
Clinical	• Presence of cough, especially lasting 3 weeks or longer • Respiratory tract disease, especially with involvement of the larynx (highly infectious) • Failure to cover the mouth and nose when coughing • Inappropriate or inadequate treatment (drugs, duration)
Procedure	• Undergoing cough-inducing or aerosol-generating procedures (e.g., bronchoscopy, sputum induction, administration of aerosolized medications)
Radiographic and laboratory	• Cavitation on chest radiograph • Positive culture for *M. tuberculosis* • Positive AFB sputum smear result

The infectiousness of a person with TB disease is directly related to the number of tubercle bacilli that he or she expels into the air. Persons who expel many tubercle bacilli are more infectious than patients who expel few or no bacilli.

Table 2.3
Environmental Factors that Enhance the Probability that *M. tuberculosis* Will Be Transmitted

Factor	Description
Concentration of infectious droplet nuclei	The more droplet nuclei in the air, the more probable that *M. tuberculosis* will be transmitted
Space	Exposure in small, enclosed spaces
Ventilation	Inadequate local or general ventilation that results in insufficient dilution or removal of infectious droplet nuclei
Air circulation	Recirculation of air containing infectious droplet nuclei
Specimen handling	Improper specimen handling procedures that generate infectious droplet nuclei
Air Pressure	Positive air pressure in infectious patient's room that causes *M. tuberculosis* organisms to flow to other areas

Table 2.4
Proximity and Length of Exposure Factors that Can Affect Transmission of *M. tuberculosis*

Factor	Description
Duration of exposure to a person with infectious TB	The longer the duration of exposure, the higher the risk for transmission
Frequency of exposure to infectious person	The more frequent the exposure, the higher the risk for transmission
Physical proximity to infectious person	The closer the proximity, the higher the risk for transmission

Young children with pulmonary and laryngeal TB disease are less likely than adults to be infectious. This is because children generally do **not** produce sputum when they cough. However, transmission from children can occur. Therefore, children and adolescents with TB disease should be evaluated for infectiousness using the same criteria as adults. These criteria include presence of cough lasting 3 weeks or longer; cavitation on chest radiograph; or respiratory tract disease with involvement of lungs, airways, or larynx (see Chapter 3, Testing for Tuberculosis Infection and Disease).

Young children with pulmonary and laryngeal TB disease are less likely than adults to be infectious.

Study Questions

2.1 How is TB spread? (circle the one best answer)

A. From sharing eating utensils with an infected person.

B. From person to person through the air.

C. From insect bites.

D. From touching surfaces that are contaminated with *M. tuberculosis*.

2.2 The probability that *M. tuberculosis* will be transmitted depends on… (circle the one best answer)

A. Susceptibility (immune status) of the exposed individual.

B. Infectiousness of the person with TB.

C. Proximity, frequency, and duration of exposure.

D. Environmental factors that affect the concentration of *M. tuberculosis* organisms.

E. A, B, C, and D are correct.

Are the following statements about infectiousness true or false? (Choose the one best answer and write the letter for the correct answer on the line next to the question number.)

Statement about Infectiousness		True or False
____ **2.3**	The infectiousness of a person with TB disease is directly related to the number of tubercle bacilli that he or she expels into the air.	**A.** True **B.** False
____ **2.4**	Persons who expel few or no tubercle bacilli are just as infectious as those who expel many bacilli.	

2.5 Which of the following environmental factors do NOT increase the probability that *M. tuberculosis* will be transmitted? (circle the one best answer)

A. Exposure in small enclosed spaces.

B. Inadequate local or general ventilation that results in insufficient dilution or removal of infectious droplet nuclei.

C. Recirculation of air containing infectious droplet nuclei.

D. Improper specimen handling procedures that generate infectious droplet nuclei.

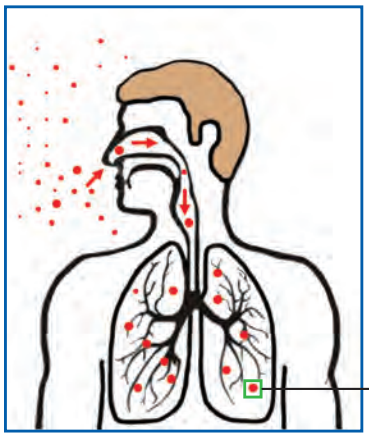
E. Negative pressure in an infectious TB patient's room.

Pathogenesis of TB

Infection occurs when a person inhales droplet nuclei containing tubercle bacilli that reach the alveoli of the lungs. These tubercle bacilli are ingested by alveolar macrophages; the majority of these bacilli are destroyed or inhibited. A small number may multiply intracellularly and are released when the macrophages die. If alive, these bacilli may spread by way of lymphatic channels or through the bloodstream to more distant tissues and organs (including areas of the body in which TB disease is most likely to develop: regional lymph nodes, apex of the lung, kidneys, brain, and bone). This process of dissemination primes the immune system for a systemic response. Further details about pathogenesis of latent tuberculosis infection (LTBI) and TB disease are described in Figure 2.3.

Figure 2.3
Pathogenesis of LTBI and TB Disease

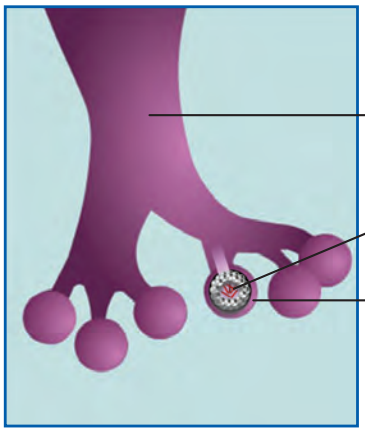
1.



Area of detail for boxes 2, 4, and 5

Droplet nuclei containing tubercle bacilli are inhaled, enter the lungs, and travel to the alveoli.

2.



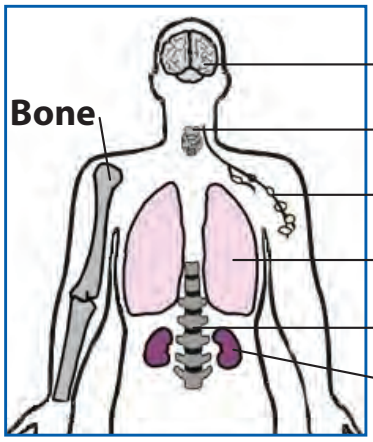
Bronchiole

Tubercle bacilli

Alveoli

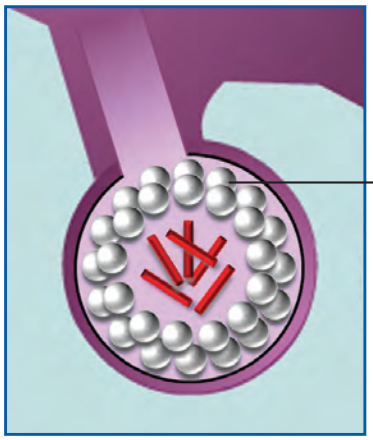
Tubercle bacilli multiply in the alveoli.

3.



A small number of tubercle bacilli enter the bloodstream and spread throughout the body. The tubercle bacilli may reach any part of the body, including areas where TB disease is more likely to develop (such as the brain, larynx, lymph node, lung, spine, bone, or kidney).

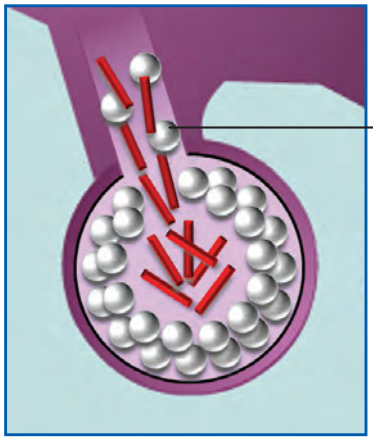
4.



Special immune cells form a barrier shell (in this example, bacilli are in the lungs)

Within 2 to 8 weeks, special immune cells called macrophages ingest and surround the tubercle bacilli. The cells form a barrier shell, called a granuloma, that keeps the bacilli contained and under control **(LTBI)**.

5.



Shell breaks down and tubercle bacilli escape and multiply

If the immune system **cannot** keep the tubercle bacilli under control, the bacilli begin to multiply rapidly (**TB disease**). This process can occur in different areas in the body, such as the lungs, kidneys, brain, or bone (see diagram in box 3).

Infection occurs when a person inhales droplet nuclei containing tubercle bacilli that reach the alveoli of the lungs.

Latent Tuberculosis Infection (LTBI)

Persons with LTBI have *M. tuberculosis* in their bodies, but do **not** have TB disease and **cannot** spread the infection to other people. A person with LTBI is **not** regarded as having a case of TB. The process of LTBI begins when extracellular bacilli are ingested by macrophages and presented to other white blood cells. This triggers the immune response in which white blood cells kill or encapsulate most of the bacilli, leading to the formation of a granuloma. At this point, LTBI has been established. LTBI may be detected by using the tuberculin skin test (TST) or an interferon-gamma release assay (IGRA) (see Chapter 3, Testing for Tuberculosis Disease and Infection). It can take 2 to 8 weeks after the initial TB infection for the body's immune system to be able to react to tuberculin and for the infection to be detected by the TST or IGRA. Within weeks after infection, the immune system is usually able to halt the multiplication of the tubercle bacilli, preventing further progression.

Persons with LTBI have *M. tuberculosis* in their bodies, but do not have TB disease and cannot spread the infection to other people.

TB Disease

In some people, the tubercle bacilli overcome the immune system and multiply, resulting in progression from LTBI to TB disease (Figure 2.4). Persons who have TB disease are usually infectious and may spread the bacteria to other people. The progression from LTBI to TB disease may occur at any time, from soon to many years later. Body fluid or tissue from the disease site should be collected for AFB smear and culture (see Chapter 5, Treatment for Latent Tuberculosis Infection). Positive culture for *M. tuberculosis* confirms the diagnosis of TB disease. Table 2.5 indicates the differences between LTBI and TB disease.

Persons who have TB disease may spread the bacteria to other people.

Figure 2.4
Progression of TB
People who are exposed to *M. tuberculosis* may or may **not** develop LTBI.
People with LTBI may or may **not** develop TB disease.

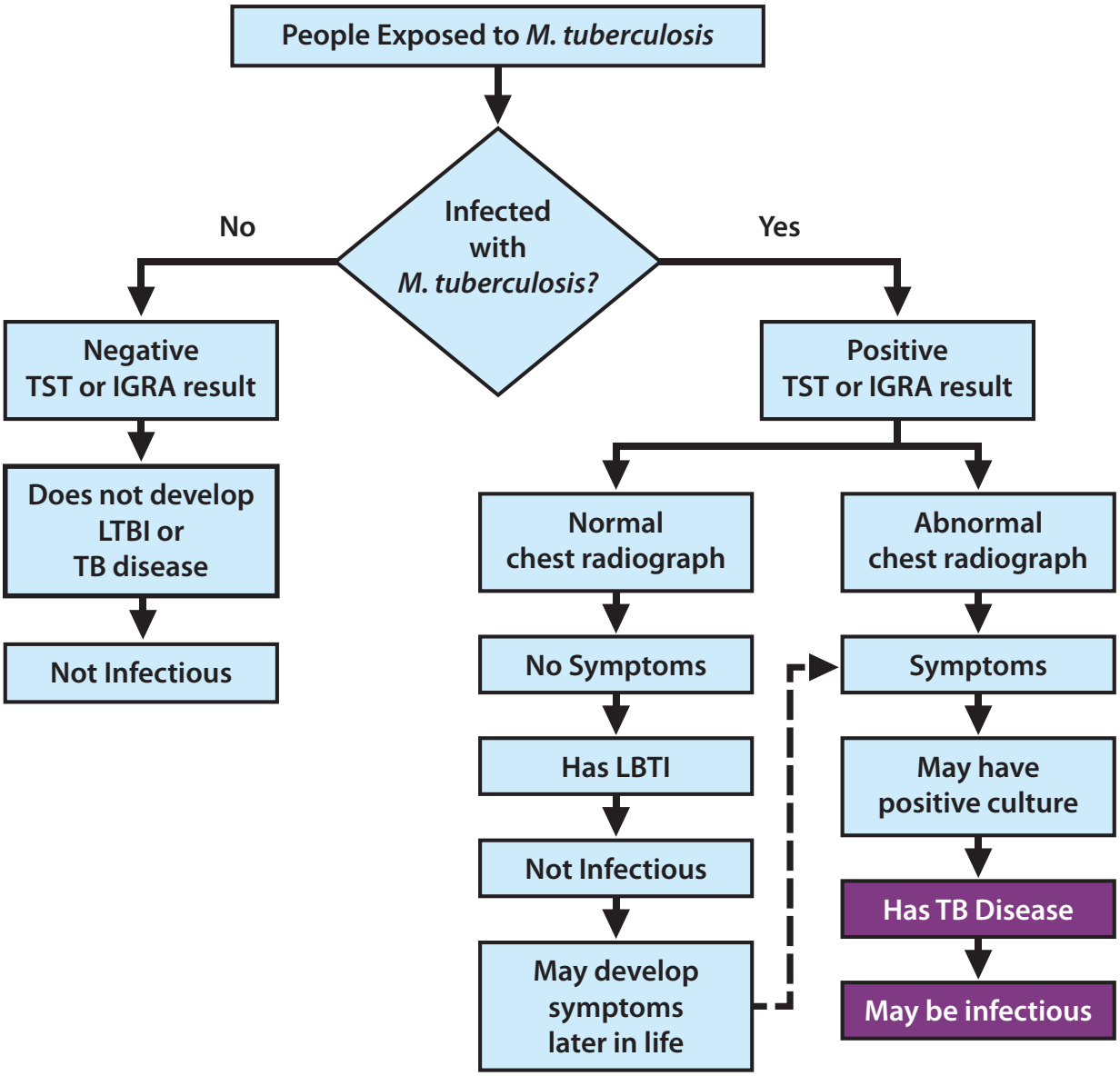


Table 2.5
LTBI vs. TB Disease

Person with LTBI (Infected)	Person with TB Disease (Infectious)
Has a small amount of TB bacteria in his/her body that are alive, but inactive	Has a large amount of active TB bacteria in his/her body
Cannot spread TB bacteria to others	May spread TB bacteria to others
Does **not** feel sick, but may become sick if the bacteria become active in his/her body	May feel sick and may have symptoms such as a cough, fever, and/or weight loss
Usually has a TB skin test or TB blood test reaction indicating TB infection	Usually has a TB skin test or TB blood test reaction indicating TB infection
Radiograph is typically normal	Radiograph may be abnormal
Sputum smears and cultures are negative	Sputum smears and cultures may be positive
Should consider treatment for LTBI to prevent TB disease	Needs treatment for TB disease
Does **not** require respiratory isolation	May require respiratory isolation
Not a TB case	A TB case

Risk of Developing TB Disease over a Lifetime

Without treatment, approximately 5% of persons who have been infected with *M. tuberculosis* will develop disease in the first year or 2 after infection, and another 5% will develop disease sometime later in life. Thus, without treatment, approximately 10% of persons with normal immune systems who are infected with *M. tuberculosis* will develop TB disease at some point in their lives.

Sites of TB Disease

TB disease can occur in pulmonary and extrapulmonary sites.

Pulmonary

TB disease most commonly affects the lungs; this is referred to as pulmonary TB. In 2011, 67% of TB cases in the United States were exclusively pulmonary. Patients with pulmonary TB usually have a cough and an abnormal chest radiograph, and may be infectious. Although the majority of TB cases are pulmonary, TB can occur in almost any anatomical site or as disseminated disease.

Extrapulmonary

Extrapulmonary TB disease occurs in places other than the lungs, including the larynx, the lymph nodes, the pleura, the brain, the kidneys, or the bones and joints. In HIV-infected persons, extrapulmonary TB disease is often accompanied by pulmonary TB. Persons with extrapulmonary TB disease usually are **not** infectious unless they have 1) pulmonary disease in addition to

extrapulmonary disease; 2) extrapulmonary disease located in the oral cavity or the larynx; or 3) extrapulmonary disease that includes an open abscess or lesion in which the concentration of organisms is high, especially if drainage from the abscess or lesion is extensive, or if drainage fluid is aerosolized. Persons with TB pleural effusions may have underlying pulmonary TB that is masked on chest radiograph because the effusion fluid compresses the lung. These patients should be considered infectious until pulmonary TB disease is excluded.

Miliary TB

Miliary TB occurs when tubercle bacilli enter the bloodstream and disseminate to all parts of the body, where they grow and cause disease in multiple sites. This condition is rare but serious. "Miliary" refers to the radiograph appearance of millet seeds scattered throughout the lung. It is most common in infants and children younger than 5 years of age, and in severely immunocompromised persons. Miliary TB may be detected in an individual organ, including the brain; in several organs; or throughout the whole body. The condition is characterized by a large amount of TB bacilli, although it may easily be missed, and is fatal if untreated. Up to 25% of patients with miliary TB may have meningeal involvement.

Central Nervous System

When TB occurs in the tissue surrounding the brain or spinal cord, it is called tuberculous meningitis. Tuberculous meningitis is often seen at the base of the brain on imaging studies. Symptoms include headache, decreased level of consciousness, and neck stiffness. The duration of illness before diagnosis is variable and relates in part to the presence or absence of other sites of involvement. In many cases, patients with meningitis have abnormalities on a chest radiograph consistent with old or current TB, and often have miliary TB.

Risk of LTBI Progressing to TB Disease

Anyone who has LTBI can develop TB disease, but some people are at higher risk than others (Table 2.6). HIV infection is the greatest risk factor for the development of TB disease in persons with LTBI, due to a weakened immune system. The risk of developing TB disease is 7% to 10% **each year** for persons who are infected with both *M. tuberculosis* and HIV and who are not receiving highly active treatment for HIV; it is 10% over a lifetime for persons infected only with *M. tuberculosis* (Figure 2.5). Children younger than 5 years of age are also at increased risk for progression of LTBI to TB disease.

Table 2.6
Persons at Increased Risk for Progression of LTBI to TB Disease

Persons at Increased Risk
• Persons infected with HIV; • Children younger than 5 years of age; • Persons who were recently infected with *M. tuberculosis* (within the past 2 years); • Persons with a history of untreated or inadequately treated TB disease, including persons with fibrotic changes on chest radiograph consistent with prior TB disease; • Persons who are receiving immunosuppressive therapy such as tumor necrosis factor-alpha (TNF) antagonists, systemic corticosteroids equivalent to/greater than 15 mg of prednisone per day, or immunosuppressive drug therapy following organ transplantation; • Persons with silicosis, diabetes mellitus, chronic renal failure, leukemia, or cancer of the head, neck, or lung; • Persons who have had a gastrectomy or jejunoileal bypass; • Persons who weigh less than 90% of their ideal body weight; • Cigarette smokers and persons who abuse drugs and/or alcohol; and • Populations defined locally as having an increased incidence of disease due to *M. tuberculosis*, including medically underserved, low-income populations.

Figure 2.5
Risk of Developing TB Disease

Risk Factor	Risk of Developing TB	Description
TB infection and no risk factors	 About 10% over a lifetime	For people with TB infection, **no risk factors**, and no treatment, the risk is about 5% in the first 2 years after infection and about 10% over a lifetime.
TB infection and diabetes	 About 30% over a lifetime	For people with TB infection and **diabetes**, and with no treatment, the risk is three times as high, or about 30% over a lifetime.
TB infection and HIV infection	 About 7% to 10% PER YEAR	For people with TB infection and **untreated HIV infection** and with no LTBI treatment, the risk is about 7% to 10% PER YEAR, a very high risk over a lifetime.

Anyone who has LTBI can develop TB disease, but some people are at higher risk than others. HIV infection is the highest risk factor for development of TB disease in persons with LTBI owing to weakening of the immune system.

Study Questions

2.6 Which statement about the difference between LTBI and TB disease is true?
(circle the one best answer)

A. Tubercle bacilli are in the body only with TB disease.

B. Persons with LTBI **cannot** spread TB bacteria to others.

C. Sputum smears and cultures are positive with LTBI but **NOT** with TB disease.

Which of the following patient characteristics indicate LTBI, TB disease, or both?
(Choose the one best answer and write the letter for the correct answer on the line next to the question number.)

Patient Characteristics	Type of TB (Answers May Be Used More Than Once)
____ **2.7** Has a positive TB skin test or TB blood test reaction.	**A.** LTBI
____ **2.8** May spread TB bacteria to others.	**B.** TB disease
____ **2.9** Has TB bacteria in his/her body.	**C.** Both LTBI and TB disease
____ **2.10** May require respiratory isolation.	
____ **2.11** Is **NOT** a case of TB.	

2.12 TB disease most commonly affects which part of the body?
(choose the one best answer)

A. Bone

B. Lungs

C. Kidneys

D. Brain

E. None of the above

The following persons have LTBI. Which persons have factors that put them either at an increased risk or NOT at an increased risk of progressing to TB disease?
(Choose the one best answer, and write the letter for the correct answer on the line next to the question number.)

Persons with LTBI	Risk of Progressing to TB Disease
____ **2.13** Susan has osteopenia.	**A.** Increased risk
____ **2.14** Andy has diabetes.	**B.** **Not** an increased risk
____ **2.15** Cindy is 3 years old.	

Case Study– Daniel

Daniel, a 30-year-old male, visits the Jackson County Health Department for a tuberculosis test because he is required to have one before he starts his new job at the Brice Nursing Home. He has a positive reaction to the test. He has no symptoms of TB and his chest x-ray findings are normal.

2.16 Should Daniel be considered a case of TB?
(circle the one best answer)

A. Yes, because he had a positive reaction to the tuberculosis test.

B. No, because he has TB infection, but no evidence of TB disease.

2.17 Should Daniel be considered infectious?
(circle the one best answer)

A. Yes, the test indicates that he has TB infection. Therefore he is infectious.

B. No, because he has TB infection, but not TB disease. Therefore he is not infectious.

Case Study– Lorena

Lorena, a 45-year-old female, is referred to the Galion County Health Department by her private physician because she was diagnosed with LTBI. She is obese, has high blood pressure, and has heart problems. She reports that she has injected illegal drugs in the past and also tested positive for HIV infection.

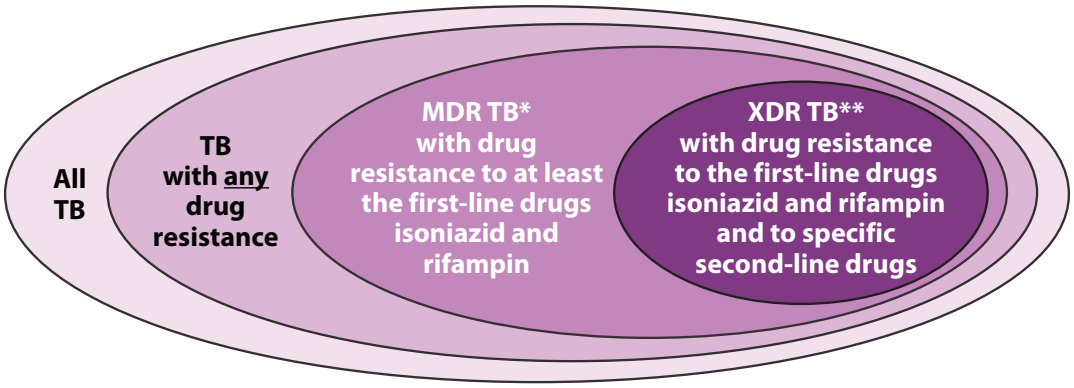
What conditions does Lorena have that increase the risk that she will develop TB disease? (Choose the one best answer and write the letter for the correct answer on the line next to the question number.)

Conditions of Persons with LTBI	Risk of Progressing to TB Disease
____ **2.18** Obesity	**A.** Increased risk
____ **2.19** High blood pressure	**B.** **Not** an increased risk
____ **2.20** Heart problems	
____ **2.21** Injection of illegal drugs	
____ **2.22** HIV	

Drug-Resistant TB (MDR and XDR)

Drug-resistant TB is caused by *M. tuberculosis* organisms that are resistant to the drugs normally used to treat the disease (Figure 2.6). Drug-resistant TB is transmitted in the same way as drug-susceptible TB, and is no more infectious than drug-susceptible TB. However, delay in the recognition of drug resistance or prolonged periods of infectiousness may facilitate increased transmission and further development of drug resistance.

Figure 2.6
Drug-Resistant Tuberculosis



* Often resistant to additional drugs

** Resistant to any fluoroquinolone and at least one of three injectable second-line drugs (i.e., amikacin, kanamycin, or capreomycin)

Drug-resistant TB is caused by *M. tuberculosis* organisms that are resistant to the drugs normally used to treat the disease. Drug-resistant TB is transmitted in the same way as drug-susceptible TB, and is no more infectious than drug-susceptible TB.

Multidrug-Resistant TB

Multidrug-resistant TB (MDR TB) is caused by organisms resistant to the most effective anti-TB drugs, isoniazid and rifampin. These drugs are considered first-line drugs and are used to treat most persons with TB disease (see Chapter 6, Treatment of Tuberculosis Disease).

Multidrug-resistant TB (MDR TB) is caused by organisms resistant to the most effective anti-TB drugs, isoniazid and rifampin.

Extensively Drug-Resistant TB

Extensively drug-resistant TB (XDR TB) is a relatively rare type of drug-resistant TB. XDR TB is resistant to isoniazid and rifampin, plus any fluoroquinolone and at least one of three injectable second-line drugs (i.e., amikacin, kanamycin, or capreomycin). Because XDR TB is resistant to first-line and second-line drugs, patients are left with treatment options that are more toxic, more expensive, and much less effective.

Types of Drug-Resistant TB Disease

Drug-resistant TB disease can develop in two different ways, called **primary** and **secondary** resistance (Table 2.7). Primary resistance occurs in persons who are initially infected with resistant organisms. Secondary resistance, or acquired resistance, develops during TB therapy, either because the patient was treated with an inadequate regimen, did **not** take the prescribed regimen appropriately, or because of other conditions such as drug malabsorption or drug-drug interactions that led to low serum levels.

Circumstances in which an exposed person is at an increased risk of infection with drug-resistant TB include the following:

- Exposure to a person who has known drug-resistant TB disease;
- Exposure to a person with TB disease who has had prior treatment for TB (treatment failure or relapse) and whose susceptibility test results are **not** known;
- Exposure to a person with TB disease from an area in which there is a high prevalence of drug resistance, or travel to one of these areas (see the World Health Organization's "Tuberculosis: MDR-TB & XDR-TB: The 2008 Report" for a list countries with highest prevalence of drug resistance at www.who.int/tb/features_archive/drs_factsheet.pdf); or
- Exposure to a person who continue to have positive smear and cultures after 2 months of combination chemotherapy.

Table 2.7
Primary and Secondary MDR TB

Primary MDR TB (Infected with Drug-Resistant Organisms)	**Secondary MDR TB** (Acquired or Developed Drug Resistance)
Caused by person-to-person transmission of drug-resistant organisms	Develops during TB treatment
• Exposure to a person who » Has known drug-resistant TB » Had prior treatment for TB (treatment failure or relapse and whose susceptibility test results are **not** known) » Is from an area in which there is a high prevalence of drug resistance » Continues to have positive smears and cultures after 2 months of combination chemotherapy • Travel in areas with a high prevalence of drug-resistant TB disease	Develops because the patient • Was **not** treated with the appropriate treatment regimen **Or** • Did **not** follow the treatment regimen as prescribed » Took the drugs incorrectly » Took the drugs irregularly • Malabsorption • Drug-drug interactions causing low serum levels

Study Questions

2.23 Which of the following statements is true about drug-resistant TB disease?
(choose the one best answer)

A. Drug-resistant TB disease is transmitted in the same way as drug-susceptible TB disease.

B. Drug-resistant TB disease is **NO** more infectious than drug-susceptible TB disease.

C. Drug-resistant TB disease is easily treated with standard drug regimens.

D. A, B, and C are all correct.

E. Only A and B are correct.

2.24 Which of the following types of TB disease is caused by the organism *M. tuberculosis?*
(choose the one best answer.)

A. Drug-susceptible TB

B. MDR TB

C. XDR TB

D. A, B, and C are all correct.

E. Only A and B are correct.

What are the characteristics for each type of TB disease?
(Choose the one best answer, and write the letter for the correct answer on the line next to the question number.)

Characteristic	Type of TB
____ **2.25** Resistant to isoniazid and rifampin, plus any fluoroquinolone, and at least one of three injectable second-line drugs.	**A.** MDR TB **B.** XDR TB
____ **2.26** Resistant to at least the two first-line drugs, isoniazid and rifampin.	

What type of drug-resistant TB does each patient have?
(Choose the one best answer, and write the letter for the correct answer on the line next to the question number.)

Patient	Type of Drug-Resistant TB
____ **2.27** Sally is diagnosed with and treated for TB by her family physician. She is not placed on directly observed therapy DOT; thus she often forgets to take her anti-TB medicine and takes only part of her prescribed regimen. Because of inadequate treatment, she now has MDR TB.	**A.** Primary resistance **B.** Secondary "acquired" resistance
____ **2.28** Li, a 13-year-old boy, immigrates from China with his family. He gets MDR TB from his older brother.	

TB Classification System

The current clinical classification system for TB used in the United States is based on the pathogenesis of the disease (Table 2.8). It is intended mainly as an operational framework for public health programs. This classification system provides clinicians the opportunity to track the development of TB in their patients. Health-care providers should comply with state and local laws and regulations requiring the reporting of TB disease. All persons with Class 3 (clinically active) or Class 5 (TB suspected) TB should be reported promptly to the local or state health department. A patient should not have a Class 5 classification for more than 3 months.

Table 2.8
TB Classification System

Class	Type	Description
0	No TB exposure **Not** infected	• No history of TB exposure and no evidence of *M. tuberculosis* infection or disease • Negative reaction to TST or IGRA
1	TB exposure No evidence of infection	• History of exposure to *M. tuberculosis* • Negative reaction to TST or IGRA (given at least 8 to 10 weeks after exposure)
2	TB infection No TB disease	• Positive reaction to TST or IGRA • Negative bacteriological studies (smear and cultures) • No bacteriological or radiographic evidence of active TB disease
3	TB clinically active	• Positive culture for *M. tuberculosis* **OR** • Positive reaction to TST or IGRA, plus clinical, bacteriological, or radiographic evidence of current active TB
4	Previous TB disease (**not** clinically active)	• May have past medical history of TB disease • Abnormal but stable radiographic findings • Positive reaction to the TST or IGRA • Negative bacteriologic studies (smear and cultures) • No clinical or radiographic evidence of current active TB disease
5	TB suspected	• Signs and symptoms of active TB disease, but medical evaluation **not** complete

Study Questions

What is the TB classification for each of the following patients?
(Choose the one best answer, and write the letter for the correct answer on the line next to the question number.)

Patient	TB Classification
____ **2.29** Sonya has a positive reaction to a TST. There is no bacteriological or radiographic evidence of TB disease.	**A.** 0 No exposure Not infected
____ **2.30** Luke has signs and symptoms of TB disease, but his medical evaluation is **not** complete.	**B.** 1 TB exposure No evidence of infection
____ **2.31** Sergei has a past medical history of TB disease. His radiographic findings are abnormal, but stable. He has a positive reaction to an IGRA. Both smear and culture results are negative and there is no clinical or radiographic evidence of current TB disease.	**C.** 2 TB infection No TB disease
____ **2.32** Joseph has a history of exposure to *M. tuberculosis* and a negative TST result.	**D.** 3 TB, clinically active
____ **2.33** Louisa has no history of TB exposure and no evidence of *M. tuberculosis* infection or disease. She had a negative IGRA result.	**E.** 4 Previous TB disease (not clinically active)
____ **2.34** Rosella has a positive culture for *M. tuberculosis.*	**F.** 5 TB disease suspected

Chapter Summary

TB is an airborne disease caused by the bacterium *Mycobacterium tuberculosis* (*M. tuberculosis*). *M. tuberculosis* and seven very closely related mycobacterial species (*M. bovis*, *M. africanum*, *M. microti*, *M. caprae*, *M. pinnipedii*, *M. canetti* and *M. mungi*) together comprise what is known as the *M. tuberculosis* complex. Most, but not all, of these species have been found to cause disease in humans. In the United States, the majority of TB cases are caused by *M. tuberculosis*. *M. tuberculosis* organisms are also called tubercle bacilli.

M. tuberculosis is carried in airborne particles, called droplet nuclei, of 1–5 microns in diameter. Infectious droplet nuclei are generated when persons who have pulmonary or laryngeal TB disease cough, sneeze, shout, or sing. Depending on the environment, these tiny particles can remain suspended in the air for several hours. *M. tuberculosis* is transmitted through the air, **not** by surface contact. Transmission occurs when a person inhales droplet nuclei containing *M. tuberculosis*, and

the droplet nuclei traverse the mouth or nasal passages, upper respiratory tract, and bronchi to reach the alveoli of the lungs.

TB disease most commonly affects the lungs; this is referred to as pulmonary TB disease. In 2009, 71% of TB cases in the United States were exclusively pulmonary. Patients with pulmonary TB disease usually have a cough and an abnormal chest radiograph, and may be infectious. Although the majority of TB cases are pulmonary, TB can occur in almost any anatomical site or as disseminated disease.

Persons with LTBI have *M. tuberculosis* in their bodies, but do not have TB disease and **cannot** spread the infection to other people. A person with LTBI is **not** regarded as a case of TB disease. The process of LTBI begins when extracellular bacilli are ingested by macrophages and presented to other white blood cells. This triggers the immune response in which white blood cells kill or encapsulate most of the bacilli, leading to the formation of a granuloma. At this point, LTBI has been established. LTBI may be detected by using the TST or IGRA. It can take 2 to 8 weeks after the initial TB infection for the body's immune system to be able to react to tuberculin and for the infection to be detected by the TST or IGRA. Within weeks after infection, the immune system is usually able to halt the multiplication of the tubercle bacilli, preventing further progression.

In some people, the tubercle bacilli overcome the immune system and multiply, resulting in progression from LTBI to TB disease. Persons who have TB disease are usually infectious and may spread the bacteria to other people. The progression from LTBI to TB disease may occur soon or many years after infection. Body fluid or tissue from the disease site should be collected for AFB smear and culture. Positive culture for *M. tuberculosis* confirms the diagnosis of TB disease.

Drug-resistant TB disease can develop in two different ways, called **primary** and **secondary** resistance. Primary resistance occurs in persons who are initially exposed to and infected with resistant organisms. Secondary resistance, or acquired resistance, develops during TB therapy, either because the patient was treated with an inadequate regimen or did not take the prescribed regimen appropriately, or because of other conditions such as drug malabsorption or drug-drug interactions that led to low serum levels.

MDR TB is caused by organisms resistant to both isoniazid and rifampin, which are the two most effective anti-TB drugs. These drugs are considered first-line drugs and are used to treat most persons with TB disease.

XDR TB is a relatively rare type of drug-resistant TB. XDR TB is resistant to both isoniazid and rifampin, plus any fluoroquinolone and at least one of three injectable second-line drugs (i.e., amikacin, kanamycin, or capreomycin). Because XDR TB disease is resistant to first-line and second-line drugs, patients are left with treatment options that are more toxic, more expensive, and much less effective.

The current clinical classification system for TB used in the United States is based on the pathogenesis of the disease. It is intended mainly as an operational framework for public health programs. This classification system provides clinicians the opportunity to track the development of TB in their patients. Health-care providers should comply with state and local laws and regulations requiring the reporting of TB disease. All persons with Class 3 (clinically active) or Class 5 (TB suspected) TB should be reported promptly to the local or state health department. A patient should not have a Class 5 classification for more than 3 months.

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