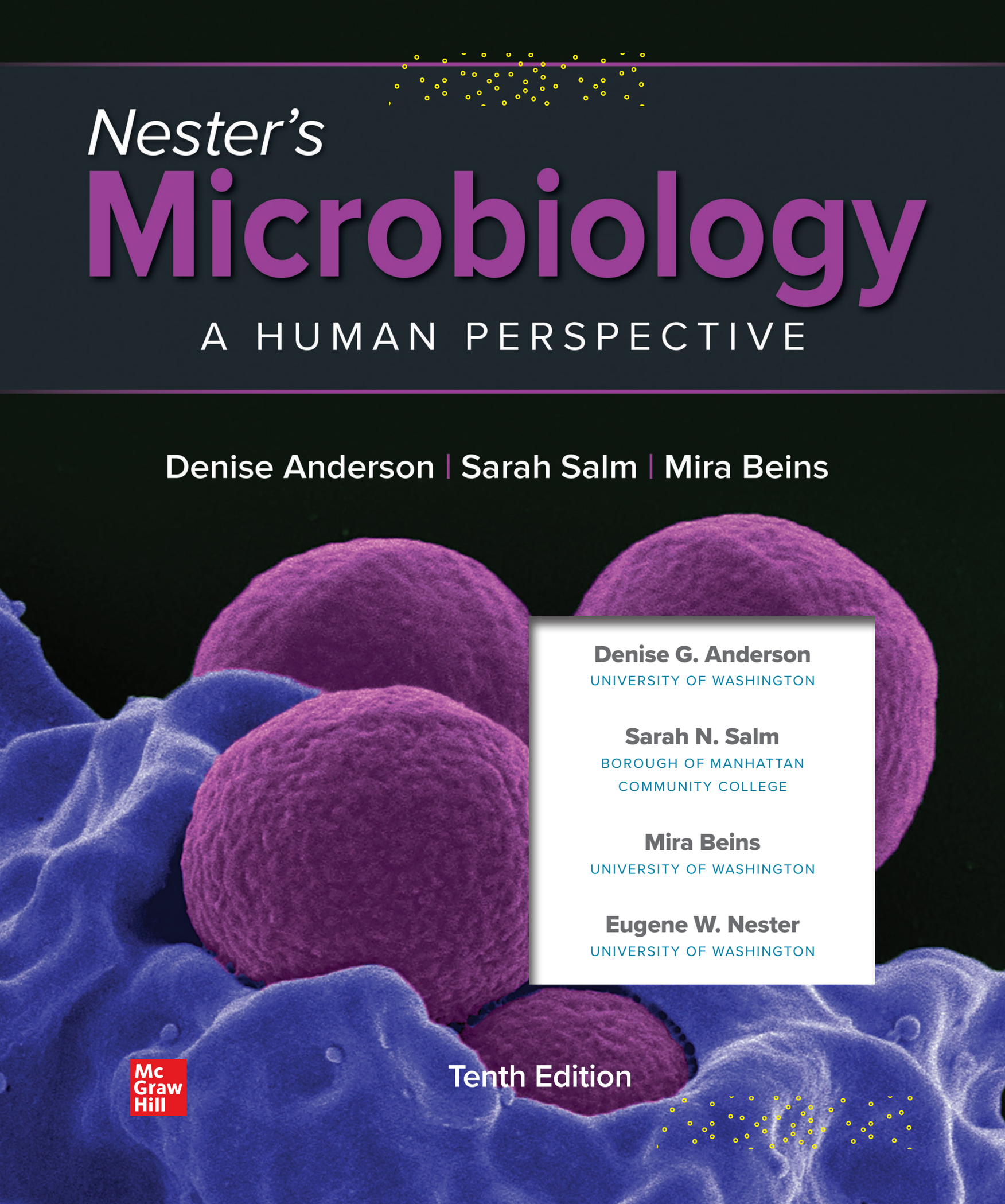
Nester's Microbiology

A HUMAN PERSPECTIVE

Denise Anderson | Sarah Salm | Mira Beins



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Brief Contents

About the Authors

The Nester Team:

Different Perspectives, One Vision, One Voice

The authors of this edition 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 chapter was edited with students in mind, using simpler words where appropriate while maintaining the scientific rigor so important for today's healthcare professionals.

Richard Moore

Denise Anderson

Denise Anderson is a Senior Lecturer Emeritus in the Department of Microbiology at the University of Washington, where she taught a variety of courses including general microbiology, medical bacteriology laboratory, recombinant DNA techniques, and medical mycology/parasitology laboratory for over 30 years. 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, received high reviews from her students.

Denise now relaxes in the Yorkshire Dales of England, where she lives with her husband, Richard Moore. When not editing textbook chapters, she can usually be found walking scenic footpaths, chatting with friends, fighting weeds in her garden, or enjoying a fermented beverage at the local pub.

Sandy Coetzee

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.

Mira Beins

Mira Beins

Mira Beins is an Associate Teaching Professor in the Department of Microbiology at the University of Washington, where she teaches general microbiology, medical bacteriology, and medical mycology/parasitology. She completed her undergraduate studies in Molecular Biology and Biotechnology at the University of the Philippines before moving to Wisconsin for graduate work in Microbiology. Her graduate and postdoctoral research both focused on virology, which solidified her belief that viruses are amazing—although she now begrudgingly admits that bacteria, fungi, and eukaryotic parasites are pretty cool, too.

Mira lives in Seattle with her husband Mike and two kids, Maya and Noah. When she's not busy teaching or driving the kids to their many activities, she enjoys reading books, watching movies, hanging out with friends and family, and planning the next family trip (which Denise hopes will be to the Yorkshire Dales!).

Mike Bohrer

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

Gene (Eugene) Nester was instrumental in establishing the text's reputation for excellence over the decades. Although no longer an active member of the author team, he 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.

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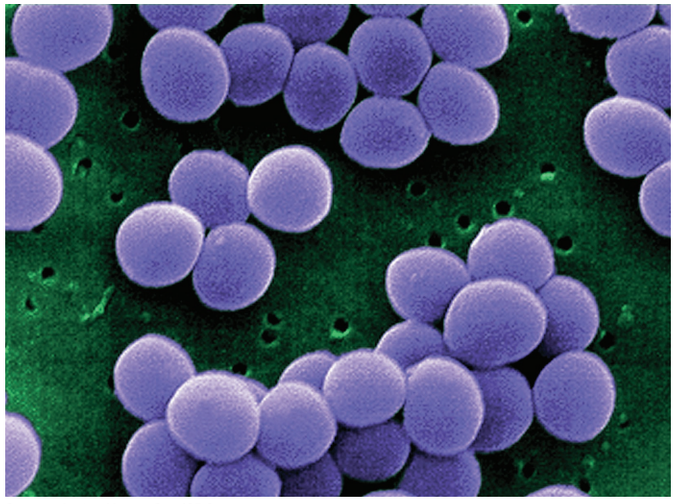

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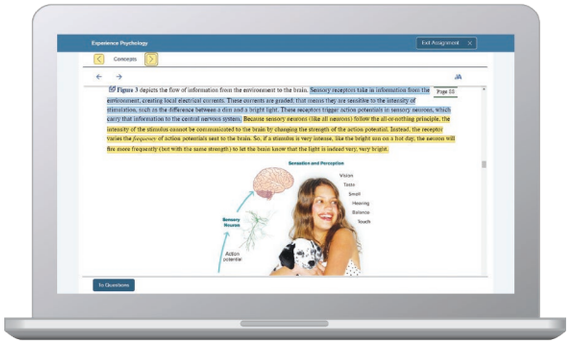

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FOCUS ON UNDERSTANDING . . .

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.

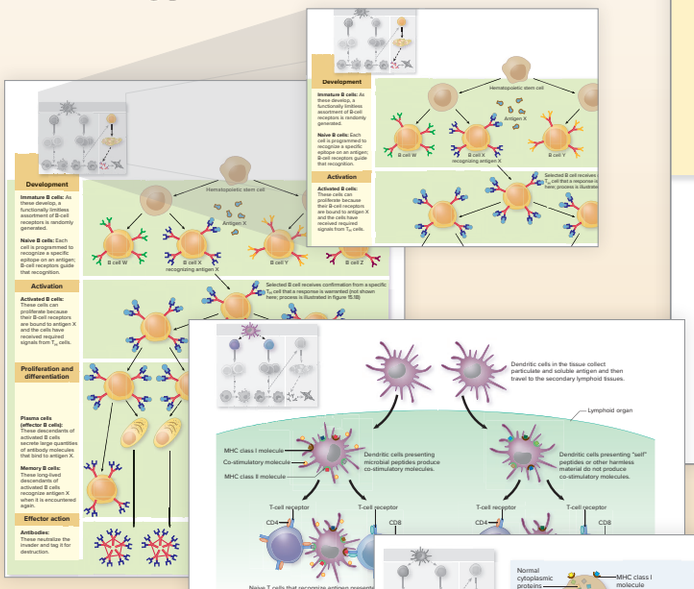

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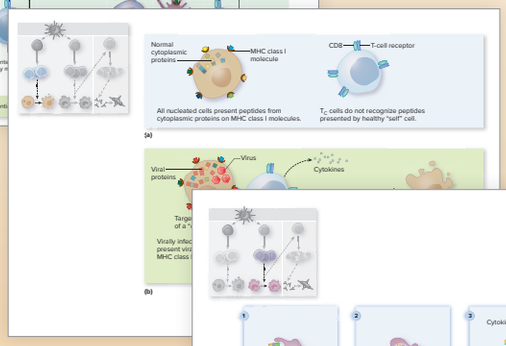
FIGURE 15.13



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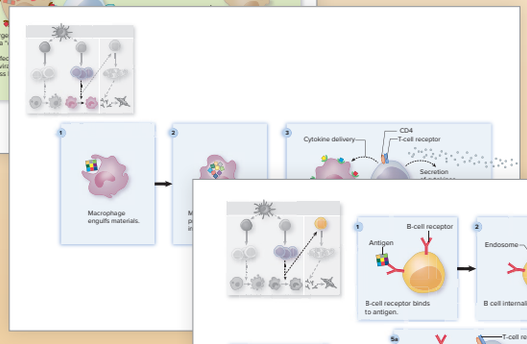

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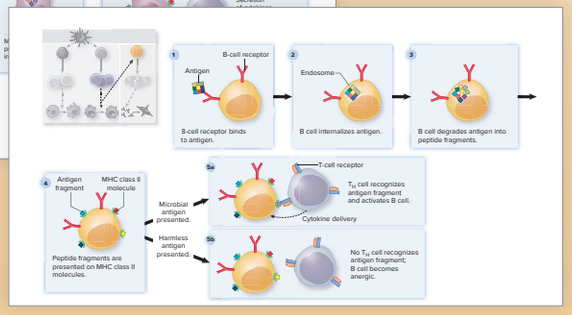

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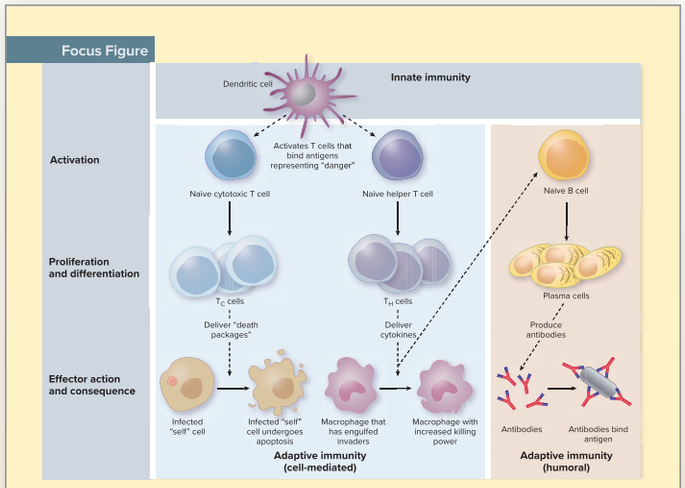

FIGURE 15.1 Overview of the Adaptive Immune Response Cell-mediated immunity protects against antigens within host cells (intracellular antigens); humoral immunity protects against antigens in blood and tissue fluid (extracellular antigens). In this diagram, solid arrows represent the path of a cell or 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?

is responsible for that recognition (**figure 15.2**). The antigen receptors on a single lymphocyte are identical and therefore recognize the same antigen, but because the body has hundreds of millions of different lymphocytes, the immune system can recognize a nearly infinite assortment of antigens. Conventional **T-cell receptors (TCRs)** only bind an antigen "presented" by one of the body's own cells, an interaction guided by a surface molecule called a CD marker (CD stands for **c**luster of **d**ifferentiation to reflect that scientists use the molecules to distinguish different groups of cells). Cytotoxic T cells have a CD marker called CD8, which is why the cells are sometimes referred to as CD8 T cells or CD8+ T cells; in contrast, helper T cells have a a CD marker called CD4, which is why the cells are sometimes referred to as CD4 T cells or CD4+ T cells. **B-cell receptors (BCRs)** are essentially membrane-anchored versions of the Y-shaped antibody molecules that the B cell is programmed to make. Unlike T-cell receptors, they bind free antigens (in other words, antigens not presented by one of the body's own cells). The two arms of the BCR are identical to each other, resulting in two antigen-binding sites.

Cell-mediated and humoral immunity are both powerful and, if misdirected, can damage the body's own tissues. To provide the immune tolerance necessary to prevent inappropriate responses, two sequential processes are used:

- **Central tolerance.** This takes place as lymphocytes mature (T cells in the thymus marrow and B cells in the bone marrow); it eliminates immature T and B cells found to recognize certain "self" molecules.

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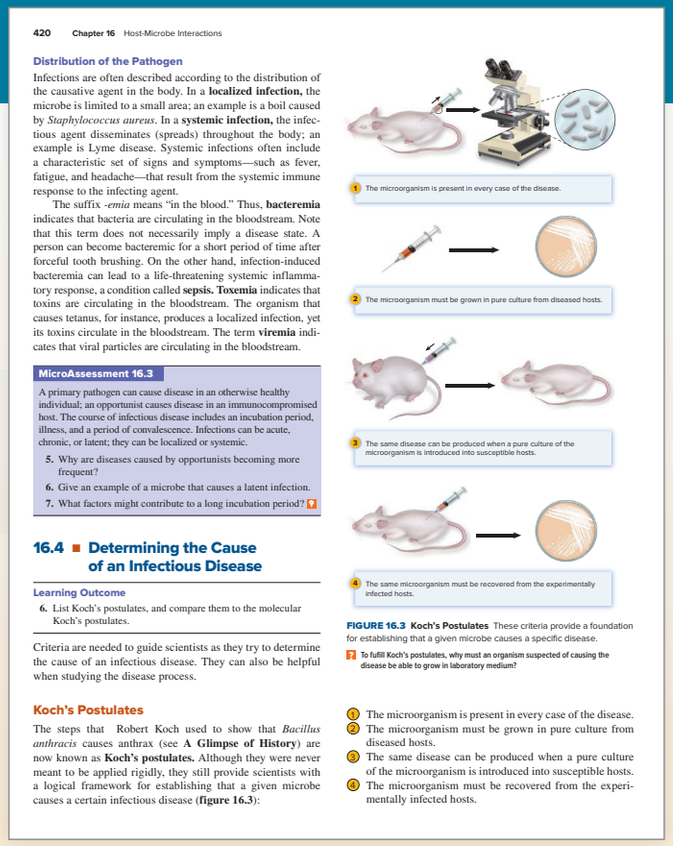
"Provides a logical unfolding conceptual framework that fosters better understanding."

—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 disseminates (spreads) 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.

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

The steps that Robert Koch used to show that *Bacillus anthracis* causes anthrax (see **A Glimpse of History**) are now known as **Koch's postulates.** Although they were never meant to be applied rigidly, they still provide scientists with a logical framework for establishing that a given microbe causes a certain infectious disease (**figure 16.3**):

1. The microorganism is present in every case of the disease.
2. The microorganism must be grown in pure culture from diseased hosts.
3. The same disease can 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 16.3 Koch's Postulates These criteria provide a foundation for establishing that a given microbe causes a specific disease.

? To fulfill Koch's postulates, why must an organism suspected of causing the disease be able to grow in laboratory medium?

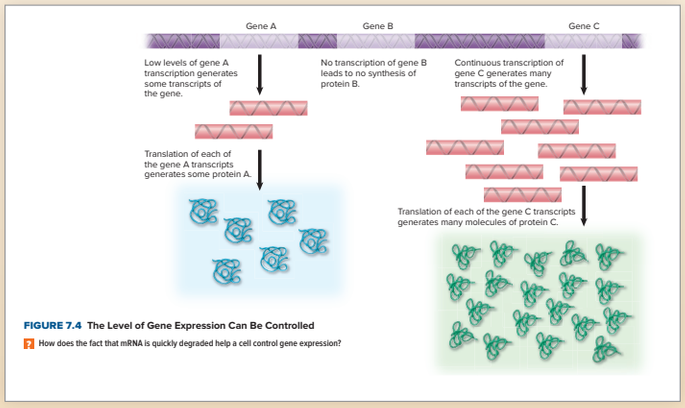


FIGURE 7.4 The Level of Gene Expression Can Be Controlled

? 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.

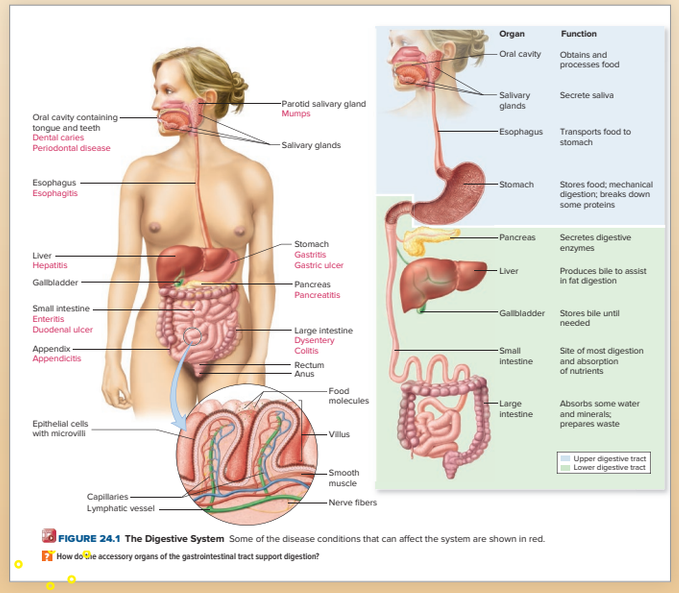


FIGURE 24.1 The Digestive System Some of the disease conditions that can affect the system are shown in red.

? How do the accessory organs of the gastrointestinal tract support digestion?

Introduce the body systems

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

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.

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.

26 Nervous System Infections

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

KEY TERMS

Blood-Brain Barrier Cells that function together to create a protective semipermeable border that separates the CNS from the bloodstream.

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"). Many historical and religious texts refer to several disfiguring skin diseases, including leprosy, and portray those suffering from the diseases as unclean and sinful. Lepers were regularly segregated from mainstream society.

Gerhard Henrik Armauer Hansen (1841–1912) was a Norwegian physician with many interests, ranging from science to religion to polar exploration. After graduating from medical school, he went to work with Dr. Daniel C. Danielson, a leading authority on leprosy. Danielson believed that leprosy was a hereditary disease and considered the idea that it was contagious to be 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 families, and they were sent to a leprosarium such as the one at Carville, Louisiana, which was surrounded by a 12-foot fence topped with barbed wire. Sufferers were separated from spouses and children and were denied the right to marry or vote. Those who tried to escape were captured and brought back in handcuffs. The Carville leprosarium was finally closed and converted to a military-style academy in 1999.

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

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.

Nerve cells work together, transmitting electrical impulses throughout the body like a highly sophisticated circuit board. Each nerve cell, or **neuron,** has three functionally distinct regions: (1) branching projections called dendrites, (2) the cell

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MicroAssessment 3.2

Peptidoglycan is a molecule unique to bacteria that provides strength to the cell wall. The Gram-positive cell wall is composed of a relatively thick layer of peptidoglycan as well as teichoic acids. Gram-negative cell walls have a thin layer of peptidoglycan and a lipopolysaccharide-containing outer membrane. Penicillin and lysozyme interfere with the structural integrity of peptidoglycan. *Mycoplasma* species lack a cell wall. Archaea have a variety of cell wall types.

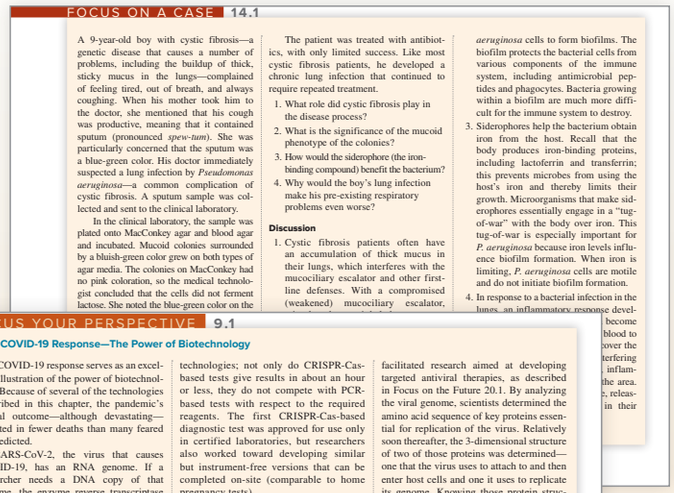
4. What is the significance of lipid A?
5. How does the action of penicillin differ from that of lysozyme?
6. Explain why penicillin kills only actively multiplying cells, whereas lysozyme kills cells in any stage of growth.

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 feeling tired, out of breath, and always coughing. 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 that the cells did not ferment lactose. She noted the blue-green color on the

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

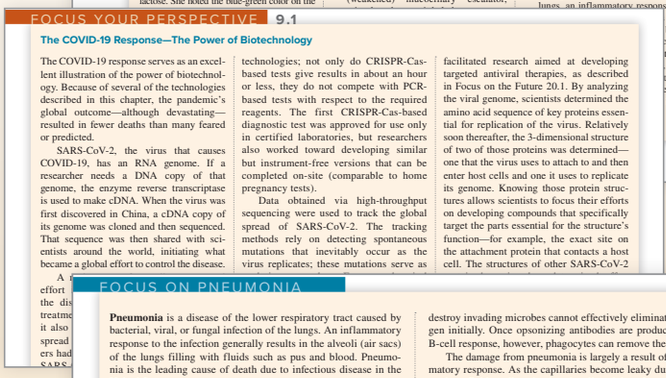
1. Cystic fibrosis patients often have an accumulation of thick mucus in their lungs, which interferes with the mucociliary escalator and other first-line defenses. With a compromised (weakened) mucociliary escalator,

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.

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 formation.
4. In response to a bacterial infection in the lungs, an inflammatory response devel-

Provide perspective

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


FOCUS YOUR PERSPECTIVE 9.1

The COVID-19 Response—The Power of Biotechnology

The COVID-19 response serves as an excellent illustration of the power of biotechnology. Because of several of the technologies described in this chapter, the pandemic's global outcome—although devastating—resulted in fewer deaths than many feared or predicted.

SARS-CoV-2, the virus that causes COVID-19, has an RNA genome. If a researcher needs a DNA copy of that genome, the enzyme reverse transcriptase is used to make cDNA. When the virus was first discovered in China, a cDNA copy of its genome was cloned and then sequenced. That sequence was then shared with scientists around the world, initiating what became a global effort to control the disease.

A

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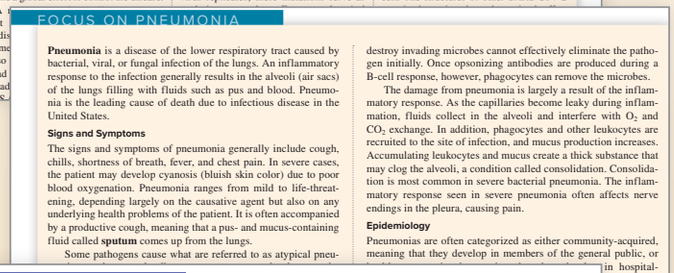
technologies; not only do CRISPR-Cas-based tests give results in about an hour or less, they do not compete with PCR-based tests with respect to the required reagents. The first CRISPR-Cas-based diagnostic test was approved for use only in certified laboratories, but researchers also worked toward developing similar but instrument-free versions that can be completed on-site (comparable to home pregnancy tests).

Data obtained via high-throughput sequencing were used to track the global spread of SARS-CoV-2. The tracking methods rely on detecting spontaneous mutations that inevitably occur as the virus replicates; these mutations serve as

facilitated research aimed at developing targeted antiviral therapies, as described in Focus on the Future 20.1. By analyzing the viral genome, scientists determined the amino acid sequence of key proteins essential for replication of the virus. Relatively soon thereafter, the 3-dimensional structure of two of those proteins was determined—one that the virus uses to attach to and then enter host cells and one it uses to replicate its genome. Knowing those protein structures allows scientists to focus their efforts on developing compounds that specifically target the parts essential for the structure's function—for example, the exact site on the attachment protein that contacts a host cell. The structures of other SARS-CoV-2

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 caused by bacterial, viral, or fungal infection of the lungs. An inflammatory response to the infection generally results in the alveoli (air sacs) of the lungs filling with fluids such as pus and blood. Pneumonia 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. It is often accompanied by a productive cough, meaning that a pus- and mucus-containing fluid called **sputum** comes up from the lungs.

Some pathogens cause what are referred to as atypical pneu-

destroy invading microbes cannot effectively eliminate the pathogen initially. Once opsonizing antibodies are produced during a B-cell response, however, phagocytes can remove the microbes.

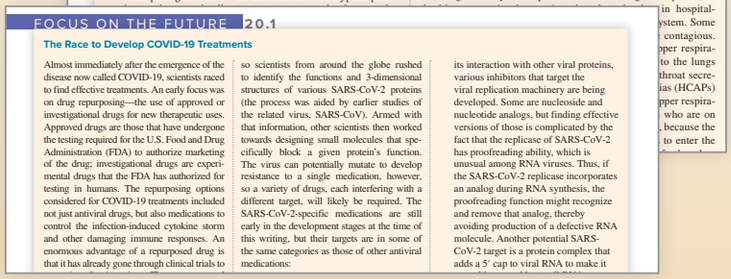
The damage from pneumonia is largely a result of the inflammatory response. As the capillaries become leaky during inflammation, fluids collect in the alveoli and interfere with O_2 and CO_2 exchange. In addition, phagocytes and other leukocytes are recruited to the site of infection, and mucus production 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

Inspire the learner

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


FOCUS ON THE FUTURE 20.1

The Race to Develop COVID-19 Treatments

Almost immediately after the emergence of the disease now called COVID-19, scientists raced to find effective treatments. An early focus was on drug repurposing—the use of approved or investigational drugs for new therapeutic uses. Approved drugs are those that have undergone the testing required for the U.S. Food and Drug Administration (FDA) to authorize marketing of the drug; investigational drugs are experimental drugs that the FDA has authorized for testing in humans. The repurposing options considered for COVID-19 treatments included not just antiviral drugs, but also medications to control the infection-induced cytokine storm and other damaging immune responses. An enormous advantage of a repurposed drug is that it has already gone through clinical trials to

so scientists from around the globe rushed to identify the functions and 3-dimensional structures of various SARS-CoV-2 proteins (the process was aided by earlier studies of the related virus, SARS-CoV). Armed with that information, other scientists then worked towards designing small molecules that specifically block a given protein's function. The virus can potentially mutate to develop resistance to a single medication, however, so a variety of drugs, each interfering with a different target, will likely be required. The SARS-CoV-2-specific medications are still early in the development stages at the time of this writing, but their targets are in some of the same categories as those of other antiviral medications:

its interaction with other viral proteins, various inhibitors that target the viral replication machinery are being developed. Some are nucleoside and nucleotide analogs, but finding effective versions of those is complicated by the fact that the replicase of SARS-CoV-2 has proofreading ability, which is unusual among RNA viruses. Thus, if the SARS-CoV-2 replicase incorporates an analog during RNA synthesis, the proofreading function might recognize and remove that analog, thereby avoiding production of a defective RNA molecule. Another potential SARS-CoV-2 target is a protein complex that adds a 5′ cap to viral RNA to make it

- **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.

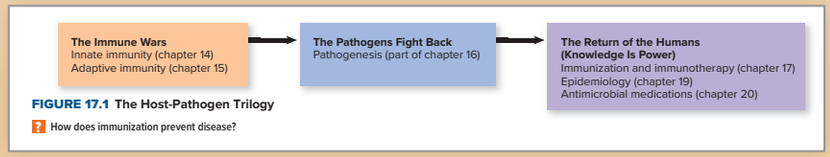


FIGURE 17.1 The Host-Pathogen Trilogy

? 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).***

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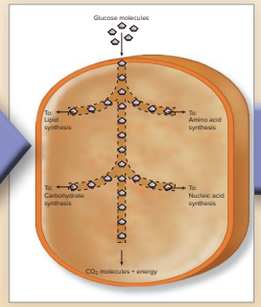
Emphasize the logic

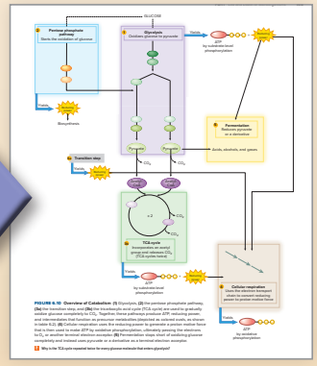
WHY? Descriptions that emphasize the logic of processes make it easier for students to understand and retain the information. Here's an example from chapter 6.

TABLE 6.2 Precursor Metabolites

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

Note: The colored icons in the table are used in figures throughout the chapter to represent the respective precursor metabolites.





Introduce the players *Certain intermediates of catabolic pathways can be used in anabolic pathways; therefore they link these two types of 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, as described by the following general reaction* ***(figure 6.10):***

$C_6H_{12}O_6 + 6\,O_2 \dashrightarrow 6\,CO_2 + 6\,H_2O$

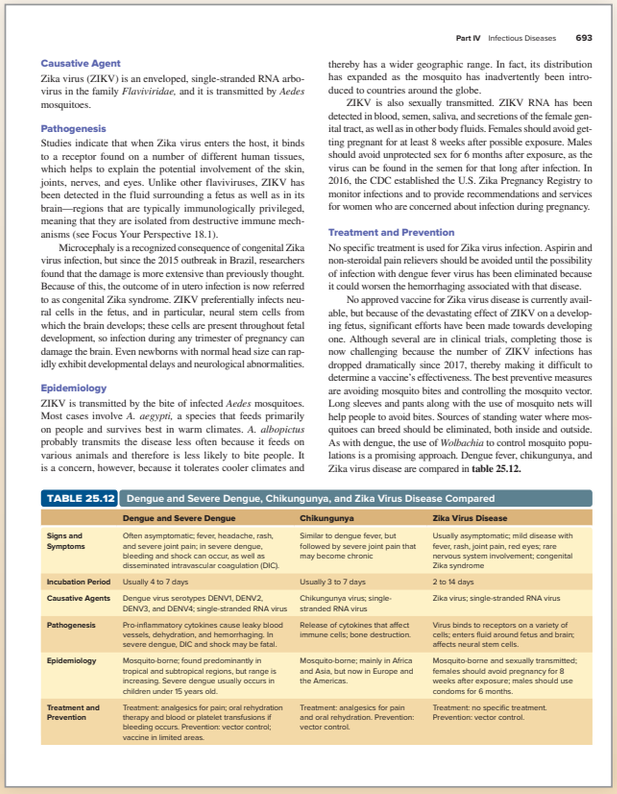
(glucose) (oxygen) (carbon dioxide) (water)

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.



Causative Agent

Zika virus (ZIKV) is an enveloped, single-stranded RNA arbovirus in the family *Flaviviridae,* and it is transmitted by *Aedes* mosquitoes.

Pathogenesis

Studies indicate that when Zika virus enters the host, it binds to a receptor found on a number of different human tissues, which helps to explain the potential involvement of the skin, joints, nerves, and eyes. Unlike other flaviviruses, ZIKV has been detected in the fluid surrounding a fetus as well as in its brain—regions that are typically immunologically privileged, meaning that they are isolated from destructive immune mechanisms (see Focus Your Perspective 18.1).

Microcephaly is a recognized consequence of congenital Zika virus infection, but since the 2015 outbreak in Brazil, researchers found that the damage is more extensive than previously thought. Because of this, the outcome of in utero infection is now referred to as congenital Zika syndrome. ZIKV preferentially infects neural cells in the fetus, and in particular, neural stem cells from which the brain develops; these cells are present throughout fetal development, so infection during any trimester of pregnancy can damage the brain. Even newborns with normal head size can rapidly exhibit developmental delays and neurological abnormalities.

Epidemiology

ZIKV is transmitted by the bite of infected *Aedes* mosquitoes. Most cases involve *A. aegypti*, a species that feeds primarily on people and survives best in warm climates. *A. albopictus* probably transmits the disease less often because it feeds on various animals and therefore is less likely to bite people. It is a concern, however, because it tolerates cooler climates and thereby has a wider geographic range. In fact, its distribution has expanded as the mosquito has inadvertently been introduced to countries around the globe.

ZIKV is also sexually transmitted. ZIKV RNA has been detected in blood, semen, saliva, and secretions of the female genital tract, as well as in other body fluids. Females should avoid getting pregnant for at least 8 weeks after possible exposure. Males should avoid unprotected sex for 6 months after exposure, as the virus can be found in the semen for that long after infection. In 2016, the CDC established the U.S. Zika Pregnancy Registry to monitor infections and to provide recommendations and services for women who are concerned about infection during pregnancy.

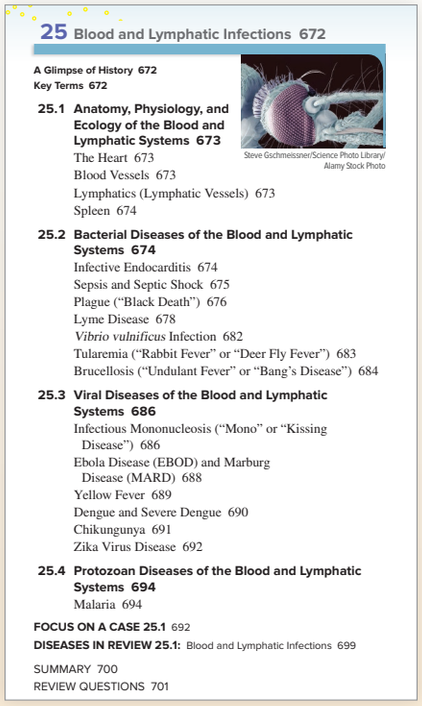
Treatment and Prevention

No specific treatment is used for Zika virus infection. Aspirin and non-steroidal pain relievers should be avoided until the possibility of infection with dengue fever virus has been eliminated because it could worsen the hemorrhaging associated with that disease.

No approved vaccine for Zika virus disease is currently available, but because of the devastating effect of ZIKV on a developing fetus, significant efforts have been made towards developing one. Although several are in clinical trials, completing those is now challenging because the number of ZIKV infections has dropped dramatically since 2017, thereby making it difficult to determine a vaccine's effectiveness. The best preventive measures are avoiding mosquito bites and controlling the mosquito vector. Long sleeves and pants along with the use of mosquito nets will help people to avoid bites. Sources of standing water where mosquitoes can breed should be eliminated, both inside and outside. As with dengue, the use of *Wolbachia* to control mosquito populations is a promising approach. Dengue fever, chikungunya, and Zika virus disease are compared in **table 25.12.**

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

	Dengue and Severe Dengue	Chikungunya	Zika Virus Disease
Signs and Symptoms	Often asymptomatic; fever, headache, rash, and severe joint pain; in severe dengue, 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; single-stranded RNA virus	Chikungunya virus; single-stranded RNA virus	Zika virus; single-stranded RNA virus
Pathogenesis	Pro-inflammatory cytokines cause leaky blood vessels, dehydration, and hemorrhaging. In severe dengue, 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. Severe dengue 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.



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Steve Gschmeissner/Science Photo Library/ Alamy Stock Photo

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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.

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
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
COVID-19, SARS and MERS	Coronaviruses	Emerging infectious diseases characterized by severe lower respiratory symptoms; zoonotic	Table 21.14
Hantavirus pulmonary syndrome	Hantaviruses	Acquired via inhaled dust contaminated with rodent saliva, urine, or feces. Frequently fatal.	Table 21.15
FUNGAL INFECTIONS OF THE RESPIRATORY TRACT			
Coccidioidomycosis ("valley fever")	*Coccidioides immitis* and *C. posadasii*	Environmental reservoir (soil in semi-arid desert areas); most infections are asymptomatic.	Table 21.16
Histoplasmosis ("spelunker's disease")	*Histoplasma capsulatum*	Environmental reservoir (bat droppings and soil enriched with bird 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

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.

UPDATES—Maintaining the Cutting Edge

Global Changes

- Added information about COVID-19 and SARS-CoV-2, including the following boxes:
  - Focus Your Perspective 9.1 *(The COVID-19 Response—The Power of Biotechnology)*
  - Focus on a Case 13.1
  - Focus on the Future 20.1 *(The Race to Develop COVID-19 Treatments)*
  - Focus Your Perspective 21.1 *(A Global Lesson in Microbiology: The COVID-19 Pandemic)*
- Updated disease statistics, vaccine recommendations, treatments, and terminology
- Rearranged some content to improve flow in the digital text (the information most relevant to a particular figure is now in the paragraph immediately preceding the figure, and summary tables have been moved to the end of the coverage)
- Converted many of the descriptions that support multi-step figures to bullet lists that correspond to the steps
- Continued "wordsmithing" to improve the clarity and readability of the descriptions

Key Changes in Individual Chapters

Chapter 1 – Humans and the Microbial World

- Added SARS-CoV-2 and *Candida auris* to the section on emerging pathogens
- Added the African swine fever to the list of epidemics in non-human populations
- Expanded the coverage of the human microbiome
- Defined the term *strain*
- Moved the information about bacterial cell shape from chapter 3 to section 1.3
- Added a MicroByte about the Microbiome Conservancy collecting/storing fecal samples from populations around the world

Chapter 2 – The Molecules of Life

- Consolidated and expanded the information on water's characteristics
- Added a subsection on short-chain fatty acids, to allow a description of butyrate
- Added a description of waxes
- Described the distinction between a Lewis symbol and a Lewis structure
- Rearranged the three-part figure showing DNA
- Added a MicroByte on the use of artificial intelligence and a video game to determine protein folding

Chapter 3 – Cells and Methods to Observe Them

- Rearranged the chapter sections so that cell structure and function is discussed before microscopy and staining methods; revised the chapter title to reflect the change
- Revised the coverage of active transport systems to place more emphasis on the concept rather than the different types
- Updated the section on gas vesicles to include information about other protein-based compartments (bacterial microcompartments and encapsulin nanocompartments)
- Introduced the term *archaellum*
- Described periplasm in Gram-positive cells
- Moved the information about bacterial cell shape to chapter 1

Chapter 4 – Dynamics of Microbial Growth

- Introduced the term *contact-dependent growth inhibition*

Chapter 5 – Control of Microbial Growth

- Combined the physical methods of microbial control into one section
- Expanded the discussion of biosafety levels
- Added the recent FDA rulings that limit the use of many previously allowed ingredients in antiseptic lotions until they are shown to be safe and effective

Chapter 6 – Microbial Metabolism: Fueling Cell Growth

- Rearranged the information about energy sources and terminal electron acceptors so that the more conceptually simple information comes first.
- Revised tables 6.2 (Precursor Metabolites) and 6.4 (Some Vitamins and Their Use in Coenzymes)
- Added new figure (6.11) to emphasize the difference in energy yield between aerobic respiration and fermentation

- Simplified the detailed discussion of the central metabolic pathways
- Simplified the discussion of photosynthesis

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

- Combined the subsections that describe DNA replication
- Added a MicroByte about the target of the new influenza medication (baloxavir marboxil)
- Added a MicroByte about the first approved RNAi-based medication
- Split the figure that illustrates the process of translation to emphasize its three phases (initiation, elongation, and termination; now figures 7.5–7.17)

Chapter 8 – Bacterial Genetics

- Changed the term *silent mutation* to *synonymous mutation*, and explained that this type of mutation is not always silent
- Changed the term *DNA-mediated transformation* to *bacterial transformation*
- Broadened the coverage of section 8.10 (now "Genome Variability") and added the term *pan-genome*
- Simplified the format of the end-of-chapter multiple choice questions

Chapter 9 – Biotechnology

- Added a new Focus Your Perspective Box: *The COVID-19 Response—The Power of Biotechnology*
- Emphasized the importance of CRISPR-Cas technologies by creating a numbered section (section 9.3); the expanded coverage includes a description of a rapid COVID-19 diagnostic test that relies on the technologies
- Expanded the chapter introduction to emphasize the applications of biotechnology
- Added a MicroByte about a bacterial enzyme engineered to efficiently break down a common type of plastic
- Changed the title of section 9.2 to "Molecular Cloning" (was "Genetic Engineering") to reflect a more narrow focus
- Added a simplified view of the cloning process (in a bullet list format) that matches figure 9.4
- Converted the description of vectors to a bullet list that matches figure 9.6 (was 9.8)
- Converted the description of how a PCR product is generated to a bullet list that matches figure 9.13 (was 9.17)
- Deleted the section on the dideoxy chain termination method of DNA sequencing
- Updated the Focus On the Future box by changing the name of the initiative described to *All of Us*

Chapter 10 – Identifying and Classifying Microorganisms

- Updated information about the new online *Bergey's Manual of Systematics of Archaea and Bacteria*
- Changed the example of nomenclature change to *Cutibacterium acnes*

Chapter 11 – The Diversity of Bacteria and Archaea

- Added information about the release of *Wolbachia*-infected mosquitoes as a means to prevent mosquito-borne diseases

Chapter 12 – The Eukaryotic Members of the Microbial World

- Extensive revision, including new photographs throughout; moved the section on protozoa forward, and increased the medical emphasis throughout
- Expanded the discussion of the difficulties of classification
- Added a disease-based grouping of fungi
- Added information about the spread of a fungal disease that destroys banana plants
- Expanded the discussion of medically important protozoa
- Added a figure that illustrates the origin of chloroplasts through primary endosymbiosis
- Simplified the figure that illustrates phylogenetic groups of eukaryotes (now figure 12.18)

Chapter 13 – Viruses, Viroids, and Prions

- Changed the topic of the Focus on a Case box to COVID-19
- Updated viral taxonomy
- Added *Pneumoviridae* to table 13.1
- Bulleted the steps of the lytic bacteriophage life cycle to match figure 13.5
- Bulleted the steps of specialized transduction to match figure 13.9
- Split the figure showing replication strategies of animal viruses into three separate figures for clarity (now figures 13.12–13.14)
- Updated information on viruses and human tumors to include oncogenic and oncolytic viruses
- Added Focus on the Future 13.1: *The Potential of Phage Therapy*

Chapter 14 – The Innate Immune Response

- Modified and updated the descriptions of granulocytes, particularly neutrophils

- Expanded the information on cell types to increase the emphasis on mast cells
- Updated the information on macrophages to indicate that tissue-resident macrophages can self-renew
- Separated the description of inflammation into vascular changes and cellular changes
- Expanded the discussion on damaging effects of inflammation
- Added necroptosis to the paragraph that describes pyroptosis

Chapter 15 – The Adaptive Immune Response

- Extensive revision; reorganized the chapter to create a more linear flow (T cells and their activation are now described before B cells)
- Expanded and rearranged the overview to reflect the new chapter organization
- Expanded the discussion of immune tolerance to distinguish between central tolerance and peripheral tolerance

Chapter 16 – Host-Microbe Interactions

- Increased the emphasis on the importance of butyrate on intestinal barrier functions
- Revised the discussion of Koch's postulates

Chapter 17 – Applications of Immune Responses

- Moved the chapter forward (was chapter 18) so that monoclonal antibodies could be described before the chapter that mentions their use in allergy therapies.
- Added a section on immunotherapies (section 17.3), particularly focusing on the new cancer therapies (checkpoint inhibitors and CAR T cells)
- Added the new the dengue disease vaccine to table 17.5
- Added information about the new combination vaccine that includes HepB

Chapter 18 – Immunological Disorders

- Bulleted the steps involved in type I hypersensitivities to match the accompanying figure
- Updated information on type II hypersensitivities
- Updated the information on immune disorder treatments, including adding information on immunotherapy
- Eliminated the section on treatment of autoimmune diseases, and instead describe the treatments in the context of the respective conditions
- Added a MicroByte on the Neurological Conditions Surveillance System (NNCSS)

Chapter 19 – Epidemiology

- Added COVID-19 as an example of the significance of asymptomatic infections in the spread of a disease
- Changed the MicroByte in section 19.1 to mention the secondary attack rate of measles
- Added measles to the factors that contribute to disease emergence
- Updated table of notifiable infectious diseases
- Updated the description of the *Morbidity and Mortality Weekly Report*
- Added the URL for the CDC's National Notifiable Diseases Surveillance System (NNDSS)
- Added COVID-19 and *Candida auris* infection to the section on emerging diseases

Chapter 20 – Antimicrobial Medications

- Added a Focus on the Future Box: *The Race to Develop COVID-19 Treatments*
- Explained that oral administration of poorly absorbed medications is useful for treating intestinal infections
- Added information about the new rifamycin for treating some types of travelers' diarrhea
- Updated the section on *Mycobacterium tuberculosis* resistance by adding information about the new combination treatment specifically for XDR-TB
- Updated the table that describes the microorganisms on the CDC's list of antibiotic resistance threats (table 20.2)
- Mentioned the resistance of *Candida auris* in the section on antifungal medications
- Updated the section on antiviral medications by adding a subsection on cap-snatching inhibitors
- Added moxidectin for treating river blindness and triclabendazole for treating liver flukes to table 20.5

Chapter 21 – Respiratory System Infections

- Added a Focus Your Perspective Box: *A Global Lesson in Microbiology: The COVID-19 Pandemic*
- Expanded the discussion of coronavirus lower respiratory tract infections to include not only SARS and MERS, but also COVID-19
- Updated the information on Group A *Streptococcus* virulence factors to include only those clearly associated with pathogenesis
- Updated the discussion of mycoplasmal pneumonia pathogenesis to include the CARDS toxin, which has been shown to be a key virulence factor
- Changed Legionellosis to Legionnaires' disease to more specifically refer to *Legionella* pneumonia

- Bulleted the discussion of TB pathogenesis to match figure 21.19
- Updated the discussion on the WHO's program to combat TB; also introduced the newly FDA-approved drug trial program for XDR-TB called Nix-TB
- Updated the pathogenesis discussion on several viral diseases, including the common cold, adenovirus respiratory infections, hantavirus pulmonary syndrome
- Updated the classification of influenza viruses to include influenza D; updated the influenza strain nomenclature to be more in line with the CDC and WHO; introduced the new anti-influenza medication baloxavir
- Updated the information on RSV classification, pathogenesis, and treatment

Chapter 22 – Skin Infections

- Added new bullet list of characteristic skin lesions and rashes, including descriptions and disease examples
- Expanded the section on acne
- Added disease summary tables for acne and hair follicle infections
- Expanded the information on impetigo
- Added information about hand-foot-and-mouth disease (HFMD)

Chapter 23 – Wound Infections

- Added a new part to figure 23.9 to illustrate the mechanism of tetanospasmin
- Reduced the coverage of streptobacillary rat bite fever, assigning it to a new section called *Other Bacterial Bite Wound Infections*

Chapter 24 – Digestive System Infections

- Added a MicroByte on the Global Microbiome Conservancy to section 24.1
- Updated the information on dental caries and modified the accompanying figure
- Updated Focus on a Case 24.1 to reflect diagnosis of *H. pylori* infections by the urea breath test
- Changed the heading *Typhoid and Paratyphoid Fevers* to *Enteric Fever (Typhoid and Paratyphoid)*

Chapter 25 – Blood and Lymphatic Infections

- Revised the section on sepsis and simplified the accompanying figure
- Updated the information on different forms of tularemia
- Updated and explained the evolving terminology of Ebola disease and Marburg disease
- Updated the terminology by changing *dengue fever* to *dengue* and *severe dengue*
- Added a description of how *Wolbachia*-infected mosquitoes can be used to control dengue and other mosquito-borne diseases

Chapter 26 – Nervous System Infections

- Changed the heading "Viral Encephalitis" to "West Nile and Other Types of Viral Encephalitis," and put the focus on West Nile encephalitis
- Changed the MicroByte topic in section 26.3 to acute flaccid myelitis (AFM)
- Updated the information on African trypanosomiasis (African sleeping sickness)

Chapter 27 – Genitourinary Tract Infections

- Updated the coverage of leptospirosis
- Updated Focus Your Perspective 27.1 and changed the title to "Conquering Syphilis"
- Added information about a new monoclonal antibody approved for use as a component of antiretroviral therapy (ART)
- Updated the information on HIV disease
- Removed tables 27.16 (People at Increased Risk for HIV Disease) and 27.18 (Behaviors that Help Control an AIDS Epidemic)

Chapter 28 – Microbial Ecology

- Added the definition of oligotroph
- Revised the section on mycorrhiza; added the terms *arbuscular mycorrhiza* and *Hartig net*, as well as information about fungal networks
- Add a MicroByte to section 28.6 about corn that produces syrup-coated aerial roots to nourish nitrogen-fixing bacteria

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

- Expanded the description of MUG/ONPG

Chapter 30 – Food Microbiology

- Bulleted the descriptions that support figures 30.4 and 30.5

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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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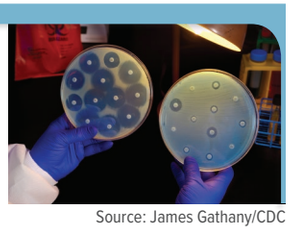

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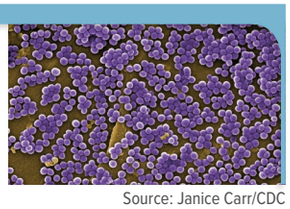

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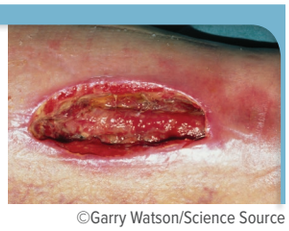

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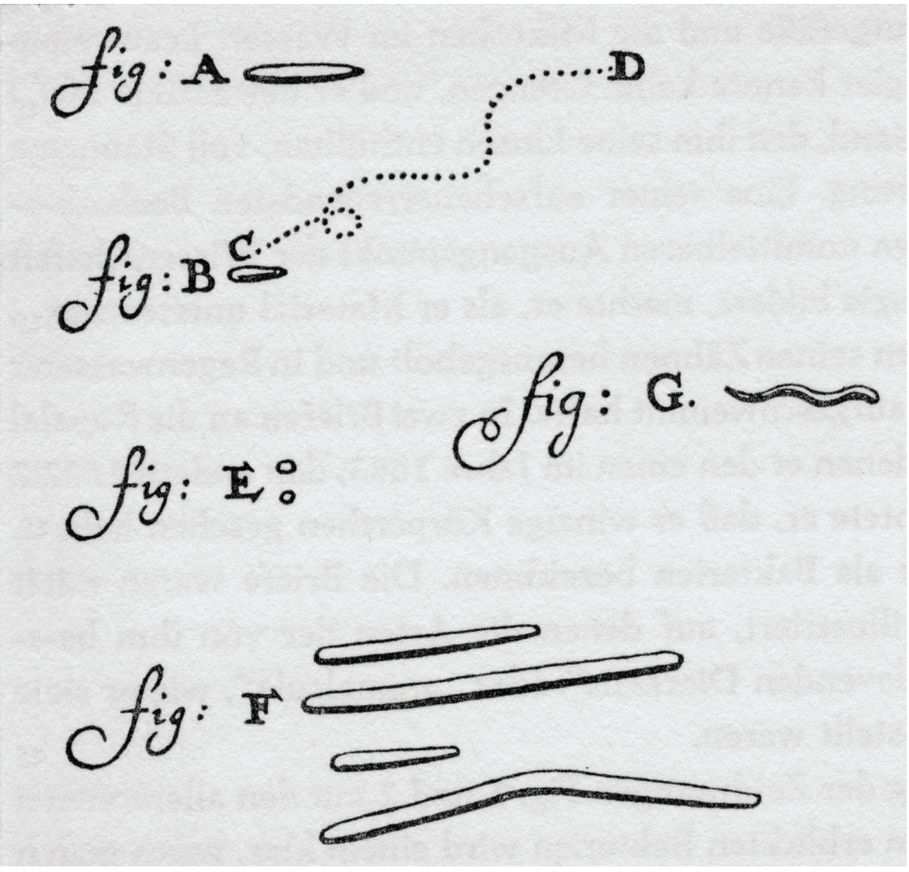
1 | Humans and the Microbial World



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. *(INTERFOTO/Alamy, Stock Photo)*

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 Antonie 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—a world you are about to study.

Microbiology is the study of an amazing world made up of members too small to be seen without the aid of a microscope. Antonie 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 life-forms arise from non-living material in a process known 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 fly eggs, 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, it took more than 200 years and many experiments to amass conclusive evidence that microorganisms did not arise by spontaneous generation.

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 the growth of 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,

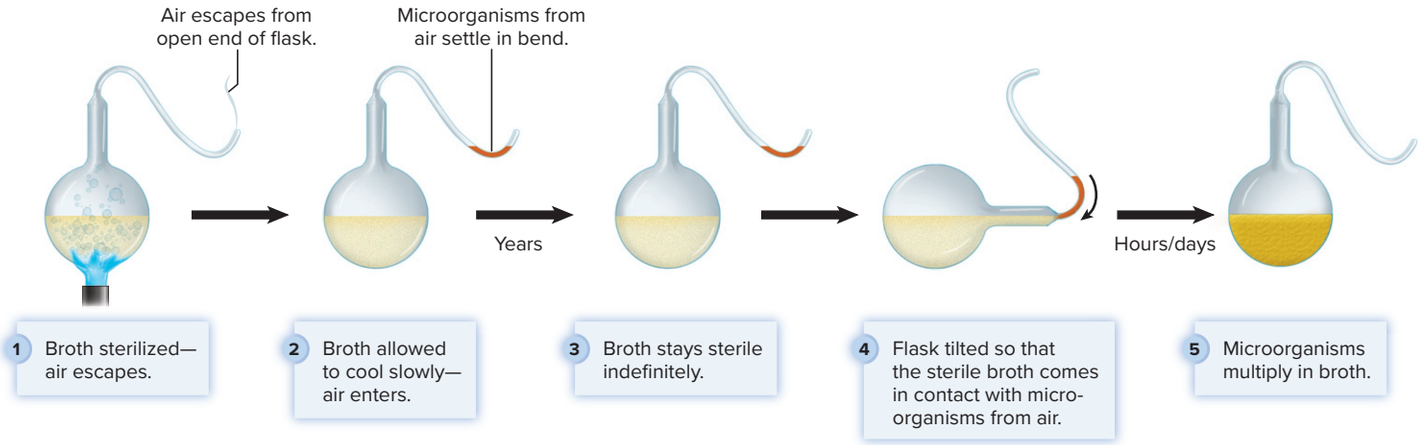


FIGURE 1.2 Pasteur's Experiment with the Swan-Necked Flask

? How did this experiment end arguments that a "vital force" in the air was necessary for spontaneous generation?

showed that Pasteur was correct. Tyndall found that various types of 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 the 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.

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. Scientists at the time 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: When repeating an experiment, all conditions must be reproduced as closely as possible. What may seem like a trivial difference might 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 the 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 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

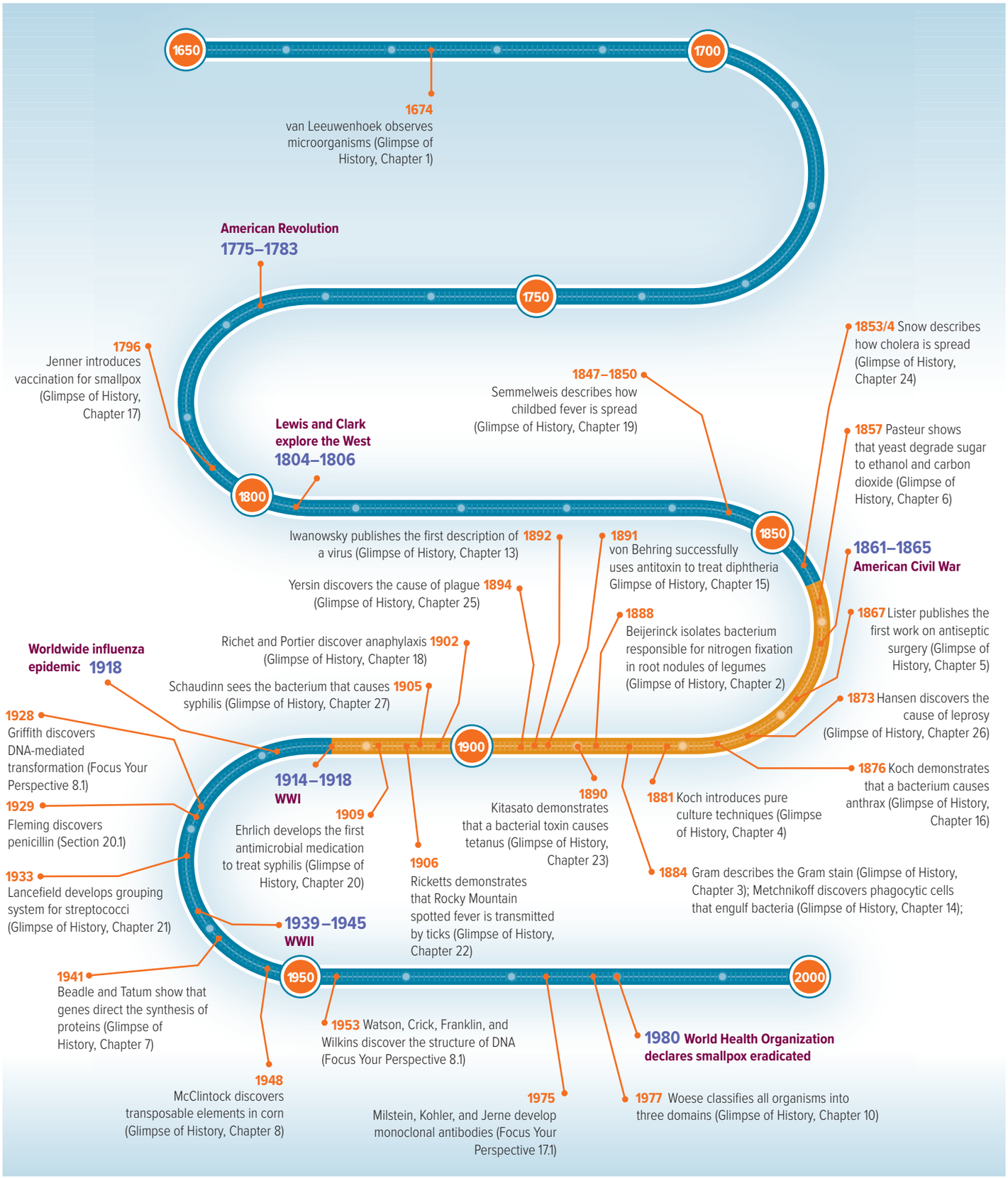


FIGURE 1.3 Historical Events in Microbiology Some major milestones in microbiology—and their timeline in relation to other historical events. The gold band indicates the Golden Age of Microbiology.

? **What is the Golden Age of Microbiology?**

microorganisms in previously sterile broths. In doing a 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 nothing in his original set-up 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 a tremendous 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 they have killed far more people than have ever been killed in war.

The Human Microbiome

Your 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 recent and probably more accurate estimates indicate that the ratio is likely closer to 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 can only be characterized using DNA sequencing technologies.

The Human Microbiome Project changed the way scientists view the human body and also revealed how much more there is to discover about our microbial partners. To understand their significance, think of 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.

The human microbiome's effect on health and disease is an exciting area of active research, but it is more difficult to understand than it might seem. For example, researchers have found that the intestinal microbiome of people diagnosed with depression differs from those who report a good quality of life, but this correlation could be an effect of mood—perhaps even dietary changes associated with certain moods—rather than a cause. Likewise, bacterial species associated with gum disease have been found in the brains of people with Alzheimer's disease, but again, this could be effect rather than cause. Continuing studies aim to clarify the situation.

MicroByte

The Global Microbiome Conservancy is collecting fecal samples from people around the world in an effort to study and preserve the diversity of intestinal bacteria.

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 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.

Microorganisms are also important because they can degrade certain materials that other organisms cannot. Cellulose (an important component of plants) is an excellent example. Although humans and other animals cannot digest cellulose, certain microorganisms can, which is why leaves and fallen trees do not pile up in the environment. Cellulose-degrading microorganisms in the specialized stomach of ruminants (a group of plant-eating animals that includes cattle, sheep, and deer) help those animals digest plant material. Without the assistance of microbes, the ruminants would starve.

In recognition of the important role that microorganisms play in all aspects of life, additional programs promise to expand the scope of existing DNA-based studies. In 2016, the National Microbiome Initiative (NMI) was started to support research on the microbiomes of humans as well as the surrounding environment. Perhaps the most ambitious DNA sequencing program so far is the Earth BioGenome Project, an international effort launched in 2018 to sequence all the known animal, plant, protozoan, and fungal species.

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. In fact, 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.

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.**

Commercially Valuable Products from Microorganisms

Microorganisms synthesize a wide variety of commercially valuable products. Examples include: antibiotics used to treat infectious 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, including the insulin used to treat diabetes. In the past, insulin was isolated from the pancreatic glands of cattle and pigs,

but 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 also allows scientists to genetically engineer plants to give them desirable qualities.

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 can result from damage caused by the pathogen's growth and products or by the body's defense mechanisms inadvertently damaging host tissues during the attempt to control the infection.

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. The COVID-19 pandemic has resulted in the death of more than 1,000,000 people worldwide, including over 200,000 Americans.

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. A bacterial disease that kills olive trees was found in southern Italy in 2013, and it has since spread to Spain and France, contributing to a recent worldwide drop in olive oil production. A fungal disease called "wheat blast" that devastated wheat crops in South America spread to Bangladesh in 2016, resulting in the loss of over 35,000 acres of crops that year. In 2001, a catastrophic outbreak of foot-and-mouth disease of livestock occurred in parts of England. To contain this viral disease, one of the most contagious known, almost 4 million pigs, sheep, and cattle were destroyed. More recently, over a million pigs in China either died from African swine fever or were killed to contain the disease, and officials in other countries are trying to limit its spread. Meanwhile, frog populations around the world have been decimated by chytridiomycosis, a fungal disease.

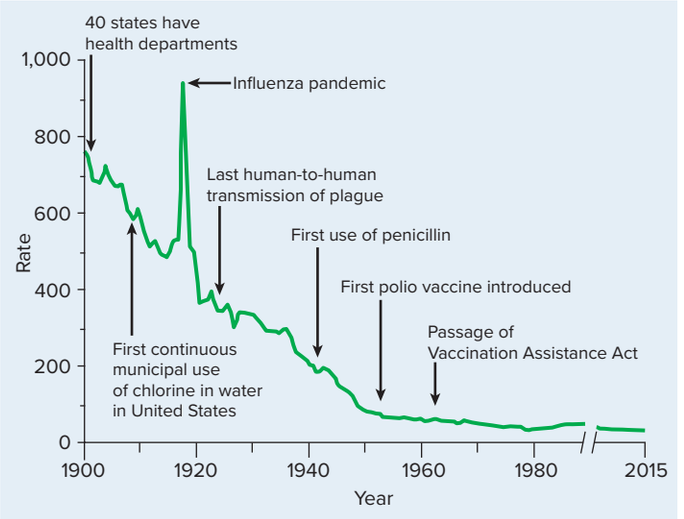


FIGURE 1.4 Trend in Death Rates Due to Infectious Diseases
Crude death rate for infectious disease, United States, per 100,000 population per year.

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

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 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. To maintain this success, we must continue to develop new medications, vaccines, and disease-prevention strategies.

Perhaps the most significant triumph with respect to disease control was the eradication (elimination) of smallpox. This viral disease was one of the most devastating the world has ever known, killing about one-third of those infected. 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. A 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.

Polio, a disease that can cause paralysis and sometimes death, was once relatively common, but it has been nearly eliminated because of vaccination. In fact, the disease now occurs in only a few countries, and the goal is to eradicate it globally.

Plague is another major killer that has largely been brought under control. In the fourteenth century, 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, fewer than 100 people worldwide die from plague in a typical 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 several decades. The EID that everyone is now likely familiar with is COVID-19 (for coronavirus disease 2019), the disease that emerged in late 2019 and then spread rapidly around the globe. COVID-19 is caused by a virus officially called SARS-CoV-2 (for severe acute respiratory syndrome coronavirus 2) but commonly referred to as the COVID-19 virus. Like COVID-19, many EIDs are new or newly recognized; examples include Ebola disease (EBOD), congenital Zika syndrome, *Candida auris* infection, hepatitis C, severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), certain types of influenza, Lyme disease, acquired immunodeficiency syndrome (AIDS), mad cow disease (bovine spongiform encephalopathy), and hantavirus pulmonary syndrome (**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 the virus that causes COVID-19 arose from a strain that infects bats. HIV-1 (**h**uman **i**mmunodeficiency **v**irus type 1), the most common type of HIV to cause AIDS, arose from a virus that infects 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

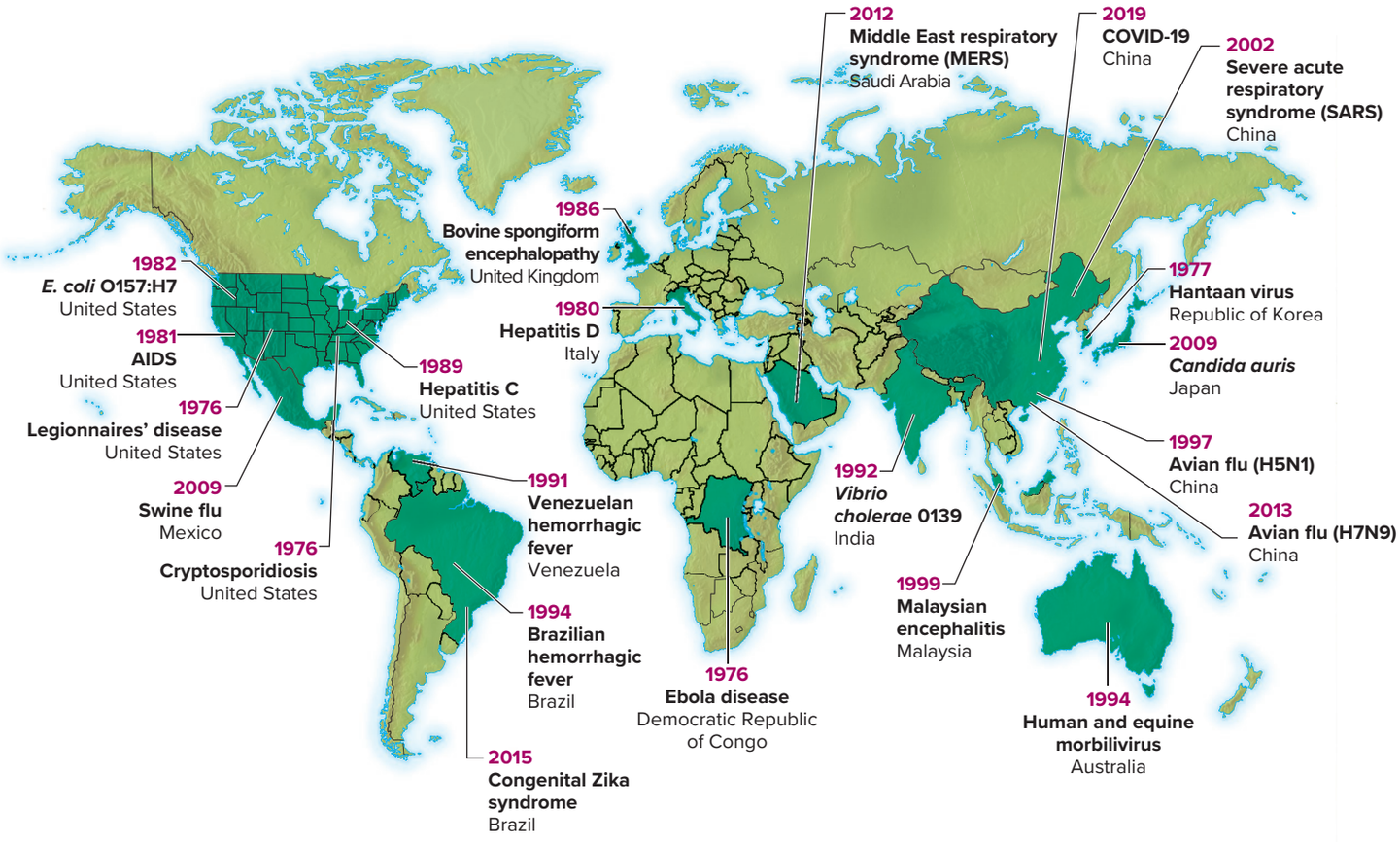


FIGURE 1.5 New and Newly Recognized Infectious Diseases or Disease Agents in Humans and Animals Since 1976 Countries where cases first appeared or were identified appear in a darker shade.

? 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 had suffered from recurrent severe episodes of an intestinal disorder called *Clostridioides (*formerly *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 *C. 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, an experimental 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, the normal microbiota quickly uses 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 by the procedure. The doctors screen the patients to ensure that they are not already infected with the pathogens. For example, if this patient developed symptoms of a *Salmonella* infection after the procedure, how would the physicians know that she acquired the infection as a result of the procedure if they had not checked 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.

incidence in recent years, in part because the causative organisms became resistant to many of the available medications.

As the rapid spread of COVID-19 around the globe certainly demonstrated, mobile populations can contribute to disease emergence as people may inadvertently carry pathogens to different regions. Even diseases such as malaria, cholera, plague, and yellow fever that have largely been eliminated from developed countries can be carried to other places if travelers to regions where they still exist become infected and then move on before recovering. Meanwhile, as city suburbs 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.

The preventive measures used to control certain infectious diseases can become victims of their own success, a situation that can also lead to disease emergence. Decades of vaccination have nearly eliminated measles, mumps, and whooping cough in developed countries, so most people no longer have first-hand knowledge of the dangers of these 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 situations where the diseases become more common again. Measles had been declared eliminated in the United States in 2000, but outbreaks in 2019 resulted in the highest number of cases in 25 years. Outbreaks generally start with unvaccinated travelers who bring the disease into the country, where it then spreads among others who are not vaccinated.

Chronic Diseases Some chronic 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.