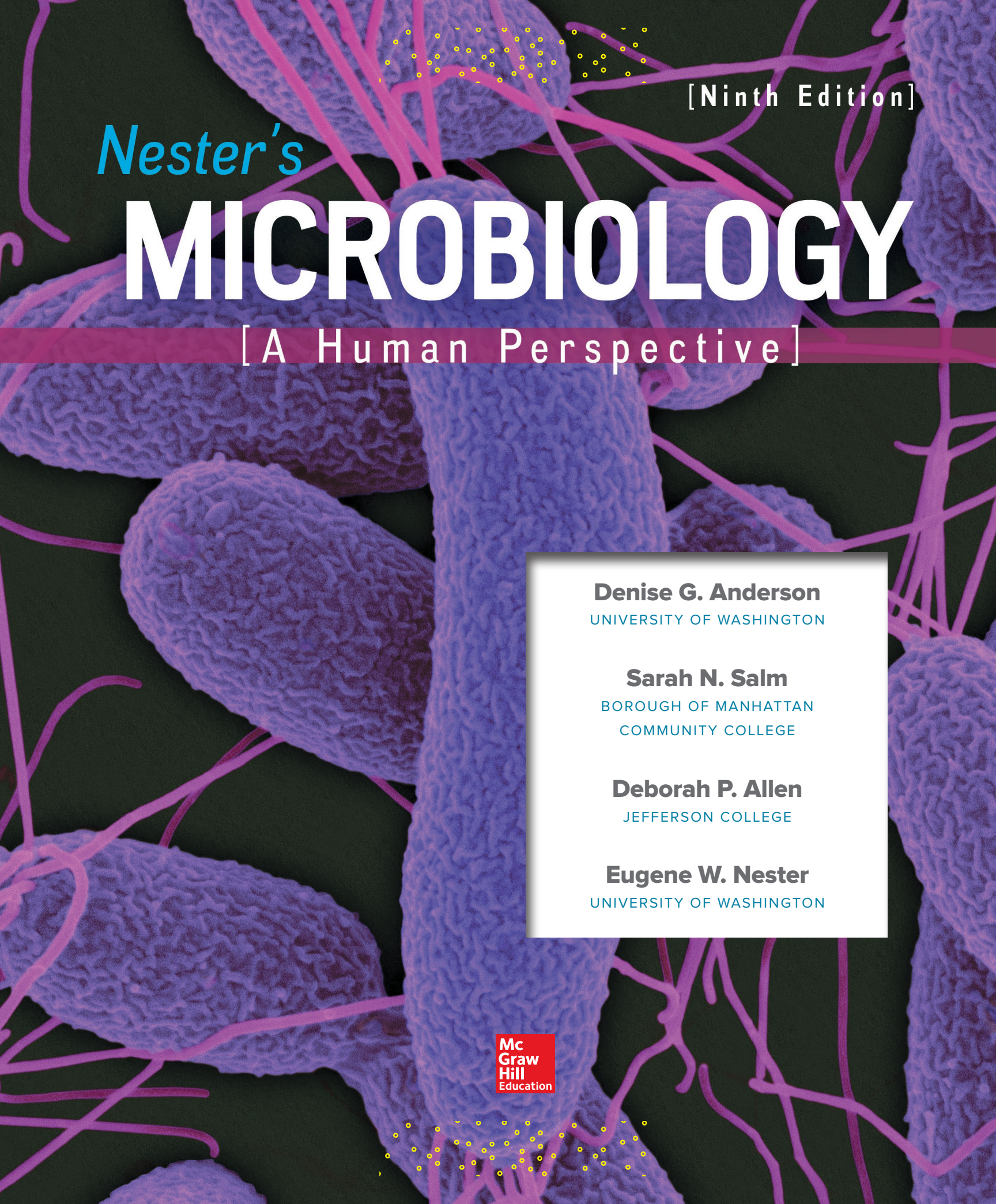

[Ninth Edition]
Nester's
MICROBIOLOGY
[A Human Perspective]
Mc Graw Hill Education
Denise Anderson | Sarah Salm | Deborah Allen



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Nester's MICROBIOLOGY

[A Human Perspective]

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NESTER'S MICROBIOLOGY: A HUMAN PERSPECTIVE, NINTH EDITION

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Brief Contents

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About the Authors

The Nester Team:

Three Perspectives, One Vision, One Voice

The three authors of this edition—Denise Anderson, Sarah Salm, and Deborah Allen—may be a set of individuals with different insights and unique experiences, but their cooperative relationship defines the word "team." What drives them is a single shared goal: to create the most learning-friendly introductory microbiology textbook available. Each author carefully read all the chapters, looking for parts that could be tweaked for clarity. They did this with students in mind, suggesting simpler words where appropriate while maintaining the scientific rigor so important for today's healthcare professionals.

Meanwhile, Gene Nester continued to serve as "team member emeritus," keeping an eagle eye out for updates that could be incorporated into the text. His work established the text's reputation for excellence over the decades, and it lives on in this edition.

©Richard Moore

Denise Anderson

Denise Anderson is a Senior Lecturer in the Department of Microbiology at the University of Washington, where she teaches a variety of courses including general microbiology, medical bacteriology laboratory, and medical mycology/parasitology laboratory. Equipped with a diverse educational background, including undergraduate work in nutrition and graduate work in food science and in microbiology, she first discovered a passion for teaching when she taught microbiology laboratory courses as part of her graduate training. Her enthusiastic teaching style, fueled by regular doses of Seattle's famous coffee, receives high reviews from her students.

Outside academic life, Denise relaxes in the Phinney Ridge neighborhood of Seattle, where she lives with her husband, Richard Moore, and dog, Riley (neither of whom is well trained). When not planning lectures, grading papers, or writing textbook chapters, she can usually be found chatting with the neighbors, fighting the weeds in her garden, or enjoying a fermented beverage at the local pub.

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Sarah Salm

Sarah Salm is a Professor at the Borough of Manhattan Community College (BMCC) of the City University of New York, where she teaches microbiology, anatomy and physiology, and general biology. She earned her undergraduate and doctoral degrees at the University of the Witwatersrand in Johannesburg, South Africa. She later moved to New York, where she did postdoctoral work at the NYU School of Medicine. Her research background is diverse, and includes plant virology, prostate cancer, and bacteria in contaminated water sources.

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Deborah Allen

Deborah Allen is a Professor at Jefferson College in Missouri, where she teaches microbiology as well as several other courses for students entering allied health careers. Her graduate work was in zoology at the University of Oklahoma and in neurobiology and behavior at Cornell University. She participated in cancer research at the University of Arkansas Medical Center before embarking on a career in publishing, working in acquisitions and development for books in the life sciences. She is now thrilled to be working on the other end of the desk with the Nester team. Away from campus, Deborah reads or listens to her favorite Eve Dallas novels, floats the rivers and listens to folk music in the Ozarks, and fully appreciates the local microbes while visiting Missouri wineries.

Courtesy Eugene Nester

Eugene Nester

Although no longer an active member of the author team, Eugene (Gene) Nester wrote the original version of the present text with Evans Roberts and Nancy Pearsall more than 30 years ago. That text, *Microbiology: Molecules, Microbes and Man,* pioneered the organ system approach to the study of infectious disease, and was developed specifically for allied health sciences.

Gene did his undergraduate work at Cornell and received his Ph.D. in microbiology from Case Western University. He then did postdoctoral work in the Department of Genetics at Stanford University with Joshua Lederberg. Following that, he joined the faculty in the Department of Microbiology at the University of Washington, where he remains active as an emeritus member. His laboratory demonstrated that *Agrobacterium* transfers DNA into plant cells—the basis for the disease crown gall—a system of gene transfer that has become a cornerstone of plant biotechnology. In recognition of his work, he was awarded the Australia Prize and the Cetus Prize in Biotechnology, and was elected to fellowship in the National Academy of Sciences, the American Academy for the Advancement of Science, the American Academy of Microbiology, and the National Academy of Sciences in India.

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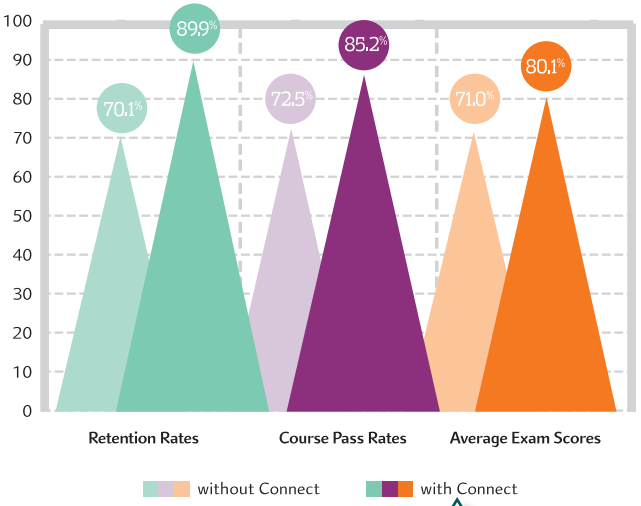

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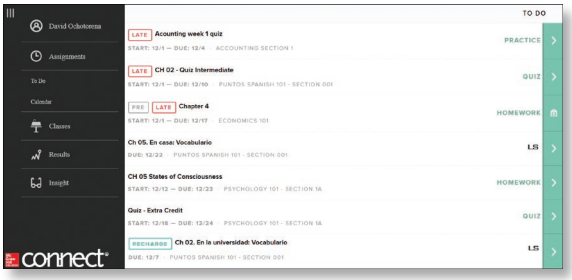

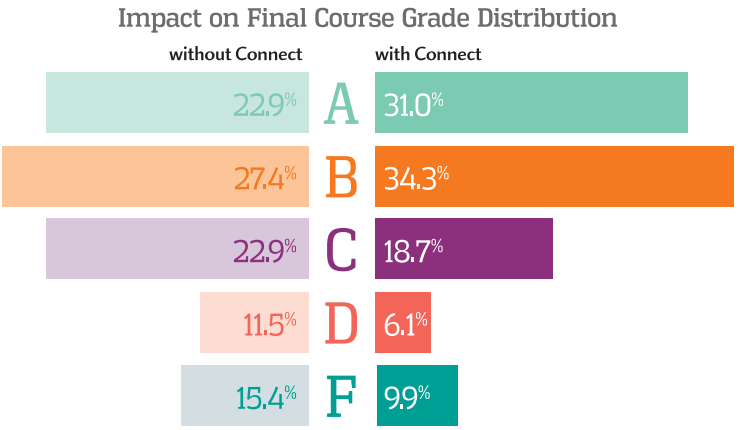

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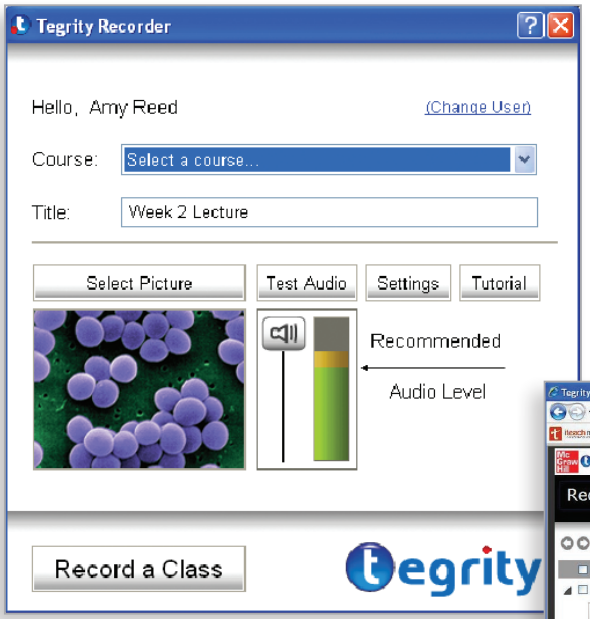
Chapter	Animations Animations/Videos (Animations and video files that can be easily downloaded and played without PowerPoint.)	Labeled Images (Art, tables, and photo files as they appear in the text as zipped files)	Base Art Images Art files, photos and table files without labels and leader lines.	*Accessible Lecture PPTs (Lecture outlines tagged for screen readers.) Chapters 1-15 are available.
Chapter 01	Ch 01 Animation (10,377 KB)	Ch 01 Labeled Images (28,687 KB)	Ch 01 Baseart Images (21,510 KB)	Ch01 Accessible Lecture PPT
Chapter 02	Ch 02 Animation (35,949 KB)	Ch 02 Labeled Images (11,405 KB)	Ch 02 Baseart Images (5,932 KB)	Ch02 Accessible Lecture PPT



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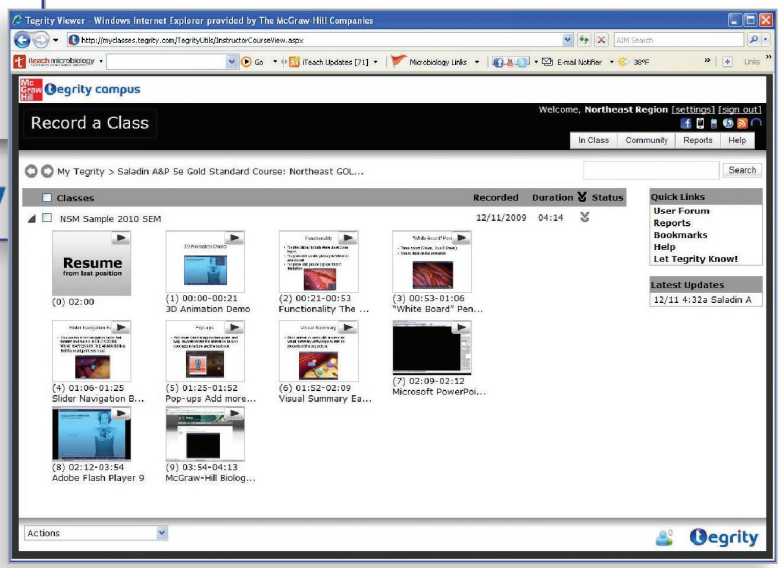


FOCUS ON UNDERSTANDING . . .

Student-Friendly Illustrations

Introduce the "big picture"

Focus figures provide an overview or highlight a key concept.

Keep the big picture in focus

A highlighted mini-version of the overview figure is often incorporated into the upper left corner of subsequent figures, helping students see how those figures fit into the big picture.

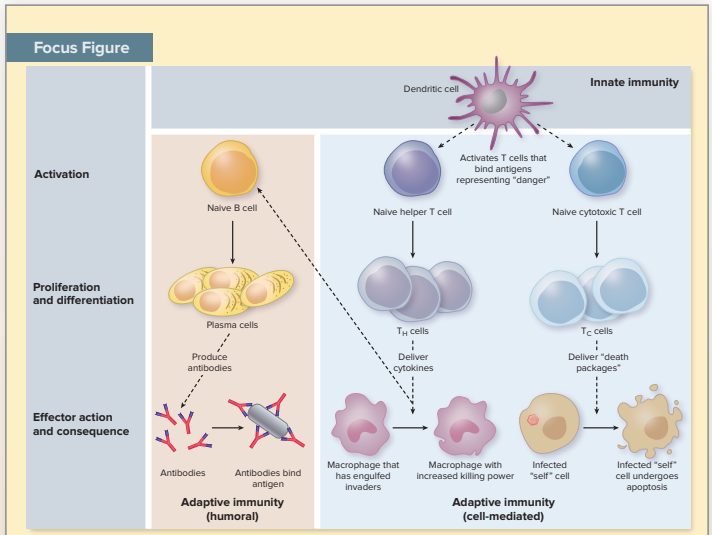


FIGURE 15.1 Overview of the Adaptive Immune Response Humoral immunity protects against antigens in blood and tissue fluid (extracellular antigens); cell-mediated immunity protects against antigens within host cells (intracellular antigens). In this diagram, solid arrows represent the path of a cell or molecule; dashed arrows represent a cell's interactions and effector functions; antigen receptors and memory cells are not shown.

? How does cell-mediated immunity eliminate intracellular antigens?

Other descendants become **memory lymphocytes,** long-lived cells that can be activated more quickly if the antigen is encountered again. Memory cells are responsible for the effectiveness of the secondary response.

Humoral Immunity

ell detects an extracellular antigen, that B cell ated, allowing it to proliferate (see figure 15.1). endants of activated B cells differentiate to **ells,** which are effector B cells. Plasma cells oteins called **antibodies.** These proteins bind f cells, toxins, viruses, and other antigens, protect the body against the effects of that mple, antibodies that bind diphtheria toxin om the effects of the toxin (see **A Glimpse**

The structure of an antibody molecule accounts for its ability to protect against an invader. An antibody has two functional regions: the two identical arms and the single stem of the Y-shaped molecule (see figure 15.1). The ends of the arms are the parts that attach to antigens. By binding to antigens, the antibodies can neutralize their effects. For example, antibody-coated viral particles cannot attach to receptors on cells and, therefore, cannot enter the cells. Antibodies are very specific with respect to their binding, so the immune system must produce many different varieties, each with a slightly different set of "arms." Although the set of arms of different antibody molecules varies, the stem portion is functionally similar—it serves as a "red flag" that sticks out from the surface of an antibody-bound antigen. This tags the antigen for rapid elimination by macrophages or other components of the immune system. ⏮ attachment of viruses

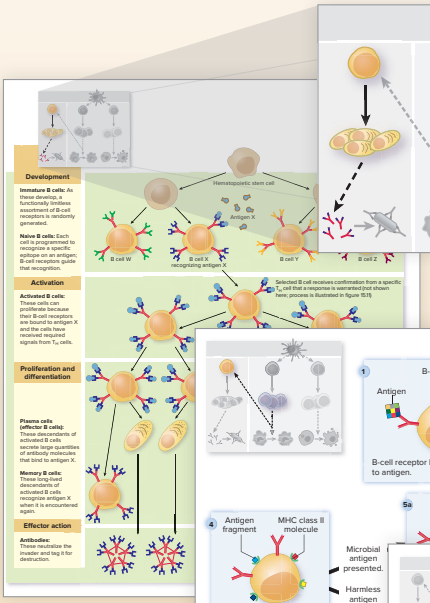


FIGURE 15.10

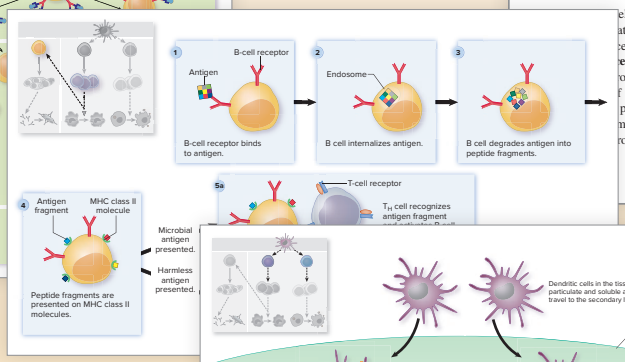


FIGURE 15.11

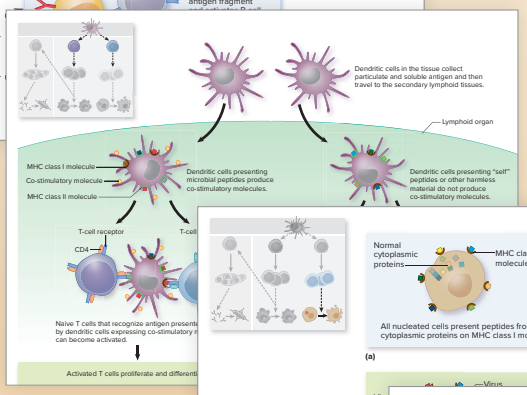


FIGURE 15.20

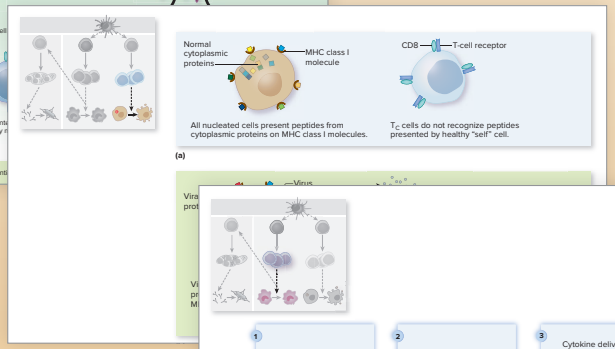


FIGURE 15.21

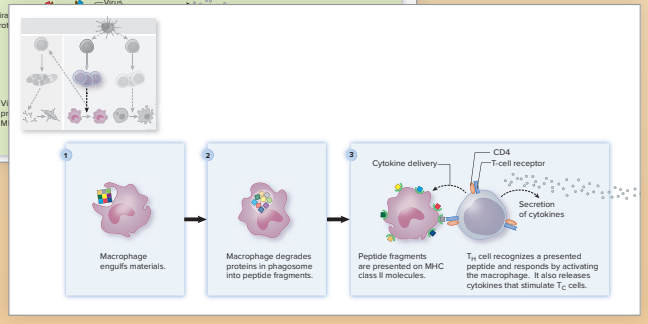


FIGURE 15.22

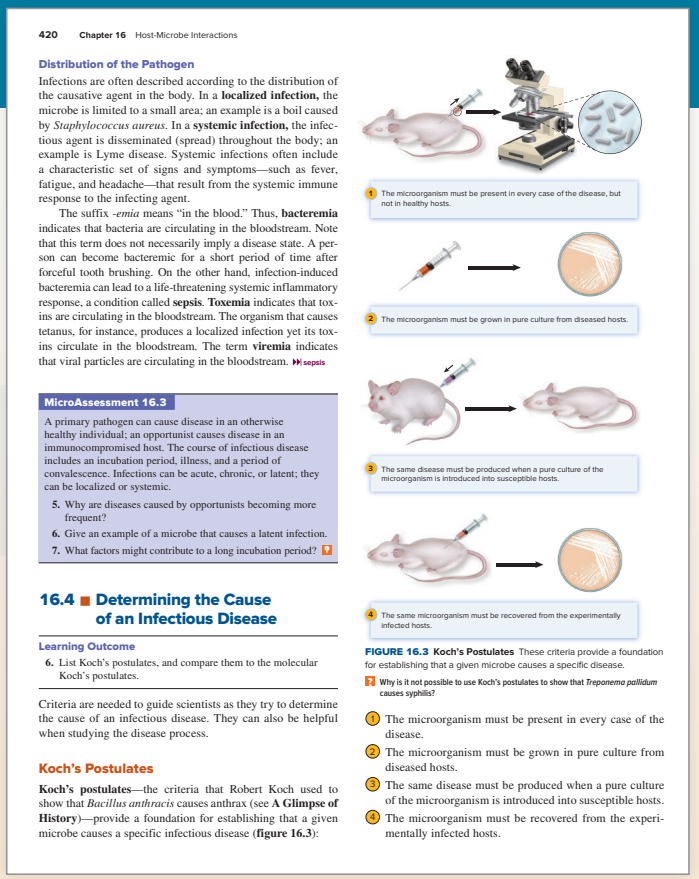
"Provides a logical unfolding conceptual framework that fosters better understanding."

—Jamal Bittar, University of Toledo

Walk through the processes

Step-by-step figures direct the student using numbered icons, often with corresponding icons in the text.

> *"The text and illustrations are 'tight' and give each other good support."*
>
> —Richard Shipee, Vincennes University



420 Chapter 16 Host-Microbe Interactions

Distribution of the Pathogen

Infections are often described according to the distribution of the causative agent in the body. In a **localized infection,** the microbe is limited to a small area; an example is a boil caused by *Staphylococcus aureus*. In a **systemic infection,** the infectious agent is disseminated (spread) throughout the body; an example is Lyme disease. Systemic infections often include a characteristic set of signs and symptoms—such as fever, fatigue, and headache—that result from the systemic immune response to the infecting agent.

The suffix *-emia* means "in the blood." Thus, **bacteremia** indicates that bacteria are circulating in the bloodstream. Note that this term does not necessarily imply a disease state. A person can become bacteremic for a short period of time after forceful tooth brushing. On the other hand, infection-induced bacteremia can lead to a life-threatening systemic inflammatory response, a condition called **sepsis**. **Toxemia** indicates that toxins are circulating in the bloodstream. The organism that causes tetanus, for instance, produces a localized infection yet its toxins circulate in the bloodstream. The term **viremia** indicates that viral particles are circulating in the bloodstream. ⏭ sepsis

MicroAssessment 16.3

A primary pathogen can cause disease in an otherwise healthy individual; an opportunist causes disease in an immunocompromised host. The course of infectious disease includes an incubation period, illness, and a period of convalescence. Infections can be acute, chronic, or latent; they can be localized or systemic.

5. Why are diseases caused by opportunists becoming more frequent?
6. Give an example of a microbe that causes a latent infection.
7. What factors might contribute to a long incubation period?

16.4 ■ Determining the Cause of an Infectious Disease

Learning Outcome

6. List Koch's postulates, and compare them to the molecular Koch's postulates.

Criteria are needed to guide scientists as they try to determine the cause of an infectious disease. They can also be helpful when studying the disease process.

Koch's Postulates

Koch's postulates—the criteria that Robert Koch used to show that *Bacillus anthracis* causes anthrax (see **A Glimpse of History**)—provide a foundation for establishing that a given microbe causes a specific infectious disease (**figure 16.3**):

1 The microorganism must be present in every case of the disease, but not in healthy hosts.

2 The microorganism must be grown in pure culture from diseased hosts.

3 The same disease must be produced when a pure culture of the microorganism is introduced into susceptible hosts.

4 The same microorganism must be recovered from the experimentally infected hosts.

FIGURE 16.3 Koch's Postulates These criteria provide a foundation for establishing that a given microbe causes a specific disease.

? Why is it not possible to use Koch's postulates to show that *Treponema pallidum* causes syphilis?

1. The microorganism must be present in every case of the disease.
2. The microorganism must be grown in pure culture from diseased hosts.
3. The same disease must be produced when a pure culture of the microorganism is introduced into susceptible hosts.
4. The microorganism must be recovered from the experimentally infected hosts.

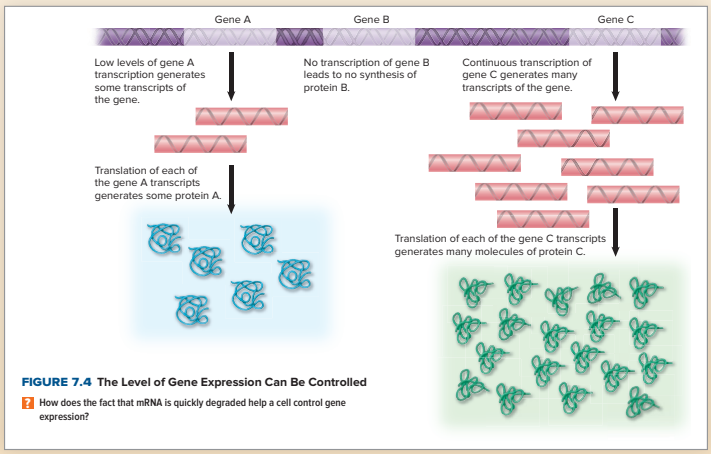


FIGURE 7.4 The Level of Gene Expression Can Be Controlled

? How does the fact that mRNA is quickly degraded help a cell control gene expression?

Encourage deeper understanding

Figures have accompanying questions that encourage students to think more carefully about the concept illustrated in a figure.

Introduce the body systems

Each disease chapter includes a stunning figure that introduces the students to the anatomy of the body system.

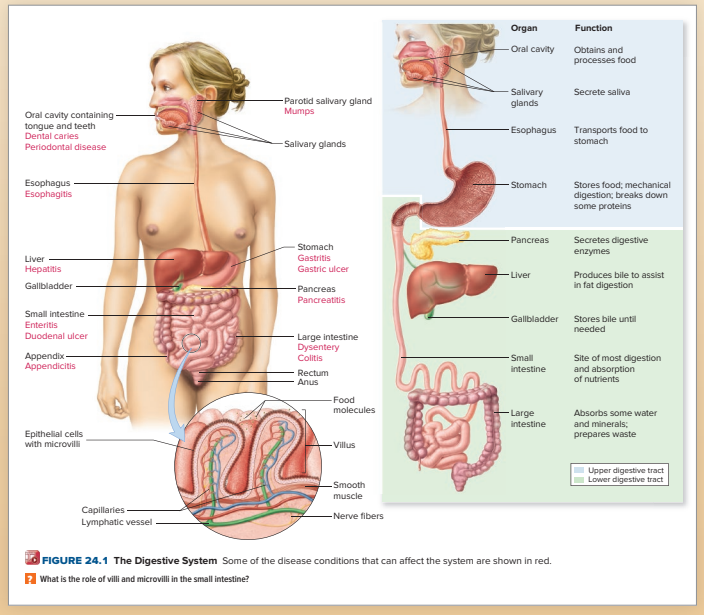


FIGURE 24.1 The Digestive System Some of the disease conditions that can affect the system are shown in red.

? What is the role of villi and microvilli in the small intestine?

FOCUS ON UNDERSTANDING . . .

Student-Friendly Chapter Features

Provide the tools for understanding

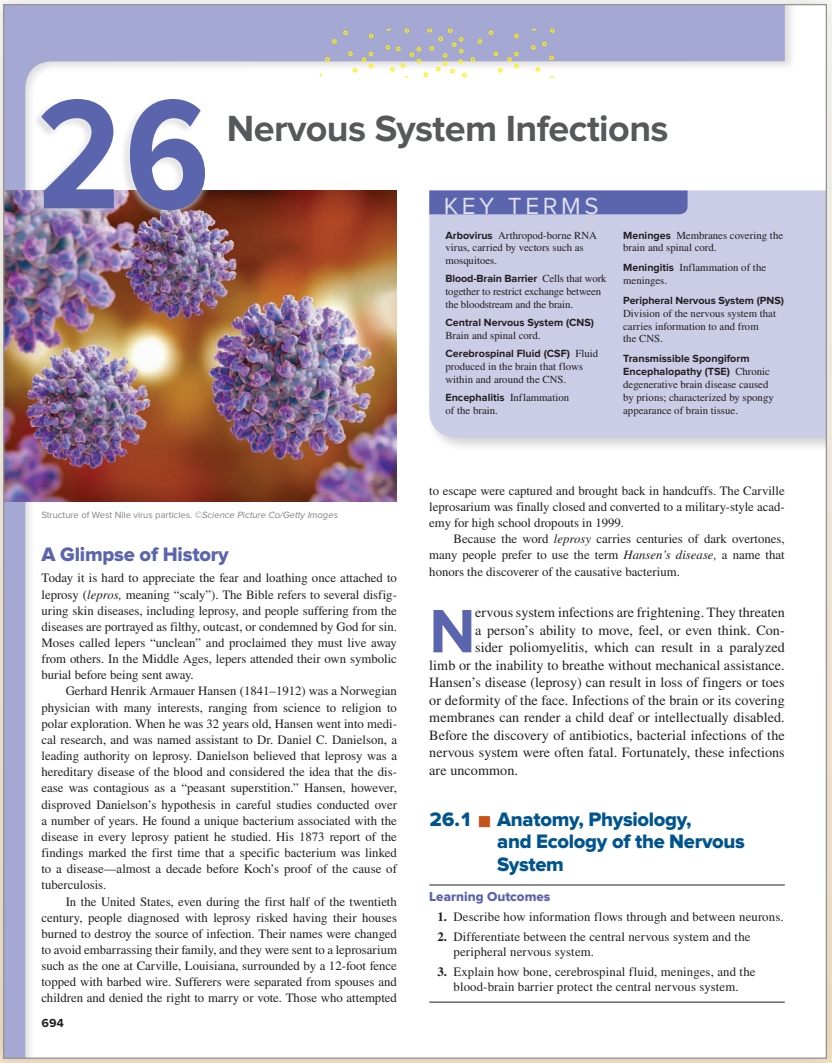
Key Terms for each chapter are defined on the opening page.

Share the history

A **Glimpse of History** opens each chapter, featuring engaging stories about the men and women who pioneered the field of microbiology.

Define the expectations

Learning outcomes are found at the beginning of each numbered section, allowing organization, evaluation, and assessment of instruction.



26 Nervous System Infections

Structure of West Nile virus particles. ©Science Picture Co/Getty Images

KEY TERMS

Arbovirus Arthropod-borne RNA virus, carried by vectors such as mosquitoes.

Blood-Brain Barrier Cells that work together to restrict exchange between the bloodstream and the brain.

Central Nervous System (CNS) Brain and spinal cord.

Cerebrospinal Fluid (CSF) Fluid produced in the brain that flows within and around the CNS.

Encephalitis Inflammation of the brain.

Meninges Membranes covering the brain and spinal cord.

Meningitis Inflammation of the meninges.

Peripheral Nervous System (PNS) Division of the nervous system that carries information to and from the CNS.

Transmissible Spongiform Encephalopathy (TSE) Chronic degenerative brain disease caused by prions; characterized by spongy appearance of brain tissue.

A Glimpse of History

Today it is hard to appreciate the fear and loathing once attached to leprosy (*lepros,* meaning "scaly"). The Bible refers to several disfiguring skin diseases, including leprosy, and people suffering from the diseases are portrayed as filthy, outcast, or condemned by God for sin. Moses called lepers "unclean" and proclaimed they must live away from others. In the Middle Ages, lepers attended their own symbolic burial before being sent away.

Gerhard Henrik Armauer Hansen (1841–1912) was a Norwegian physician with many interests, ranging from science to religion to polar exploration. When he was 32 years old, Hansen went into medical research, and was named assistant to Dr. Daniel C. Danielson, a leading authority on leprosy. Danielson believed that leprosy was a hereditary disease of the blood and considered the idea that the disease was contagious as a "peasant superstition." Hansen, however, disproved Danielson's hypothesis in careful studies conducted over a number of years. He found a unique bacterium associated with the disease in every leprosy patient he studied. His 1873 report of the findings marked the first time that a specific bacterium was linked to a disease—almost a decade before Koch's proof of the cause of tuberculosis.

In the United States, even during the first half of the twentieth century, people diagnosed with leprosy risked having their houses burned to destroy the source of infection. Their names were changed to avoid embarrassing their family, and they were sent to a leprosarium such as the one at Carville, Louisiana, surrounded by a 12-foot fence topped with barbed wire. Sufferers were separated from spouses and children and denied the right to marry or vote. Those who attempted to escape were captured and brought back in handcuffs. The Carville leprosarium was finally closed and converted to a military-style academy for high school dropouts in 1999.

Because the word *leprosy* carries centuries of dark overtones, many people prefer to use the term *Hansen's disease,* a name that honors the discoverer of the causative bacterium.

694

Nervous system infections are frightening. They threaten a person's ability to move, feel, or even think. Consider poliomyelitis, which can result in a paralyzed limb or the inability to breathe without mechanical assistance. Hansen's disease (leprosy) can result in loss of fingers or toes or deformity of the face. Infections of the brain or its covering membranes can render a child deaf or intellectually disabled. Before the discovery of antibiotics, bacterial infections of the nervous system were often fatal. Fortunately, these infections are uncommon.

26.1 ■ Anatomy, Physiology, and Ecology of the Nervous System

Learning Outcomes

1. Describe how information flows through and between neurons.
2. Differentiate between the central nervous system and the peripheral nervous system.
3. Explain how bone, cerebrospinal fluid, meninges, and the blood-brain barrier protect the central nervous system.

MicroAssessment 3.2

Dyes are used to stain cells so they can be seen against an unstained background. The Gram stain is the most commonly used differential stain. The acid-fast stain is used to detect *Mycobacterium* species. Specific dyes and techniques are used to observe cell structures such as capsules, endospores, and flagella. Fluorescent dyes and tags can be used to observe total cells, a subset of cells, or cells that have certain proteins on their surface.

4. What are the functions of a primary stain and a counterstain?
5. Describe one error in the staining procedure that would result in a Gram-positive bacterium appearing pink.
6. What color would a Gram-negative bacterium be in an acid-fast stain?

Assess understanding

A **MicroAssessment** at the end of each numbered section summarizes the concepts and includes review questions, usually featuring one that stimulates critical thinking (indicated by a light bulb icon).

Engage the reader

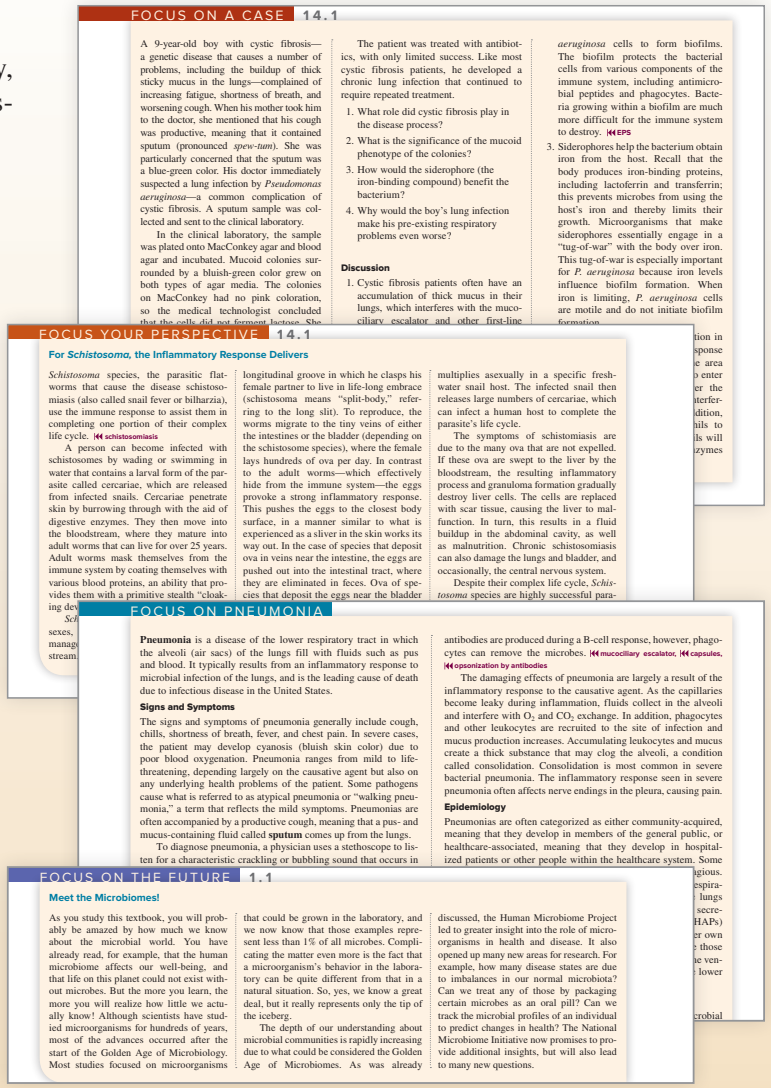
MicroBytes found throughout the chapter provide small "bytes" of information, capturing the reader's attention.

MicroByte

There are more bacteria in just one person's mouth than there are people in the world!

Highlight the relevance

Focus on a Case boxes describe realistic clinical, veterinary, or environmental situations, along with questions and discussions designed to highlight the relevance of the information.


FOCUS ON A CASE 14.1

A 9-year-old boy with cystic fibrosis—a genetic disease that causes a number of problems, including the buildup of thick sticky mucus in the lungs—complained of increasing fatigue, shortness of breath, and worsening cough. When his mother took him to the doctor, she mentioned that his cough was productive, meaning that it contained sputum (pronounced *spew-tum*). She was particularly concerned that the sputum was a blue-green color. His doctor immediately suspected a lung infection by *Pseudomonas aeruginosa*—a common complication of cystic fibrosis. A sputum sample was collected and sent to the clinical laboratory.

In the clinical laboratory, the sample was plated onto MacConkey agar and blood agar and incubated. Mucoid colonies surrounded by a bluish-green color grew on both types of agar media. The colonies on MacConkey had no pink coloration, so the medical technologist concluded

The patient was treated with antibiotics, with only limited success. Like most cystic fibrosis patients, he developed a chronic lung infection that continued to require repeated treatment.

1. What role did cystic fibrosis play in the disease process?
2. What is the significance of the mucoid phenotype of the colonies?
3. How would the siderophore (the iron-binding compound) benefit the bacterium?
4. Why would the boy's lung infection make his pre-existing respiratory problems even worse?

Discussion

1. Cystic fibrosis patients often have an accumulation of thick mucus in their lungs, which interferes with the muco-

aeruginosa cells to form biofilms. The biofilm protects the bacterial cells from various components of the immune system, including antimicrobial peptides and phagocytes. Bacteria growing within a biofilm are much more difficult for the immune system to destroy. EPS

3. Siderophores help the bacterium obtain iron from the host. Recall that the body produces iron-binding proteins, including lactoferrin and transferrin; this prevents microbes from using the host's iron and thereby limits their growth. Microorganisms that make siderophores essentially engage in a "tug-of-war" with the body over iron. This tug-of-war is especially important for *P. aeruginosa* because iron levels influence biofilm formation. When iron is limiting, *P. aeruginosa* cells are motile and do not initiate biofilm

Provide perspective

Focus Your Perspective boxes show how microorganisms and their products influence our lives in many different ways.

FOCUS YOUR PERSPECTIVE 14.1

For *Schistosoma*, the Inflammatory Response Delivers

Schistosoma species, the parasitic flatworms that cause the disease schistosomiasis (also called snail fever or bilharzia), use the immune response to assist them in completing one portion of their complex life cycle. schistosomiasis

A person can become infected with schistosomes by wading or swimming in water that contains a larval form of the parasite called cercariae, which are released from infected snails. Cercariae penetrate skin by burrowing through with the aid of digestive enzymes. They then move into the bloodstream, where they mature into adult worms that can live for over 25 years. Adult worms mask themselves from the immune system by coating themselves with various blood proteins, an ability that provides them with a primitive stealth "cloak-

longitudinal groove in which he clasps his female partner to live in life-long embrace (schistosoma means "split-body," referring to the long slit). To reproduce, the worms migrate to the tiny veins of either the intestines or the bladder (depending on the schistosome species), where the female lays hundreds of ova per day. In contrast to the adult worms—which effectively hide from the immune system—the eggs provoke a strong inflammatory response. This pushes the eggs to the closest body surface, in a manner similar to what is experienced as a sliver in the skin works its way out. In the case of species that deposit ova in veins near the intestine, the eggs are pushed out into the intestinal tract, where they are eliminated in feces. Ova of species that deposit the eggs near the bladder

multiplies asexually in a specific freshwater snail host. The infected snail then releases large numbers of cercariae, which can infect a human host to complete the parasite's life cycle.

The symptoms of schistomiasis are due to the many ova that are not expelled. If these ova are swept to the liver by the bloodstream, the resulting inflammatory process and granuloma formation gradually destroy liver cells. The cells are replaced with scar tissue, causing the liver to malfunction. In turn, this results in a fluid buildup in the abdominal cavity, as well as malnutrition. Chronic schistosomiasis can also damage the lungs and bladder, and occasionally, the central nervous system.

Despite their complex life cycle, *Schistosoma* species are highly successful para-

Introduce the concepts

Focus on a Disease boxes introduce a general category of disease (pneumonia, diarrheal disease, meningitis, sexually transmitted infections), giving students a framework for understanding specific diseases.

FOCUS ON PNEUMONIA

Pneumonia is a disease of the lower respiratory tract in which the alveoli (air sacs) of the lungs fill with fluids such as pus and blood. It typically results from an inflammatory response to microbial infection of the lungs, and is the leading cause of death due to infectious disease in the United States.

Signs and Symptoms

The signs and symptoms of pneumonia generally include cough, chills, shortness of breath, fever, and chest pain. In severe cases, the patient may develop cyanosis (bluish skin color) due to poor blood oxygenation. Pneumonia ranges from mild to life-threatening, depending largely on the causative agent but also on any underlying health problems of the patient. Some pathogens cause what is referred to as atypical pneumonia or "walking pneumonia," a term that reflects the mild symptoms. Pneumonias are often accompanied by a productive cough, meaning that a pus- and mucus-containing fluid called **sputum** comes up from the lungs.

To diagnose pneumonia, a physician uses a stethoscope to listen for a characteristic crackling or bubbling sound that occurs in

antibodies are produced during a B-cell response, however, phagocytes can remove the microbes. mucociliary escalator, capsules, opsonization by antibodies

The damaging effects of pneumonia are largely a result of the inflammatory response to the causative agent. As the capillaries become leaky during inflammation, fluids collect in the alveoli and interfere with O_2 and CO_2 exchange. In addition, phagocytes and other leukocytes are recruited to the site of infection and mucus production increases. Accumulating leukocytes and mucus create a thick substance that may clog the alveoli, a condition called consolidation. Consolidation is most common in severe bacterial pneumonia. The inflammatory response seen in severe pneumonia often affects nerve endings in the pleura, causing pain.

Epidemiology

Pneumonias are often categorized as either community-acquired, meaning that they develop in members of the general public, or healthcare-associated, meaning that they develop in hospitalized patients or other people within the healthcare system. Some

Inspire the learner

Focus on the Future boxes describe pending challenges facing current and future microbiologists.

FOCUS ON THE FUTURE 1.1

Meet the Microbiomes!

As you study this textbook, you will probably be amazed by how much we know about the microbial world. You have already read, for example, that the human microbiome affects our well-being, and that life on this planet could not exist without microbes. But the more you learn, the more you will realize how little we actually know! Although scientists have studied microorganisms for hundreds of years, most of the advances occurred after the start of the Golden Age of Microbiology. Most studies focused on microorganisms

that could be grown in the laboratory, and we now know that those examples represent less than 1% of all microbes. Complicating the matter even more is the fact that a microorganism's behavior in the laboratory can be quite different from that in a natural situation. So, yes, we know a great deal, but it really represents only the tip of the iceberg.

The depth of our understanding about microbial communities is rapidly increasing due to what could be considered the Golden Age of Microbiomes. As was already

discussed, the Human Microbiome Project led to greater insight into the role of microorganisms in health and disease. It also opened up many new areas for research. For example, how many disease states are due to imbalances in our normal microbiota? Can we treat any of those by packaging certain microbes as an oral pill? Can we track the microbial profiles of an individual to predict changes in health? The National Microbiome Initiative now promises to provide additional insights, but will also lead to many new questions.

- **Summary** briefly reviews the key points.
- **Short Answer** questions review major chapter concepts.
- **Multiple Choice** questions allow self-testing; answers are provided in Appendix IV.
- **Application** questions provide an opportunity to use knowledge of microbiology to solve real-world problems.
- **Critical Thinking** questions encourage practice in analysis and problem solving that can be used by the student in any subject.

Review the information

End-of-chapter review encourages students to revisit the information.

Build the story

Logical chapter order helps students understand and connect the concepts.

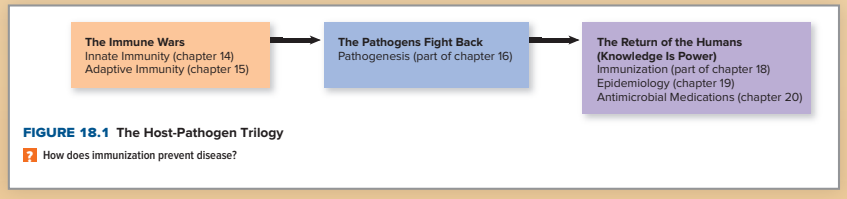


FIGURE 18.1 The Host-Pathogen Trilogy

? How does immunization prevent disease?

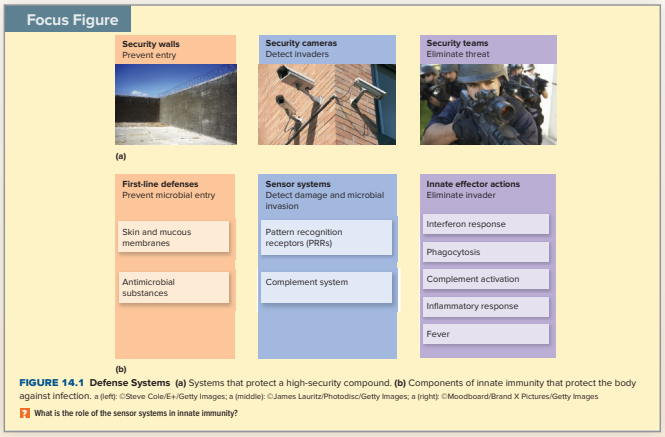
FOCUS ON UNDERSTANDING . . .

Student-Friendly Descriptions

Include analogies

WHY? Analogies provide students a comfortable framework for making sense of difficult topics. Here's an example from chapter 14.

Innate Immunity *The innate immune system has three general components: first-line defenses, sensor systems, and innate effector actions. As a useful analogy, think of the defense systems of a high-security building or compound: The first-line defenses are the security walls surrounding the property; the sensor systems are the security cameras scattered throughout the property, monitoring the environment for signs of invasion; and the effector actions are the security teams sent to remove any invaders that have been detected, thereby eliminating the threat* ***(figure 14.1a).***

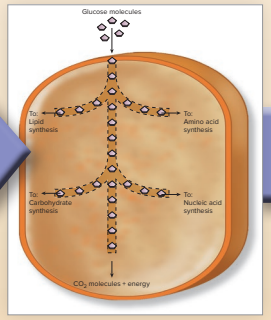


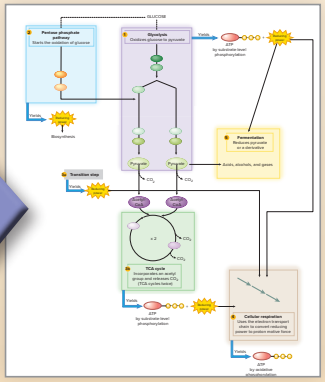
Emphasize the logic

WHY? Descriptions that emphasize the logic of processes make it easier for students to understand and retain the information. Here's an example from chapter 6.

TABLE 6.2 Precursor Metabolites

Precursor Metabolite	Pathway Generated	Biosynthetic Role
Glucose-6-phosphate	Glycolysis	Lipopolysaccharide
Fructose-6-phosphate	Glycolysis	Peptidoglycan
Dihydroxyacetone phosphate	Glycolysis	Lipids (glycerol component)
3-Phosphoglycerate	Glycolysis	Proteins (the amino acids cysteine, glycine, and serine)
Phosphoenolpyruvate	Glycolysis	Proteins (the amino acids phenylalanine, tryptophan, and tyrosine)
Pyruvate	Glycolysis	Proteins (the amino acids alanine, leucine, and valine)
Ribose-5-phosphate	Pentose phosphate cycle	Nucleic acids and proteins (the amino acid histidine)
Erythrose-4-phosphate	Pentose phosphate cycle	Proteins (the amino acids phenylalanine, tryptophan, and tyrosine)
Acetyl-CoA	Transition step	Lipids (fatty acids)
α-Ketoglutarate	TCA cycle	Proteins (the amino acids arginine, glutamate, glutamine, and proline)
Oxaloacetate	TCA cycle	Proteins (the amino acids aspartate, asparagine, isoleucine, lysine, methionine, and threonine)





Introduce the players *Certain intermediates of catabolic pathways can be used in anabolic pathways. These intermediates—****precursor metabolites****—serve as carbon skeletons from which subunits of macromolecules can be made* ***(table 6.2).***

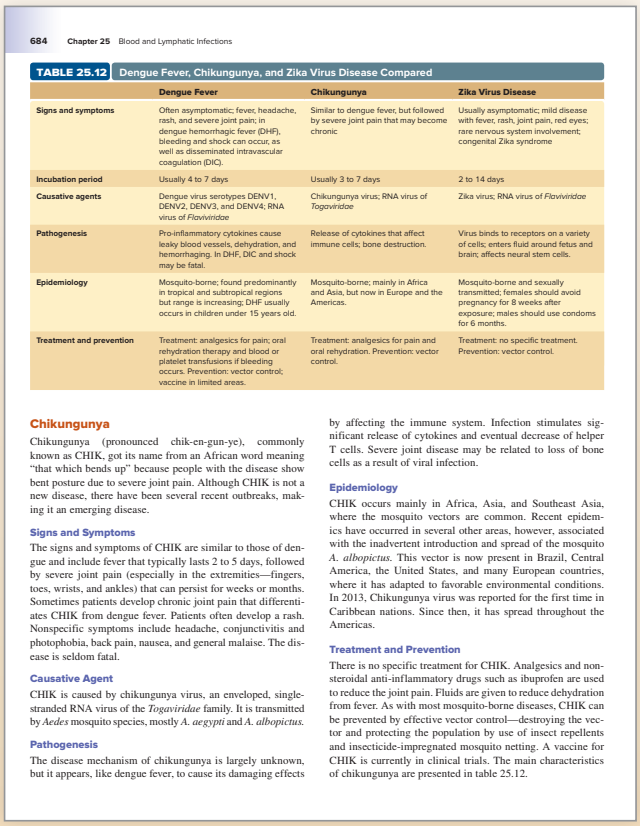
Reinforce the concept *A cell's metabolic pathways make it easy for that cell to use glucose for multiple purposes. Think of the cells as extensive biological recycling centers that routinely process millions of glucose molecules* ***(figure 6.9).*** *Molecules that remain on the central deconstruction line are oxidized completely to CO_2, releasing the maximum amount of energy. Some breakdown intermediates, however, can exit that line to be used in biosynthesis.*

Put the pieces together *Three key metabolic pathways—the* ***central metabolic pathways****—gradually oxidize glucose to CO_2* ***(figure 6.10).*** *The pathways are catabolic, but the precursor metabolites and reducing power they generate can also be diverted for use in biosynthesis.*

Student-Friendly Disease Presentations

Help students think like experts

Within each body system chapter, diseases are separated by major taxonomic category (bacteria, viruses, fungi, protozoa). This organization reflects a major consideration with respect to treatment options, an important consideration for students going into healthcare-related fields.



684 Chapter 25 Blood and Lymphatic Infections

TABLE 25.12 Dengue Fever, Chikungunya, and Zika Virus Disease Compared

	Dengue Fever	Chikungunya	Zika Virus Disease
Signs and symptoms	Often asymptomatic; fever, headache, rash, and severe joint pain; in dengue hemorrhagic fever (DHF), bleeding and shock can occur, as well as disseminated intravascular coagulation (DIC).	Similar to dengue fever, but followed by severe joint pain that may become chronic	Usually asymptomatic; mild disease with fever, rash, joint pain, red eyes; rare nervous system involvement; congenital Zika syndrome
Incubation period	Usually 4 to 7 days	Usually 3 to 7 days	2 to 14 days
Causative agents	Dengue virus serotypes DENV1, DENV2, DENV3, and DENV4; RNA virus of *Flaviviridae*	Chikungunya virus; RNA virus of *Togaviridae*	Zika virus; RNA virus of *Flaviviridae*
Pathogenesis	Pro-inflammatory cytokines cause leaky blood vessels, dehydration, and hemorrhaging. In DHF, DIC and shock may be fatal.	Release of cytokines that affect immune cells; bone destruction.	Virus binds to receptors on a variety of cells; enters fluid around fetus and brain; affects neural stem cells.
Epidemiology	Mosquito-borne; found predominantly in tropical and subtropical regions but range is increasing; DHF usually occurs in children under 15 years old.	Mosquito-borne; mainly in Africa and Asia, but now in Europe and the Americas.	Mosquito-borne and sexually transmitted; females should avoid pregnancy for 8 weeks after exposure; males should use condoms for 6 months.
Treatment and prevention	Treatment: analgesics for pain; oral rehydration therapy and blood or platelet transfusions if bleeding occurs. Prevention: vector control; vaccine in limited areas.	Treatment: analgesics for pain and oral rehydration. Prevention: vector control.	Treatment: no specific treatment. Prevention: vector control.

Chikungunya

Chikungunya (pronounced chik-en-gun-ye), commonly known as CHIK, got its name from an African word meaning "that which bends up" because people with the disease show bent posture due to severe joint pain. Although CHIK is not a new disease, there have been several recent outbreaks, making it an emerging disease.

Signs and Symptoms

The signs and symptoms of CHIK are similar to those of dengue and include fever that typically lasts 2 to 5 days, followed by severe joint pain (especially in the extremities—fingers, toes, wrists, and ankles) that can persist for weeks or months. Sometimes patients develop chronic joint pain that differentiates CHIK from dengue fever. Patients often develop a rash. Nonspecific symptoms include headache, conjunctivitis and photophobia, back pain, nausea, and general malaise. The disease is seldom fatal.

Causative Agent

CHIK is caused by chikungunya virus, an enveloped, single-stranded RNA virus of the *Togaviridae* family. It is transmitted by *Aedes* mosquito species, mostly *A. aegypti* and *A. albopictus.*

Pathogenesis

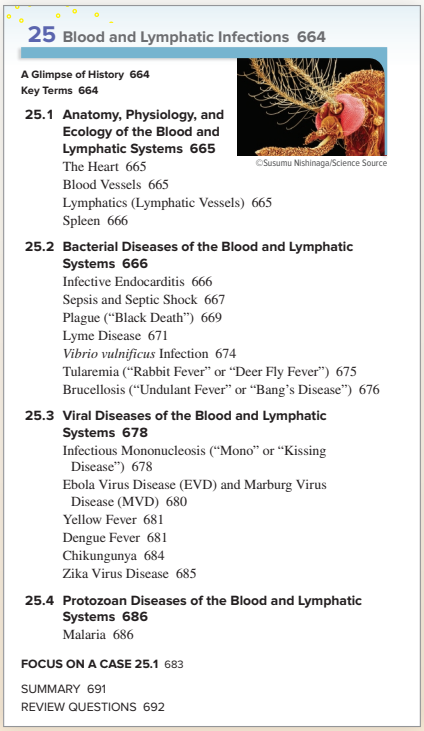
The disease mechanism of chikungunya is largely unknown, but it appears, like dengue fever, to cause its damaging effects by affecting the immune system. Infection stimulates significant release of cytokines and eventual decrease of helper T cells. Severe joint disease may be related to loss of bone cells as a result of viral infection.

Epidemiology

CHIK occurs mainly in Africa, Asia, and Southeast Asia, where the mosquito vectors are common. Recent epidemics have occurred in several other areas, however, associated with the inadvertent introduction and spread of the mosquito *A. albopictus.* This vector is now present in Brazil, Central America, the United States, and many European countries, where it has adapted to favorable environmental conditions. In 2013, Chikungunya virus was reported for the first time in Caribbean nations. Since then, it has spread throughout the Americas.

Treatment and Prevention

There is no specific treatment for CHIK. Analgesics and non-steroidal anti-inflammatory drugs such as ibuprofen are used to reduce the joint pain. Fluids are given to reduce dehydration from fever. As with most mosquito-borne diseases, CHIK can be prevented by effective vector control—destroying the vector and protecting the population by use of insect repellents and insecticide-impregnated mosquito netting. A vaccine for CHIK is currently in clinical trials. The main characteristics of chikungunya are presented in table 25.12.



Provide a consistent conceptual framework

Disease discussions are separated into consistent subsections, providing a conceptual framework and breaking the material into "bite-sized" pieces.

Summarize each disease's characteristics

Summary tables serve as brief reminders of the important features of each disease. Major diseases are represented with an enhanced summary table that includes an outline of the disease process keyed to a human figure, showing the entry and exit of the pathogen.

Review the diseases as a group

Each disease chapter ends with a table that summarizes the key features of the diseases discussed in that chapter.

Diseases in Review 21.1

Respiratory System Diseases

Disease	Causative Agent	Comment	Summary Table
BACTERIAL INFECTIONS OF THE UPPER RESPIRATORY TRACT			
Conjunctivitis (pink eye), otitis media (earache), sinus infection	Usually *Haemophilus influenzae* or *Streptococcus pneumoniae*	Often occur together; factors involved in the transmission are unknown.	
Streptococcal pharyngitis ("strep throat")	*Streptococcus pyogenes* (group A streptococcus)	Treated with antibiotics, partly to avoid sequelae; must be distinguished from viral pharyngitis, which cannot be treated with antibiotics.	Table 21.3
Diphtheria	*Corynebacterium diphtheriae*	Toxin-mediated disease characterized by pseudomembrane in the upper respiratory tract. Preventable by vaccination.	Table 21.4
VIRAL INFECTIONS OF THE UPPER RESPIRATORY TRACT			
Common cold	Rhinoviruses and other viruses	Runny nose, sore throat, and cough are due to the inflammatory response and cell destruction.	Table 21.5
Adenovirus pharyngitis	Adenoviruses	Similar to the common cold but with fever; spread to the lower respiratory tract can result in severe disease.	Table 21.6
BACTERIAL INFECTIONS OF THE LOWER RESPIRATORY TRACT			
Pneumococcal pneumonia	*Streptococcus pneumoniae*	Organism common in the throat of healthy people; causes disease when mucociliary escalator is impaired or with underlying conditions. Vaccine that protects against multiple strains is available.	Table 21.7
***Klebsiella* pneumonia**	*Klebsiella* species, commonly *K. pneumoniae*	Common hospital-acquired bacterium; characterized by thick, bloody, jelly-like sputum. Drug resistance is a major problem.	Table 21.7
Mycoplasmal pneumonia ("walking pneumonia")	*Mycoplasma pneumoniae*	Relatively mild pneumonia; common among college students and military recruits. Cannot be treated with medications that inhibit cell wall synthesis.	Table 21.7
Pertussis ("whooping cough")	*Bordetella pertussis*	Characterized by frequent violent coughing. Preventable by vaccination.	Table 21.8
Tuberculosis ("TB")	*Mycobacterium tuberculosis*	Most infections result in latent tuberculosis infection (LTBI), but these can reactivate to cause tuberculosis disease (TB disease). Treated using combination drug therapy, but drug resistance is an increasing problem.	Table 21.9
Legionellosis ("legionnaires' disease")	*Legionella pneumophila*	Transmitted via aerosolized water drops; smokers and those with impaired defenses are most at risk of developing disease.	Table 21.10
Inhalation anthrax	*Bacillus anthracis*	Rare zoonotic disease; may be associated with bioterrorism; high case-fatality rate.	Table 21.11
VIRAL INFECTIONS OF THE LOWER RESPIRATORY TRACT			
Influenza ("flu")	Influenza viruses	New vaccine developed yearly; viruses change seasonally due to antigenic drift; antigenic shifts cause pandemics.	Table 21.12
Respiratory syncytial virus infections	RSV	Serious disease in infants, young children, and the elderly.	Table 21.13
Hantavirus pulmonary syndrome	Hantaviruses	Acquired via inhaled dust contaminated with rodent saliva, urine, or feces. Frequently fatal.	Table 21.14
SARS and MERS	Coronaviruses	Emerging zoonotic diseases.	Table 21.15
FUNGAL INFECTIONS OF THE RESPIRATORY TRACT			
Coccidioidomycosis ("valley fever")	*Coccidioides immitis*	Environmental reservoir (soil in semi-arid desert areas); most infections are asymptomatic.	Table 21.16
Histoplasmosis ("spelunker's disease")	*Histoplasma capsulatum*	Environmental reservoir (soil enriched with bird or bat droppings); most infections are asymptomatic.	Table 21.17
***Pneumocystis* pneumonia (PCP)**	*Pneumocystis jirovecii* (formerly *carinii*)	Organism is an opportunistic fungus that causes serious lung disease in immunocompromised people, such as those with HIV/AIDS.	Table 21.18

UPDATES—Maintaining the Cutting Edge

Global Changes

- Continued "wordsmithing" to improve the clarity and readability of the descriptions
- Updated disease statistics, vaccine recommendations, treatments, and terminology
- Replaced former "Future Opportunities" boxes with "Focus on the Future" boxes
- Deleted some boxes to make room for updates and other changes

New! "Focus on . . . " Disease Boxes

These boxes cover a general category of disease, giving students a framework and the terminology for understanding the more focused coverage of individual diseases. In essence, they help students see the "forest" before learning about the "trees."

- Chapter 21—Focus on Pneumonia
- Chapter 24—Focus on Diarrheal Diseases
- Chapter 26—Focus on Meningitis
- Chapter 27—Focus on Sexually Transmitted Infections

Key Changes in Individual Chapters

Chapter 1 – Humans and the Microbial World

- Retitled and expanded the section on the normal microbiota (now The Human Microbiome)
- Added information about the National Microbiome Initiative (NMI)
- Added congenital Zika syndrome to the list of emerging diseases
- Substituted MERS for SARS in the discussion of evolution of pathogens to infect new hosts

Chapter 2 – The Molecules of Life

- Simplified the discussion of polysaccharide structures
- Updated the discussion of D-amino acids
- Added a table showing relative electronegativities of common atoms in biology (table 2.3)

Chapter 3 – Microscopy and Cell Structure

- New section on super-resolution microscopes, including an accompanying figure (figure 3.9)
- Retitled the section on atomic force microscopes (now Scanning Probe Microscopes)
- Modified the headings in the cell structure sections to provide clearer distinction between sections on prokaryotic and eukaryotic cells

Chapter 4 – Dynamics of Microbial Growth

- Created a new figure to illustrate the principles of selective and differential media (figure 4.10)
- Added a new MicroByte on the global agar shortage

Chapter 5 – Control of Microbial Growth

- Updated the information about the EPA's efforts to encourage the use of less toxic options for germicidal chemicals, and added a figure (figure 5.9) showing the new "Safer Choice" label
- Enhanced the coverage of high pressure processing (HPP)
- Updated the coverage of triclosan to include restrictions on its use in personal care products
- Updated coverage of the use of chlorine and iodine as disinfectants

Chapter 6 – Microbial Metabolism: Fueling Cell Growth

- Revised the description of vitamins

Chapter 7 – The Blueprint of Life, from DNA to Protein

- New chapter opening photo
- Modified figure 7.13 so that reading frame #1 starts with AUG
- Revised the description of capping of eukaryotic pre-mRNA

Chapter 8 – Bacterial Genetics

- Added an overview figure showing the three mechanisms of horizontal gene transfer (figure 8.18), in place of the previous summary table (was table 8.3)
- Created a new section, "Bacterial Defenses Against Invading DNA" (section 8.10), by moving and revising what was section 13.4. This change introduces restriction enzymes and CRISPR systems before they are discussed in section 9.1 (Fundamental Tools Used in Biotechnology)
- Simplified the table on DNA repair (table 8.2)
- Simplified the summary table on mobile genetic elements (now table 8.3)

Chapter 9 – Biotechnology

- Added a subsection that describes the use of CRISPR in biotechnology, including a supporting figure (figure 9.3)
- Combined what was sections 9.1–9.3 (Applications of Genetic Engineering, Techniques Used in Genetic Engineering, and Concerns Regarding Genetic Engineering)
- Retitled the subsection on next-generation sequencing methods (now High-Throughput Sequencing Methods) and expanded to include nanopore sequencing and its use in the International Space Station
- Expanded the section on PCR by adding information about RT-PCR and q-PCR
- Added a "Focus on the Future" box about Precision Medicine

Chapter 10 – Identifying and Classifying Microorganisms

- Updated figure 10.1 to include a part that illustrates the new Tree of Life based on ribosomal protein sequences
- Expanded the information about whole genome sequencing to characterize strain differences, and added information about the Genome Trakr Network

Chapter 11 – The Diversity of *Bacteria* and *Archaea*

- Added *Methanopyrus kandleri,* the current record-holder for high-temperature growth, to the section on methane-generating hyperthermophiles
- Updated the information on *Chlamydia* species to no longer state that they lack detectable peptidoglycan; also changed the question that accompanies the figure showing *Chlamydia* (now figure 11.26)

Chapter 12 – The Eukaryotic Members of the Microbial World

- Updated the description of lichens to indicate that genetic and molecular evidence suggests that they may include more than two partners
- Revised figure 12.12 to accompany an updated presentation of eukaryotic phylogeny
- Reduced the coverage of arthropod groups (some information was moved to chapters that describe arthropod-borne diseases)

Chapter 13 – Viruses, Viroids, and Prions

- Added icons that correlate steps in figure 13.5 (steps in the replication of lytic phage T4 in *E. coli*) with descriptions in the accompanying narrative
- Moved the previous section on bacterial defenses against phages to chapter 8, so that restriction enzymes and CRISPR systems are covered earlier (before chapter 9, which describes their use in biotechnology)
- Added a new rendition of the figure that illustrates animal virus replication strategies (figure 13.12) for easier understanding

Chapter 14 – The Innate Immune Response

- Moved the Focus Figure (figure 14.1) into section 14.1
- Simplified figure 14.5

Chapter 15 – The Adaptive Immune Response

- Changed the critical thinking question in MicroAssessment 15.5
- Expanded the legend for figure 15.25

Chapter 16 – Host-Microbe Interactions

- Added the definition of microbiome to the key terms
- Changed the title of section 16.2 to The Human Microbiome (was The Normal Microbiota)
- Introduced the term *dysbiosis*
- Added a subsection on damage to the host in section 16.9 (Mechanisms of Viral Pathogenesis)

Chapter 17 – Immunological Disorders

- Updated coverage of hypersensitivity reactions, particularly asthma, systemic anaphylaxis, and immune complex diseases

- Updated and increased coverage of immunotherapy to treat allergic reactions
- Added MicroByte on sublingual immunotherapy (SLIT) as an alternative to allergy shots
- Moved coverage of tuberculin skin test to the presentation of tuberculosis in section 21.4

Chapter 18 – Applications of Immune Responses

- Updated the information about polio eradication efforts by including the switch from trivalent to bivalent OPV
- Reorganized and refined the section on vaccines (section 18.2) by incorporating a new subsection titled "The Importance of Vaccines," rearranging the order of the tables, and separating the list of non-routine vaccines into a new table (table 18.5); also updated the table entries
- Added information about the monoclonal antibody recently approved for use as part of the protocol for treating inhalation anthrax
- Created a new "Focus on the Future" box that describes cancer immunotherapies, including CAR T cells

Chapter 19 – Epidemiology

- Updated the table of notifiable infectious diseases (table 19.1)
- Added a new table that lists the most common nosocomial infections (table 19.3)
- Added a subsection on visitors to the section that describes potential reservoirs for nosocomial infections
- Added new coverage of National Healthcare Safety Network (NHSN)

Chapter 20 – Antimicrobial Medications

- Expanded the section on development of antibiotics by adding information about Generating Antibiotic Incentives Now (GAIN)
- Added information about the newest glycopeptide antibiotics (dalbavancin and oritavancin) and the newest oxazolidinone (tedizolid)
- Updated the list of antiviral medications by adding NS5A inhibitors (used to treat HCV)
- Changed the "Focus on the Future" box to cover the *National Action Plan for Combating Antibiotic Resistant Bacteria*

Chapter 21 – Respiratory System Infections

- Added new box, "Focus on Pneumonia," presenting general characteristics of this important category of respiratory diseases
- Added a new section on inhalation anthrax
- Added a new section on SARS and MERS
- Rearranged section 21.2 to begin with milder diseases (pink eye, earache, sinus infections)
- Updated and focused the coverage of pneumococcal pneumonia and *Klebsiella* pneumonia
- Pertussis: revised the information about the epidemiology and the treatment and prevention; added a new photo (figure 21.16)
- Tuberculosis: increased the coverage of tuberculin skin test and added an accompanying figure (figure 21.21)

Chapter 22 – Skin Infections

- Added new section on cutaneous anthrax
- Added mention of ceftaroline as a new β-lactam antibiotic that can be used for treating MRSA
- Moved section on Lyme disease to chapter 25 (Blood and Lymphatic Infections)
- Rocky Mountain spotted fever: revised the information on the signs and symptoms and the pathogenesis
- Rubeola: revised the introduction and the information about the epidemiology and the prevention

Chapter 23 – Wound Infections

- Deleted coverage of actinomycosis (lumpy jaw)
- Removed photo showing an individual with sporotrichosis (was figure 23.14)

Chapter 24 – Digestive System Infections

- Added new box, "Focus on Diarrheal Diseases," presenting general characteristics of this important category of intestinal disease
- Periodontal disease and ANUG: revised the descriptions of causative agents
- Mumps: revised the description of epidemiology
- Cholera: added information about the new FDA-approved vaccine
- Shigellosis: updated the description of treatment
- *Clostridium difficile* infection (CDI): added information about fidaxomicin for treatment

- Norovirus: added update about the recent cultivation of the virus in the laboratory
- Hepatitis C: revised the introduction and added information about the new treatments

Chapter 25 – Blood and Lymphatic Infections

- Reorganized coverage throughout
- Revised coverage of anatomy, especially the lymphatics
- Added new section on Zika virus disease
- Dengue fever: added information about the new vaccine
- Chikungunya: standardized the organization of the section
- Added a new table that compares Dengue fever, Chikungunya, and Zika Virus disease (table 25.12)
- Added a section on Lyme disease (moved from chapter 22)
- Revised the coverage of infective endocarditis (previously SBE)

Chapter 26 – Nervous System Infections

- Added new box, "Focus on Meningitis," presenting general characteristics of this important category of nervous system diseases
- Reorganized to separate central nervous system (CNS) diseases from peripheral nervous system (PNS) diseases; superheadings added
- Pneumococcal and meningococcal meningitis: updated and focused the coverage
- Polio: updated the coverage
- Changed African sleeping sickness to African trypanosomiasis; revised the descriptions of the epidemiology and the treatment

Chapter 27 – Genitourinary Tract Infections

- Added new box, "Focus on Sexually Transmitted Infections," presenting general characteristics of this important category of genitourinary infections
- Added coverage on *Mycoplasma genitalium* infections
- Updated figure 27.21 (The Global HIV/AIDS Epidemic) to reflect changes in numbers
- Updated figure 27.25 (HIV Replication)
- Updated and modified figure 27.26 (was Deaths Due to AIDS) to include global number of people receiving ART

Chapter 28 – Microbial Ecology

- Revised the section on terrestrial habitats to emphasize the microbiome
- Changed the order of the questions in MicroAssessment 28.4

Chapter 29 – Environmental Microbiology: Treatment of Water, Wastes, and Polluted Habitats

- Deleted the "Focus on the Future" box ("Better Identification of Pathogens in Water and Wastes")

Chapter 30 – Food Microbiology

- Moved the description of starter culture
- Updated the names of the organisms used to make fermented foods
- Revised the section on making beer
- Deleted the "Focus on the Future" box ("Using Microorganisms to Nourish the World")

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We hope that this text will be interesting and educational for students and helpful to instructors. Our goal is excellence, so with that in mind we would appreciate any comments and suggestions from our readers.

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Contents

PROKARYOTIC CELLS

EUKARYOTIC CELLS

4 Dynamics of Microbial Growth 92


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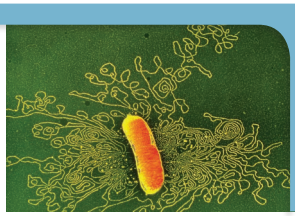

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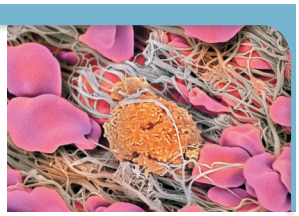

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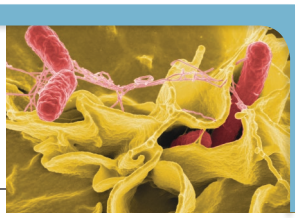

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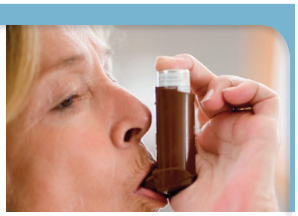
MECHANISMS OF PATHOGENESIS



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IMMUNIZATION

IMMUNOLOGICAL TESTING

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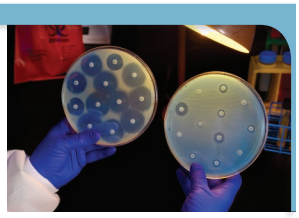
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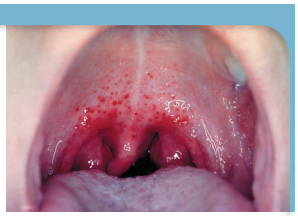
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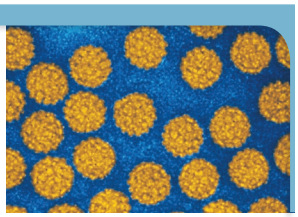

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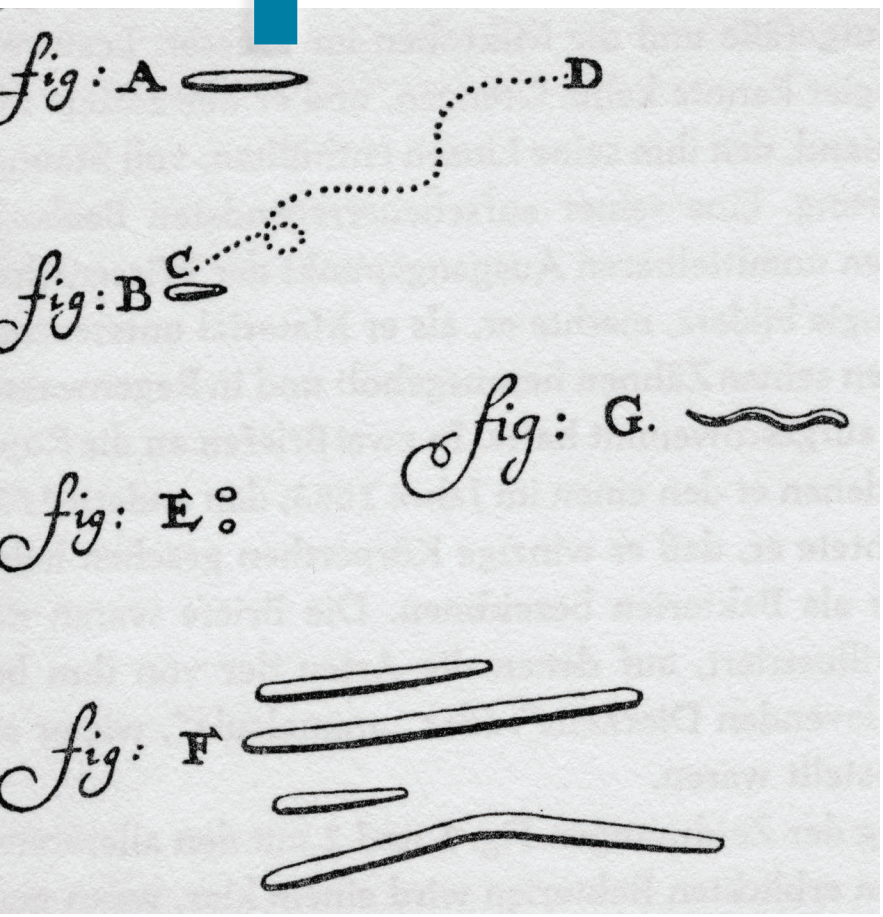
1 Humans and the Microbial World



Drawings that van Leeuwenhoek made in 1683 of microorganisms he saw through his single lens microscope. He also observed organism B moving from position C to D.
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KEY TERMS

Domain The highest level in biological classification. There are three domains: *Bacteria, Archaea,* and *Eukarya.*

Eukaryote Organism composed of one or more eukaryotic cells; members of the domain *Eukarya* are eukaryotes.

Eukaryotic Cell Cell type characterized by a membrane-bound nucleus.

Prion An acellular infectious agent consisting only of protein.

Prokaryote Single-celled organism consisting of a prokaryotic cell; members of the domains *Bacteria* and *Archaea* are prokaryotes.

Prokaryotic Cell Cell type characterized by the lack of a membrane-bound nucleus.

Viroid An acellular infectious agent consisting only of RNA.

Virus An acellular infectious agent consisting of nucleic acid surrounded by a protein coat.

A Glimpse of History

Microbiology as a science was born in 1674 when Antony van Leeuwenhoek, an inquisitive Dutch fabric merchant, looked at a drop of lake water through a glass lens he had carefully made. Although many people before him had used curved glass to magnify objects, Leeuwenhoek's skilled hands made a lens that uncovered a startling and amazing sight—the world of microbes. As van Leeuwenhoek wrote in a letter to the Royal Society of London, he saw

> Very many little animalcules, whereof some were roundish, while others a bit bigger consisted of an oval. On these last, I saw two little legs near the head, and two little fins at the hind most end of the body. Others were somewhat longer than an oval, and these were very slow a-moving, and few in number. These animalcules had diverse colours, some being whitish and transparent; others with green and very glittering little scales, others again were green in the middle, and before and behind white; others yet were ashed grey. And the motion of most of these animalcules in the water was so swift, and so various, upwards, downwards, and round about, that 'twas wonderful to see.

Before van Leeuwenhoek made these observations, Robert Hooke, an English microscopist, saw another kind of microorganism. In 1665, he described what he called a "microscopical mushroom." His drawing was so accurate that his specimen could later be identified as a common bread mold. Hooke also described how to make the kind of microscope that van Leeuwenhoek constructed almost 10 years later. Both men deserve equal credit for revealing the world of microbes—the organisms you are about to study.

Microbiology is the study of the microbial world—an amazing world made up of members too small to be seen without the aid of a microscope. Antony van Leeuwenhoek described this world when he observed what he called "animalcules" through his simple microscope (**figure 1.1**). What he saw were **microorganisms** (organisms too small to see with the naked eye), including bacteria, protozoa, and some fungi and algae. The microbial world also includes viruses and other infectious agents that are not considered organisms because they are not composed of cells; they are acellular. When referring to general members of the microbial world, the term **microbe** is often used.

Microorganisms are the foundation for all life on Earth. They have existed on this planet for about 3.5 billion years, and over this time, plants, animals, and modern microorganisms have evolved from them. Even today, they continue to be a driving force in the evolution of all living things. Microorganisms may be small, but as you are about to learn, our life depends on their activities.

FIGURE 1.1 Model of van Leeuwenhoek's Microscope
The original made in 1673 could magnify an object almost 300 times. The object is brought into focus with the adjusting screws. ©Tetra Images/Alamy Stock Photo

? What kinds of organisms did van Leeuwenhoek observe through his microscope?

1.1 ■ The Dispute over Spontaneous Generation

Learning Outcomes

1. Describe the key experiments of scientists who disproved spontaneous generation.
2. Explain how the successful challenge to the idea of spontaneous generation led to the Golden Age of Microbiology.
3. Describe the scientific method, using Pasteur's swan-necked flask experiment as an example.

The discovery of microorganisms in various specimens raised an interesting question: "Where did these microscopic forms originate?" Some people believed that worms and other forms of life arise from non-living material in a process referred to as **spontaneous generation.** This was challenged by an Italian biologist and physician, Francesco Redi. In 1668, he used a simple experiment to show that worms found on rotting meat originated from the eggs of flies, not from the decaying meat as supporters of spontaneous generation believed. In his experiment, Redi covered the meat with fine gauze that prevented flies from depositing their eggs. When he did this, no worms appeared.

Despite Redi's work that explained the source of worms on decaying meat, conclusive evidence that microorganisms did not arise by spontaneous generation took more than 200 years and many experiments.

Early Experiments

In 1749, John Needham, a scientist and Catholic priest, showed that flasks containing various broths (made by soaking a nutrient source such as hay or chicken in water) gave rise to microorganisms even when the flasks were boiled and sealed with a cork. At that time, brief boiling was thought to kill all organisms, so this suggested that microorganisms did indeed arise spontaneously.

In 1776, the animal physiologist and priest Lazzaro Spallanzani obtained results that contradicted Needham's experiments; no bacteria appeared in Spallanzani's broths after boiling. His experiments differed from Needham's in two significant ways: Spallanzani boiled the broths for longer periods and he sealed the flasks by melting their glass necks closed. Using these techniques, he repeatedly demonstrated that broths remained sterile (free of microorganisms). However, if the neck of the flask cracked, the broth rapidly became cloudy due to growth of the organisms. Spallanzani concluded that microorganisms had entered the broth with the air, and the corks used by Needham and other investigators did not keep them out.

Spallanzani's experiments did not stop the controversy. Some people argued that the heating process destroyed a "vital force" in the air that was necessary for spontaneous generation, and so the debate continued.

Experiments of Pasteur

One giant in science who helped disprove spontaneous generation was Louis Pasteur, the French chemist considered by many to be the father of modern microbiology. In 1861, he did a series of clever experiments. First, he demonstrated that air contains microorganisms. He did this by filtering air through a cotton plug, trapping microorganisms. He then examined the trapped microorganisms with a microscope and found that many looked identical to those described by others who had been studying broths. When Pasteur dropped the cotton plug into a sterilized broth, the broth became cloudy from the growth of these microorganisms.

Most important, Pasteur demonstrated that sterile broths in specially constructed swan-necked flasks remained sterile even when left open to air (**figure 1.2**). Microorganisms from the air settled in the bends of the flask necks, never reaching the broth. Only when the flasks were tipped would microorganisms enter the broth and grow. Pasteur's simple and elegant experiments ended the arguments that unheated air or the broths themselves contained a "vital force" necessary for spontaneous generation. They led to the theory of **biogenesis,** the production of living things from other living things (*bio* means "life"; *genesis* means "to create").

Experiments of Tyndall

Although most scientists were convinced by Pasteur's experiments, some remained skeptical because they could not reproduce his results. An English physicist, John Tyndall, finally explained the conflicting data and, in turn, showed that Pasteur was correct. Tyndall found that various types of

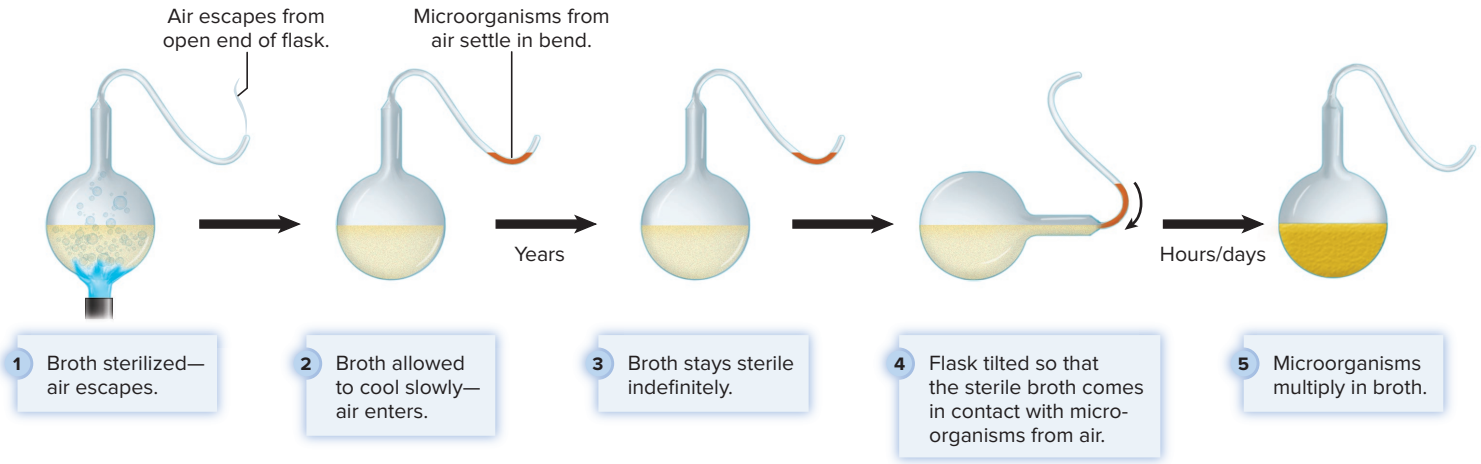

FIGURE 1.2 Pasteur's Experiment with the Swan-Necked Flask If the flask remains upright, no microbial growth occurs. If the flask is tipped, the microorganisms trapped in the neck reach the sterile broth and grow.

? If the broth in Pasteur's swan-necked flasks had contained endospores, what results would have been observed?

broths required different boiling times to be sterilized. Some were sterilized by boiling for 5 minutes, whereas others, most notably broths made from hay, still contained living microorganisms even after boiling for 5 hours! Even when hay was merely present in the laboratory, broths that had previously been sterilized by boiling for 5 minutes could not be sterilized by boiling for several hours. What was going on? Tyndall finally realized that hay contained heat-resistant forms of microorganisms. When hay was brought into the laboratory, dust particles must have transferred these heat-resistant forms to the broths.

Tyndall concluded that some microorganisms exist in two forms: a cell easily killed by boiling, and one that is heat resistant. In the same year (1876), a German botanist, Ferdinand Cohn, discovered **endospores,** the heat-resistant forms of some bacteria. ⏭ endospores

The extreme heat resistance of endospores explains the differences between Pasteur's results and those of other investigators. Organisms that produce endospores are commonly found in the soil and were likely present in broths made from hay. Pasteur used only broths made with sugar or yeast extract, so his experiments probably did not have endospores. At the time, scientists did not appreciate the importance of the source of the broth, but in hindsight, the source was critical. This points out an important lesson for all scientists. In repeating an experiment, it is essential to reproduce all conditions as closely as possible. What may seem like a trivial difference may be extremely important.

The Golden Age of Microbiology

The work of Pasteur and others in disproving spontaneous generation started an era called the Golden Age of Microbiology, during which time the field of microbiology blossomed. Many important advances were made during this period, including discoveries that led to acceptance of the suggestion that microorganisms cause certain diseases, a principle now called the Germ Theory of Disease.

Figure 1.3 lists some of the important advances in microbiology made over the years in the context of other historical events. Rather than cover more history now, we will return to many of these milestones in brief stories called "A Glimpse of History" that open each chapter.

The Scientific Method

The dispute over spontaneous generation offers an excellent example of the process of science. This process, called the **scientific method,** separates science from intuition and beliefs. The scientific method involves a series of steps, including:

- **Making an observation about something and asking a question about that situation.** An example from this chapter was the observation that microorganisms were present in various examined specimens. This observation led to the question "Where did the microorganisms originate?"
- **Developing an explanation and then devising an experiment that tests the explanation.** A testable explanation of an observation is called a **hypothesis,** and experiments are done to test the hypothesis. The dispute over spontaneous generation led to two opposing hypotheses: biogenesis and spontaneous generation. Various people designed different experiments to test the hypotheses.
- **Doing the experiment, collecting the data, and drawing a conclusion.** Experiments such as the one illustrated in figure 1.2 provided data about the growth of microorganisms in previously sterile broths. In doing a

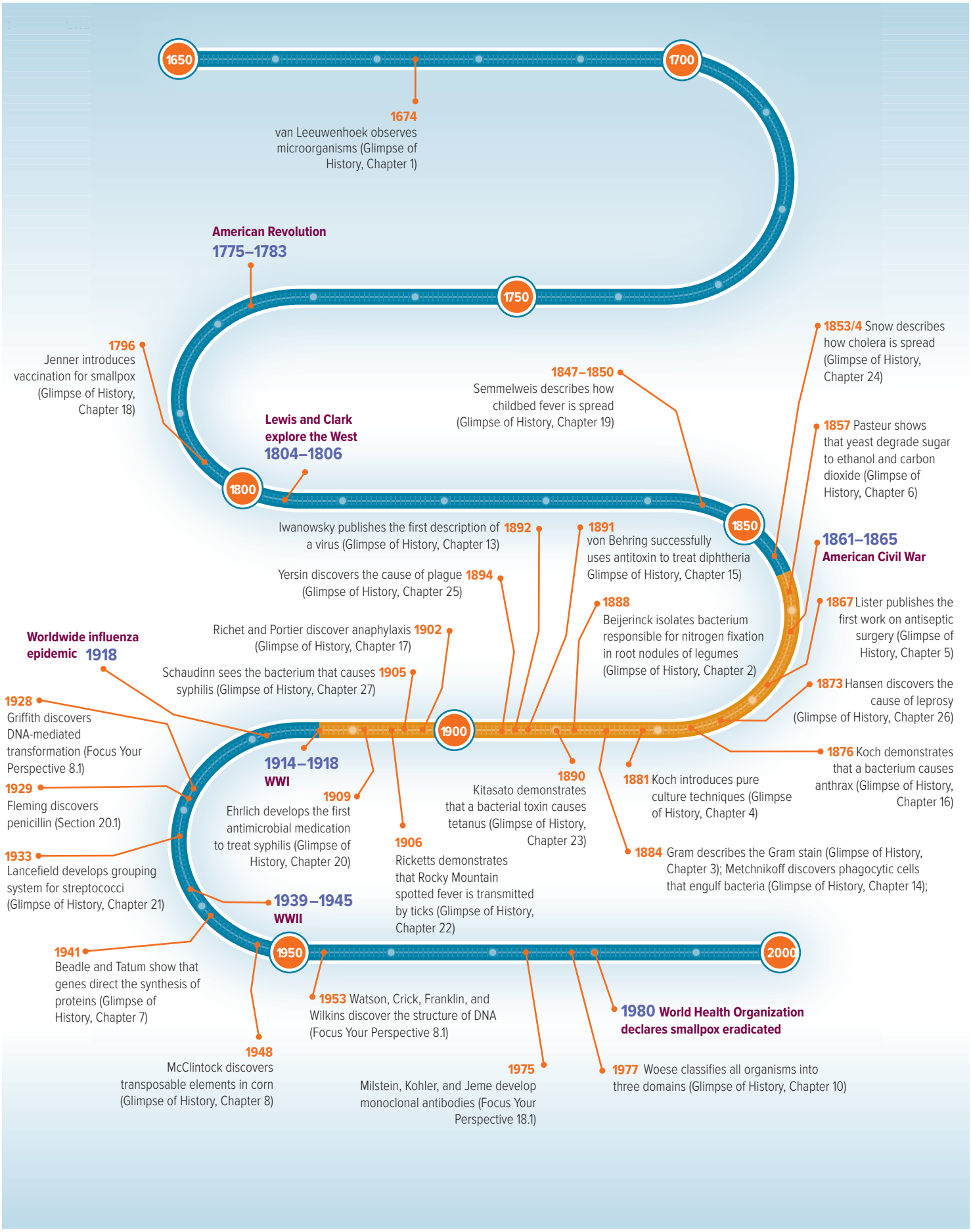

FIGURE 1.3 Historical Events in Microbiology Some major milestones in microbiology—and their timeline in relation to other historical events. The gold band indicates the Golden Age of Microbiology.

? What is the Golden Age of Microbiology?

scientific experiment, a critical component is a **control.** A control helps rule out alternative explanations of the results by showing that the only feature that varied in the experiment was the characteristic being tested. Pasteur's swan-necked flask experiment was brilliantly designed because it provided the following control: After showing that the fluid in the swan-necked flasks remained sterile even when opened to air, he tipped the flasks so that bacteria could enter the fluid. By doing this, he showed that there was nothing in his original set-up that would have prevented bacteria from growing in the broth.

- **Communicating the methods, results, and conclusions.** Scientists share their work by publishing it in scientific journals. This step is particularly important because it allows other scientists to repeat the experiment to ensure the validity of the findings. Today, the respected scientific journals use a review process in which other experts in the field read communications before they are published. If deficiencies or flaws are noticed, the reviewers give suggestions for improving the experiments.

When an extensive amount of experimental evidence supports a hypothesis, that explanation may become a scientific **theory,** such as the Germ Theory of Disease. Note that the scientific meaning of the word *theory* is far different from the meaning of the word in common language, which is "a speculation or guess."

As you read the information in this textbook, continually challenge yourself by asking questions about what you have learned. If you find yourself asking a question such as "How does that happen?" try to develop a hypothesis and then devise an experiment. As you do this, consider the controls you could use. Start learning to think like a scientist!

MicroAssessment 1.1

Experiments of Pasteur and Tyndall helped disprove spontaneous generation by showing that life arises from life. Many important discoveries were made during the Golden Age of Microbiology, including ones that led to the acceptance of the Germ Theory of Disease. The scientific method uses experimental evidence, including proper controls, to support or refute hypotheses.

1. Describe Pasteur's experiment that disproved the idea that a "vital force" in air was responsible for spontaneous generation.
2. How is the meaning of the word "theory" in science different from its meaning in everyday conversation?
3. Why is it important for scientists to repeat the experiments of others?

1.2 ■ Microbiology: A Human Perspective

Learning Outcomes

4. Explain the importance of microorganisms in the health of humans and the surrounding environment.
5. List three commercial benefits of microorganisms.
6. Describe why microorganisms are useful research tools.
7. Describe the role of microbes in disease, including examples of past triumphs and remaining challenges.

Microorganisms have an enormous impact on all living things. We could not survive without them, and they also make our lives much more comfortable. At the same time, microbes can be harmful, and have killed far more people than have ever been killed in war.

The Human Microbiome

The human body carries an enormous population of microorganisms—tens of trillions of bacterial cells alone. Many sources claim that the body carries 10 times as many microbial cells as human cells, but that number is just a guess. Recent and probably more accurate estimates indicate that the ratio is likely closer to 3:1 or even 1:1. Regardless, scientists have known for years that these microorganisms, collectively referred to as the **normal microbiota** or normal flora, play an essential role in human health. For example, they prevent disease by competing with disease-causing microbes, help to degrade foods that the body otherwise could not digest, and promote the development of the immune system. In fact, studies indicate that early exposure to certain common microorganisms lessens the likelihood that an individual will develop allergies, asthma, and some other diseases. According to what is sometimes referred to as the "Old Friends" hypothesis, this early exposure helps the immune system learn to distinguish "friendly" microbes from those that can cause severe disease. In addition, animal studies suggest that the composition of the normal microbiota can affect brain chemistry and behavior, as well as the tendency to gain or lose weight.

The important role of the normal microbiota became even more obvious in recent years, thanks in part to the **Human Microbiome Project.** This coordinated set of studies, started in 2007, used DNA sequencing technologies to characterize the microbial communities that inhabit the human body. The term **microbiome** has two overlapping meanings: (1) the total genetic content of a microbial community, and (2) the microbial community itself. While the different meanings might seem confusing, they are actually quite similar because at this point the communities must be examined by studying their genetic material. The reason for this is that less than 1% of microorganisms can currently be grown in the laboratory.

So for every microbe that had been studied in the laboratory, more than 99 others could not be characterized until DNA sequencing technologies were developed.

The Human Microbiome Project has changed the way scientists view the human body and is also revealing how much more there is to discover about our microbial partners. To understand their significance, think of the earth's ecosystems (the environments and their interacting inhabitants). Over time, an interacting assortment of organisms has evolved to live in a given environment, resulting in a relatively stable community. Sudden changes can alter individual populations, often with negative consequences to the community as a whole. In turn, a disturbance in one ecosystem can affect the overall health of the planet. The human body, like a planet, is composed of various ecosystems—for example, the desert-like dry areas of the skin, and the nutrient-rich environment of the intestinal tract. An important part of these ecosystems is a population of interacting microbes. Disturbances in a microbial population can create an imbalance that may have negative consequences to that community, which, in turn, can harm a person's health. Observations such as these have led some scientists to suggest that the human body be considered a superorganism, meaning that our own cells interact with the body's normal microbiota to form a single cooperative unit.

Microorganisms in the Environment

Microorganisms are the masters of recycling, and without them we would run out of certain nutrients. For instance, humans and other animals all require oxygen gas (O_2) to breathe. However, the supply of O_2 in the atmosphere would run out if it were not continually replenished. Plants produce O_2 during photosynthesis, but so do many photosynthetic microorganisms. Another example involves nitrogen, an essential part of nucleic acids and proteins. A plentiful source of nitrogen is N_2—the most common gas in the atmosphere—yet neither plants nor animals can use it. Instead, we depend on certain microbes that convert N_2 into a form of nitrogen that other organisms can use, a process called nitrogen fixation. Without nitrogen-fixing microbes, life as we know it would not exist. ⏭ nitrogen fixation

Microorganisms are also important because they can degrade certain materials that other organisms cannot. For instance, humans and other animals cannot digest cellulose—an important component of plants. Certain microorganisms degrade cellulose, however, which is why leaves and fallen trees do not pile up in the environment. Many of the billions of microorganisms in the digestive tracts of a group of animals that includes cattle, sheep, and deer degrade cellulose; by doing so, the microorganisms help the animals digest plant material. Without cellulose-degrading microbes in their digestive tracts, these plant-eating animals would starve.

In recognition of the important role that microorganisms play in all aspects of life, the **National Microbiome Initiative (NMI)** expands the scope of microbiome research. Started in 2016, the program supports research on the microbiomes of humans as well as those of our surrounding environment.

Commercial Benefits of Microorganisms

In addition to the crucial roles microorganisms play in our very existence, they also have made life more comfortable for humans over the centuries.

Food Production

Microorganisms have been used in food production since ancient times. For example, Egyptians used yeast to make bread and beer. Virtually every population that raised milk-producing animals such as cows and goats also developed procedures to ferment milk. This allowed them to make foods such as yogurt, cheeses, and buttermilk. Today, the bacteria added to some fermented milk products are advertised as probiotics (live microorganisms that provide a health benefit), protecting against digestive disruptions. ⏭ bread, ⏭ beer, ⏭ fermented milk products, ⏭ probiotics

Biodegradation

Microorganisms play essential roles in degrading various environmental pollutants. These include materials in wastewater, as well as toxic chemicals in contaminated soil and water. Bacteria also lessen the damage from oil spills. In some cases, microorganisms are added to pollutants to hasten their decay, a process called **bioremediation.** ⏭ wastewater treatment, ⏭ bioremediation

Commercially Valuable Products from Microorganisms

Microorganisms synthesize a wide variety of different products, some of which are commercially valuable. Examples include antibiotics used in the treatment of diseases; ethanol used as a biofuel; hydrogen gas and certain oils potentially used as biofuels; amino acids used as dietary supplements; insect toxins used in insecticides; cellulose used in headphones; and polyhydroxybutyrate used in the manufacture of disposable diapers and plastics.

Biotechnology

Biotechnology—the use of microbiological and biochemical techniques to solve practical problems—depends on members of the microbial world. Information learned by studying microorganisms led to easier production of many medications, such as insulin (used to treat diabetes). In the past, insulin was isolated from pancreatic glands of cattle and pigs. Now, certain microorganisms have been genetically engineered to make human insulin. The microbe-produced insulin is easier

to obtain, and patients who use it have fewer allergic reactions than occurred with the animal-derived product. Biotechnology has also led to techniques that scientists now use to genetically engineer plants to give them desirable qualities.

genetic engineering

Microbes as Research Tools

Microorganisms are wonderful model organisms to study because they have the same fundamental metabolic and genetic properties as higher life forms. All cells are composed of the same chemical elements and they synthesize their cell structures by similar mechanisms. They all duplicate their DNA, and when they degrade foods to harvest energy, they do so via the same metabolic pathways. To paraphrase a Nobel Prize–winning microbiologist, Dr. Jacques Monod—what is true of elephants is also true of bacteria, and bacteria are much easier to study! In addition, bacteria can be used to obtain results very quickly because they grow rapidly and form billions of cells per milliliter on simple inexpensive growth media. In fact, most major advances made in the last century toward understanding life have come through the study of microbes.

Microbes and Disease

Although most microbes are beneficial or not harmful, some are **pathogens,** meaning they can cause disease (a noticeable impairment in body function). The disease symptoms result from damage to the body tissues. This damage can occur either as a direct result of the pathogen's growth and products, or as a result of the body's defense mechanisms, which can inadvertently harm the host while attempting to control the pathogen.

To appreciate the effect an infectious disease can have on a population, consider that more Americans died of influenza in 1918–1919 than were killed in World Wars I and II, and the Korean, Vietnam, and Iraq wars combined. Fortunately, technological advances such as sanitation, vaccination, and antibiotic treatments have dramatically reduced the incidence of many of the most feared infectious diseases. To maintain this success, however, we must continue to develop new medications, vaccines, and disease-prevention strategies.

Past Triumphs

The Golden Age of Microbiology included an important period when scientists learned a great deal about pathogens. Between 1876 and 1918, most pathogenic bacteria were identified, and early work on viruses had begun. Once people realized that microbes could cause disease, they tried to prevent their spread. As illustrated in **figure 1.4,** the death rate due to infectious diseases has decreased dramatically over the last

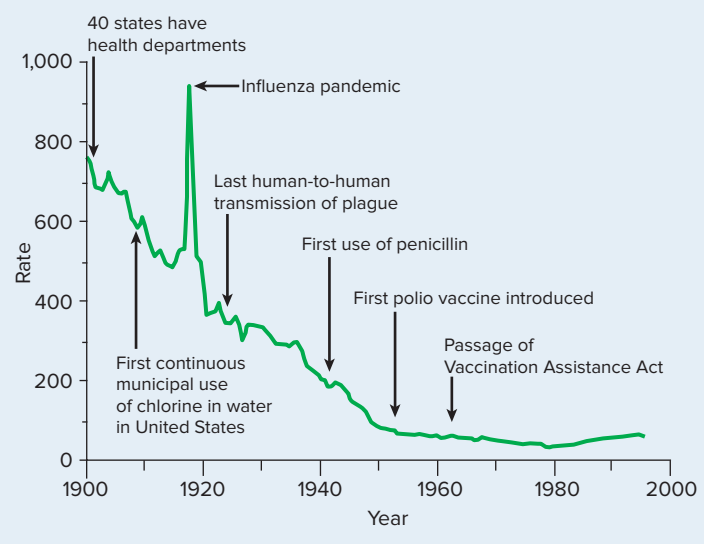

FIGURE 1.4 Trend in Death Rates Due to Infectious Diseases
Crude death rate for infectious disease, United States, per 100,000 population per year.

? **Why would the creation of health departments lower the disease rate?**

100 years or so, due largely to preventing the spread of pathogens, developing vaccines to provide immunity, and using antibiotics to treat bacterial diseases when they do occur.

The viral disease smallpox was one of the most devastating diseases the world has ever known, killing about one-third of people who got it. Survivors were sometimes blinded and often left with disfiguring scars. When Europeans carried the disease to the Americas, the effect on the populations of native inhabitants who had not been exposed before was catastrophic. In recent times, an active worldwide vaccination program eliminated the disease in nature, with no cases being reported since 1977. Laboratory stocks of the smallpox virus remain, however, raising the possibility that the virus could be used in bioterrorist attacks.

Plague has been another major killer. One-third of the population of Europe, or approximately 25 million people, died of this bacterial disease in only 4 years (1347–1351). We now know that rodents can carry the bacterium, and their fleas can transmit the disease, so we take measures to control the rodent populations. We have also learned that the pneumonic form of the disease (meaning that it is in the lungs) can spread from human to human through respiratory secretions, so special precautions are taken when a patient has pneumonic plague. In addition, the discovery of antibiotics in the twentieth century made treatment possible. As a result, less than 100 people worldwide die from plague in a typical year.

Polio can cause paralysis, leading to death or disability. The disease was once relatively common, but it has been nearly eliminated because of vaccination. In fact, polio now

occurs in only a few countries, and the goal is to eradicate (eliminate) the disease globally.

Epidemics are not limited to human populations. The great famine in Ireland in the 1800s was due, in part, to a microbial disease of potatoes. In 2001, a catastrophic outbreak of foot-and-mouth disease of animals occurred in England. To contain this viral disease, one of the most contagious known, almost 4 million pigs, sheep, and cattle were destroyed. In 2016, a fungal disease called "wheat blast" that devastated wheat crops in South America spread to Bangladesh, resulting in the loss of over 35,000 acres of crops that year.

Remaining Challenges

Although progress has been impressive against infectious diseases, much more still needs to be done. On a worldwide basis, infectious diseases remain too common, particularly in developing countries. Even in developed countries with sophisticated healthcare systems, infectious diseases remain a serious threat, costing lives and money.

Emerging Infectious Diseases An **emerging infectious disease (EID)** is an infectious disease that has become more common in the last 35 years. Many of these are new or newly recognized; examples include Ebola virus disease, congenital Zika syndrome, hepatitis C, Middle East respiratory syndrome (MERS), certain types of influenza, Lyme disease, acquired immunodeficiency syndrome (AIDS), hantavirus pulmonary syndrome, and mad cow disease (bovine spongiform encephalopathy) (**figure 1.5**). Others such as malaria and tuberculosis have been present for years, but have spread or become more common recently.

Some diseases arise as infectious agents evolve to infect new hosts, cause different types of damage, or become more difficult to treat because of antibiotic resistance. Genetic analysis indicates that HIV-1 (**h**uman **i**mmunodeficiency **v**irus type 1), the most common type of HIV to cause AIDS, arose from a virus that infected chimpanzees. A bacterium called *E. coli* O104:H4, which caused a severe foodborne diarrheal outbreak in Europe, appears to have gained the ability to make a specific toxin by acquiring genes from a related organism. Tuberculosis and malaria have increased in incidence in recent years, in part because the causative organisms became resistant to many of the available medications.

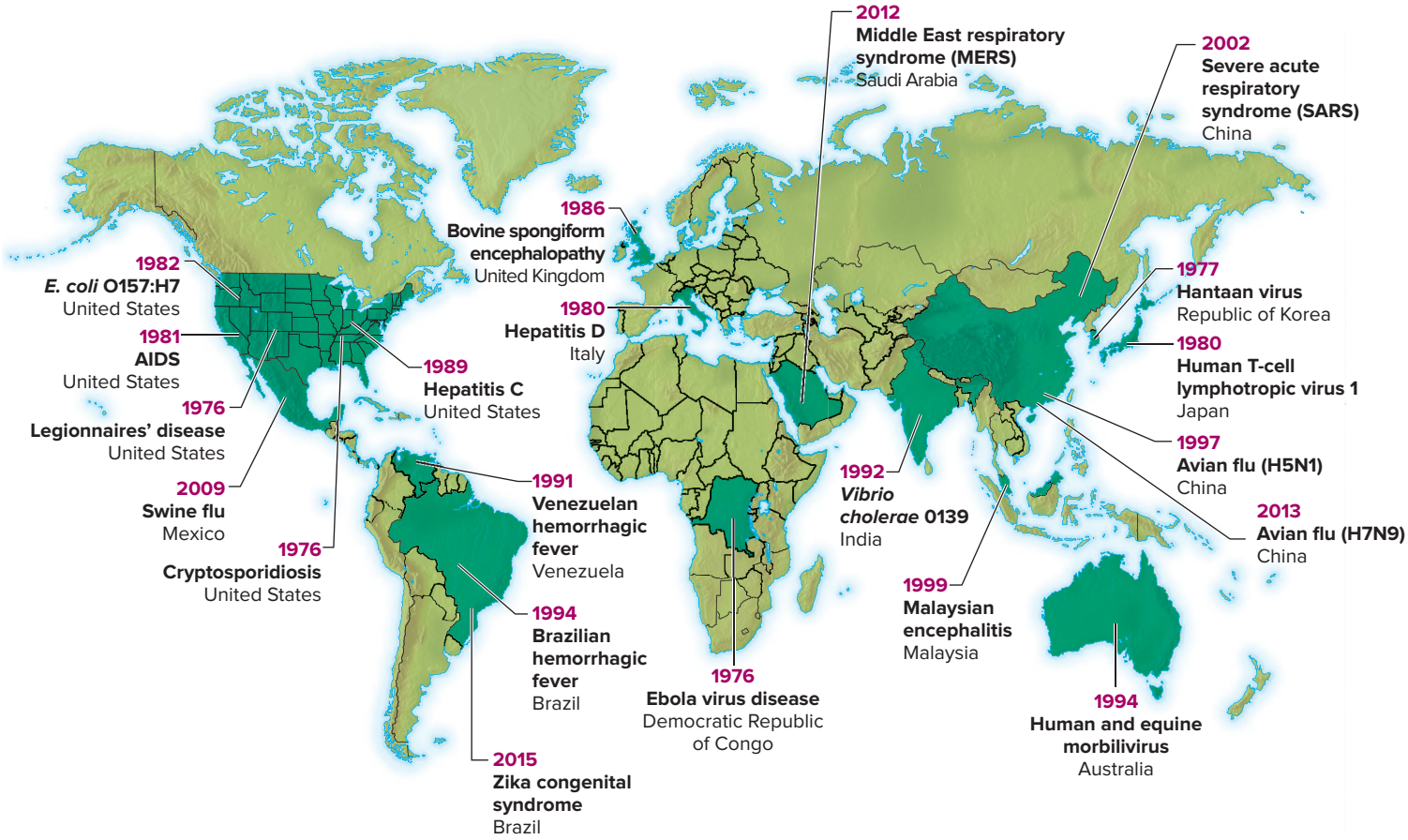

FIGURE 1.5 New and Newly Recognized Infectious Diseases or Disease Agents in Humans and Animals Since 1976 Countries where cases first appeared or were identified appear in a darker shade.

? Why might so many of the diseases first appear or be identified in the United States and Western European countries?

FOCUS ON A CASE 1.1

A 24-year-old woman suffered from recurrent severe episodes of an intestinal disorder called *Clostridium difficile* infection (CDI) for the past 13 months. She routinely experienced profuse watery diarrhea, abdominal pain, and fever. In addition, she was feeling tired and hopeless because she did not seem to be getting well, despite long attempts at multiple different treatments.

As with most patients who develop CDI, the woman had been taking an oral antibiotic shortly before her symptoms began—in this case, to treat a tooth infection. The antibiotic had successfully killed the bacteria that caused her tooth infection, but it also killed some members of her normal intestinal microbiota. As a result, the bacterium *Clostridium difficile*—often referred to simply as "C. diff"—thrived in her intestinal tract, growing to much higher numbers than it could before. The strain that caused her infection was able to make a toxin that damaged the lining of her intestinal tract.

When the patient first started experiencing CDI, her doctor told her to stop taking the antibiotic prescribed for her tooth infection, hoping that her CDI would resolve on its own. When that did not help, the doctor prescribed a different antibiotic that is often effective in treating CDI. The patient started feeling better, but the symptoms quickly returned when she stopped taking the medication. She also tried oral supplements containing *Lactobacillus* GG, a bacterium that sometimes appears to be effective in preventing antibiotic-associated diarrhea.

Because the patient's health was declining, doctors suggested a fecal transplant, a procedure that involves inserting feces from a healthy person into the patient's intestinal tract in order to repopulate that environment with appropriate microbes. They chose to use her sister as a fecal donor, screening both the donor and the patient to ensure that neither was infected with certain microbes, including various intestinal pathogens and HIV. Approximately ¼ cup of fresh feces was mixed with 1 quart of water and delivered to her intestinal tract via a colonoscope. Within days after the transplant, the patient began feeling better, and she soon recovered completely.

1. Why would certain oral antibiotics allow *C. difficile* to thrive in the intestinal tract?
2. Why would the doctors screen both the patient and the fecal donor for certain infectious agents?
3. Why would the doctors transplant feces rather than introducing isolated bacteria from feces to repopulate the colon?

Discussion

1. Antibiotics kill or inhibit not just pathogens, but also beneficial members of the normal microbiota, a group that protects against infection in at least two general ways. First, they quickly use nutrients that would otherwise be available to *C. difficile* and other pathogens. Also, some members of the normal microbiota make compounds that are toxic or inhibitory to other organisms. The environment of the intestinal tract is quite complex, however, so other factors might also be playing a role.
2. Physicians screen the fecal donor to decrease the likelihood that disease-causing microbes could be transferred to the patient via the procedure. The doctors screen the patient to ensure that she was not already infected with the pathogens. For example, if the patient developed symptoms of a *Salmonella* infection after the procedure, how would physicians know that she acquired the infection as a result of the procedure if they had not checked her beforehand?
3. Feces contain many types of bacteria that cannot yet be grown in the laboratory. In addition, scientists do not yet know which types of fecal bacteria protect against CDI.

Changes in society bring opportunities for infectious agents to spread, resulting in an emerging disease. More mobile populations can contribute to disease emergence as people may inadvertently carry pathogens around the globe. Diseases such as malaria, cholera, plague, and yellow fever have largely been eliminated from developed countries, but they still exist in many parts of the world. Newly infected international travelers could theoretically circle the globe, touch down in several countries, and expose many people before becoming ill themselves. Meanwhile, as suburbs of cities expand into rural areas, human populations come into closer contact with animals as well as the mosquitoes and other arthropods that normally feed on those animals. Consequently, people are exposed to pathogens they might not have encountered previously.

Infectious diseases that were under control can spread again, resulting in increased numbers of cases. Sometimes, the preventive measures become victims of their own success. For instance, decades of vaccination have nearly eliminated measles, mumps, and whooping cough in developed countries, so that most people no longer have first-hand knowledge of the dangers of the diseases. Couple this with misinformation about vaccines, and some people develop irrational fears, falsely believing that vaccines are more harmful than the diseases they prevent. When this happens, parents often refuse to vaccinate their children appropriately, leading to a situation where the diseases become more common again.

Chronic Diseases In addition to the diseases long recognized as being caused by pathogens, some illnesses once attributed to other causes may be due to microorganisms. Perhaps the best-known example is stomach ulcers, once thought to be due to stress. We now know that stomach ulcers are often caused by a bacterium *(Helicobacter pylori)* and are treatable with antibiotics. Chronic indigestion may be caused by the same bacterium. Another example is cervical cancer, which we now know is caused by human papillomavirus (HPV) infection; a vaccine against HPV prevents that cancer. Infectious microbes may play important roles in other chronic diseases as well.