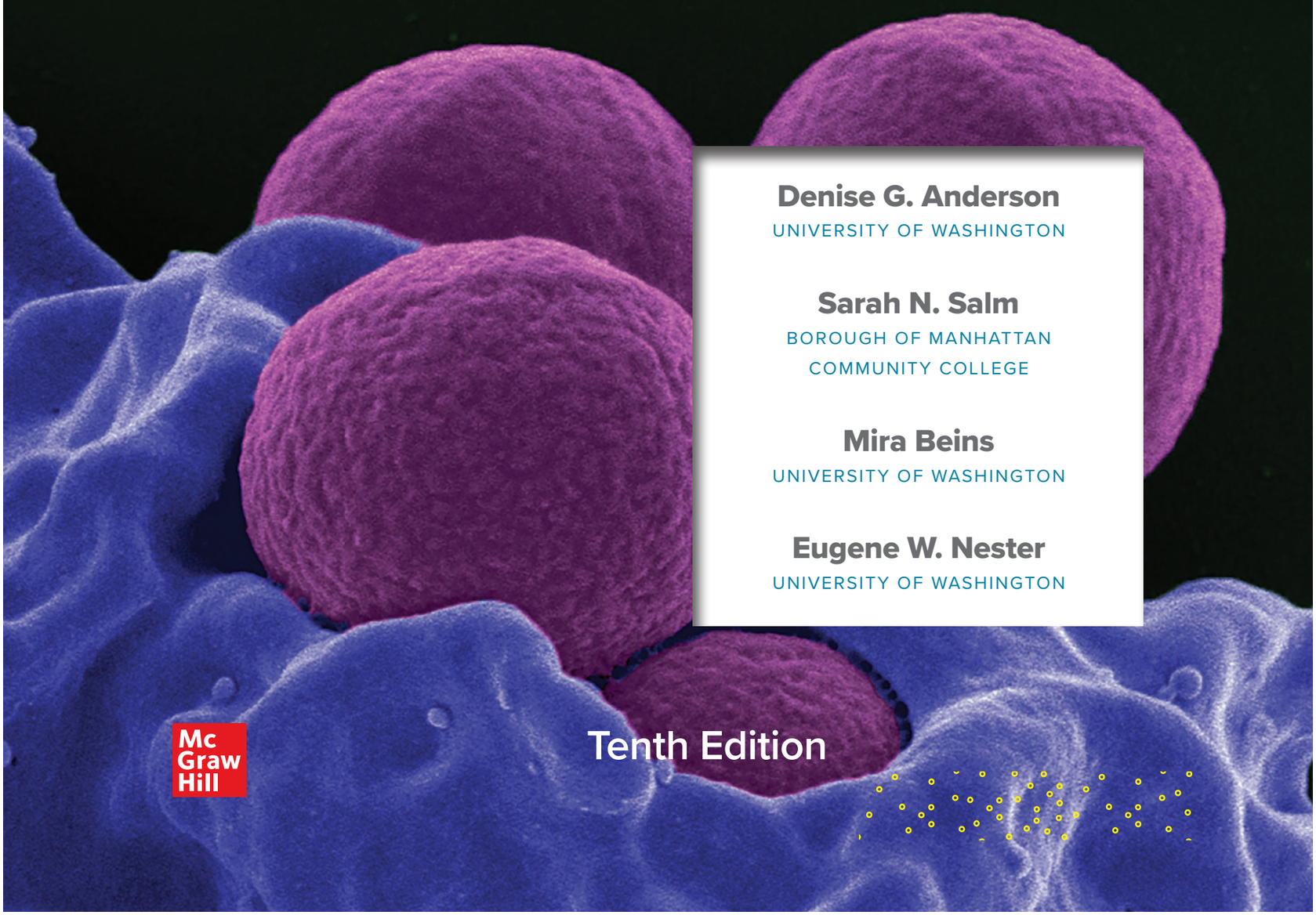
Nester's Microbiology

A HUMAN PERSPECTIVE

Denise Anderson | Sarah Salm | Mira Beins



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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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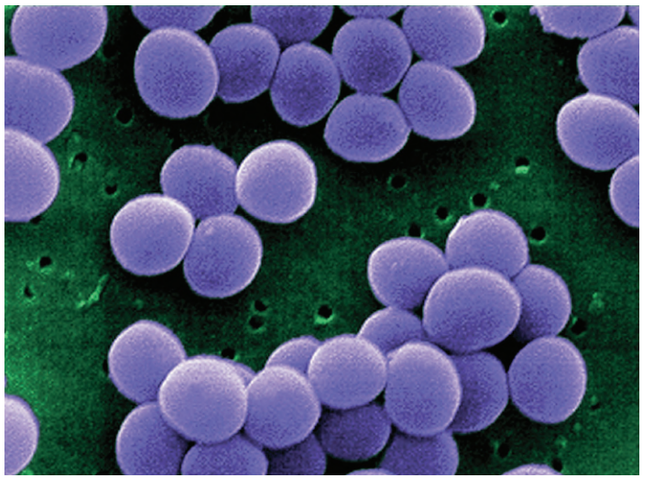

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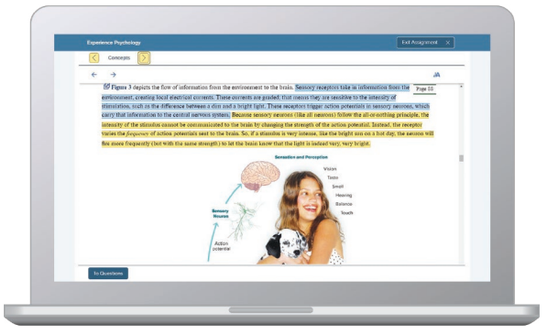

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>
> - Jordan Cunningham, Eastern Washington University

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FOCUS ON UNDERSTANDING . . .

Student-Friendly Illustrations

Introduce the "big picture"

Focus figures provide an overview or highlight a key concept.

Keep the big picture in focus

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

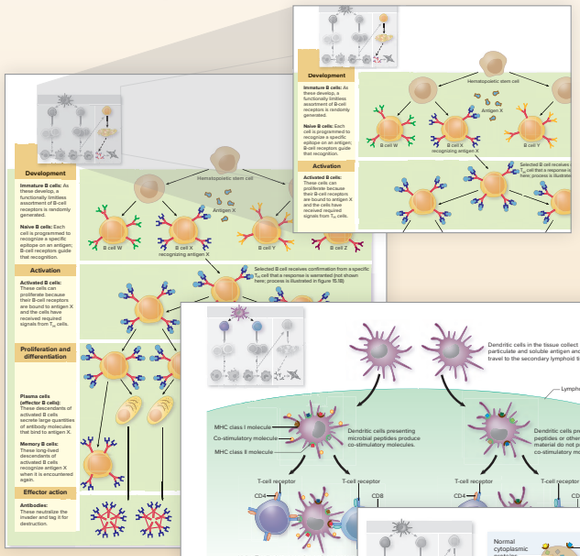
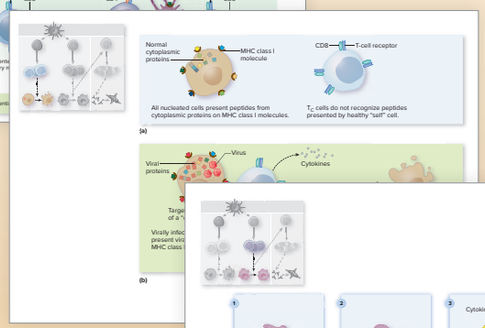


FIGURE 15.10

FIGURE 15.13



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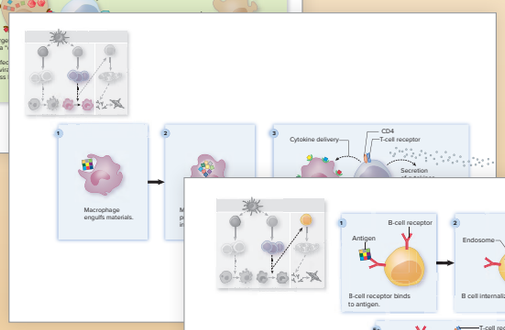

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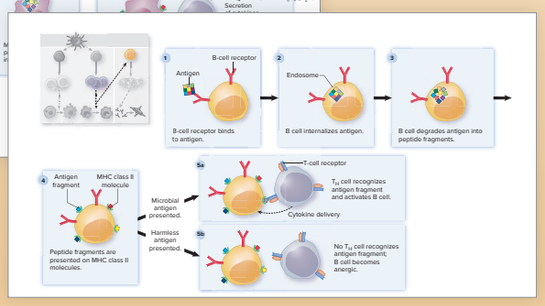

FIGURE 15.18

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

—Jamal Bittar, University of Toledo

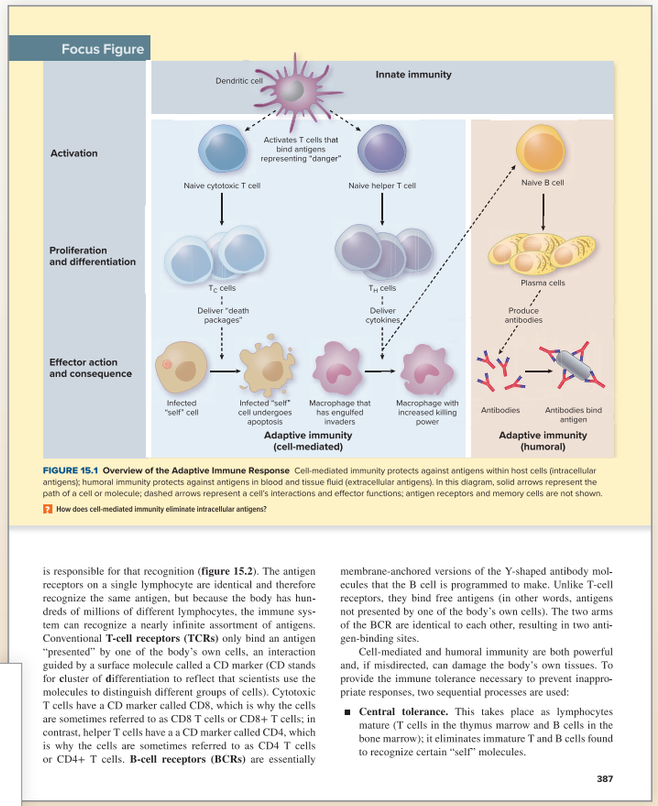

FIGURE 15.1 Overview of the Adaptive Immune Response Cell-mediated immunity protects against antigens within host cells (intracellular antigens); humoral immunity protects against antigens in blood and tissue fluid (extracellular antigens). In this diagram, solid arrows represent the path of a cell or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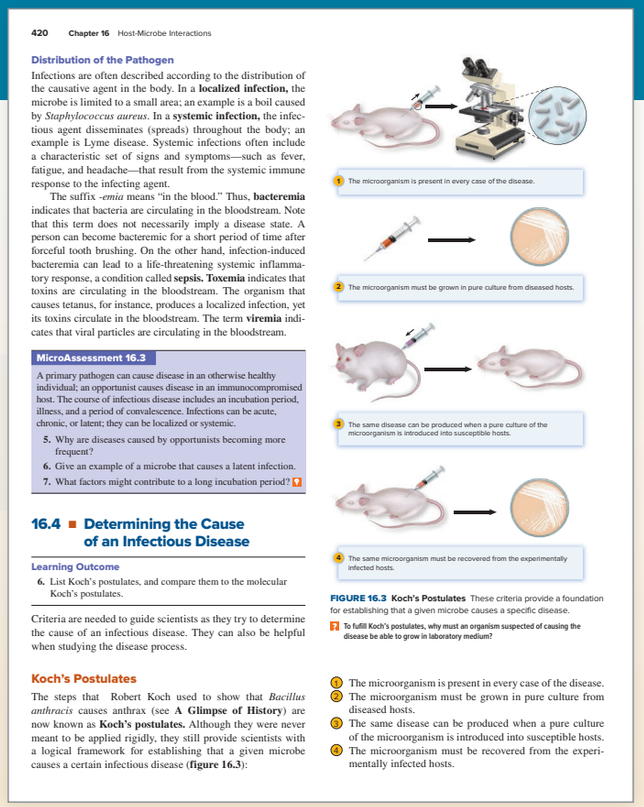
Walk through the processes

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?

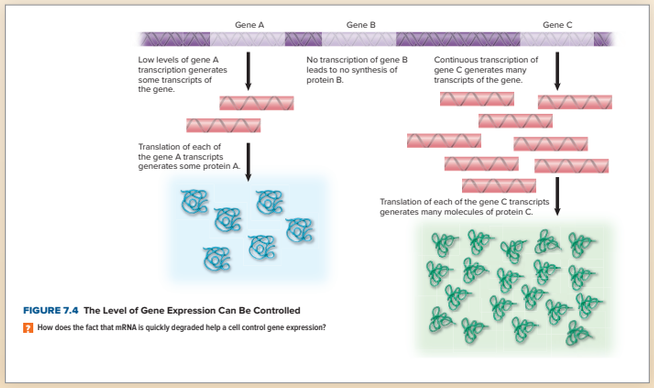


FIGURE 7.4 The Level of Gene Expression Can Be Controlled

? 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.

Introduce the body systems

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

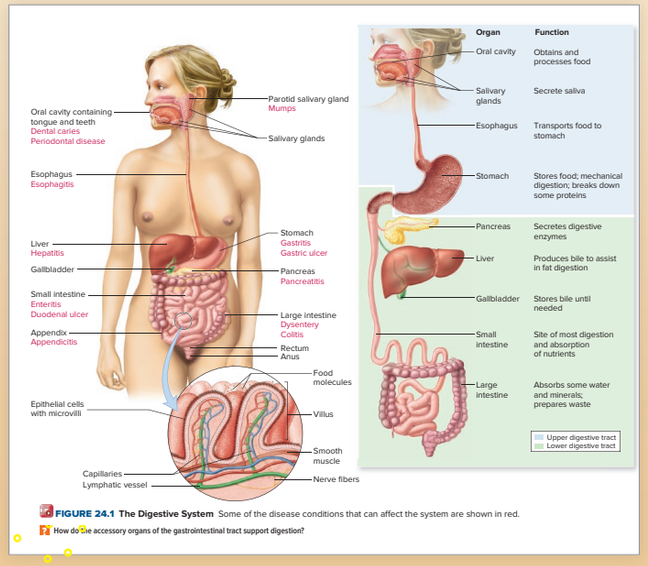


FIGURE 24.1 The Digestive System Some of the disease conditions that can affect the system are shown in red.

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

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.

Provide perspective

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

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.

Inspire the learner

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

- **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.

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-

become
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terfering
inflam-
the area.
releas-
in their

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

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

in hospital-
ystem. Some
contagious.
pper respira-
to the lungs
throat secre-
ias (HCAPs)
pper respira-
who are on
because the
to enter the

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

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.

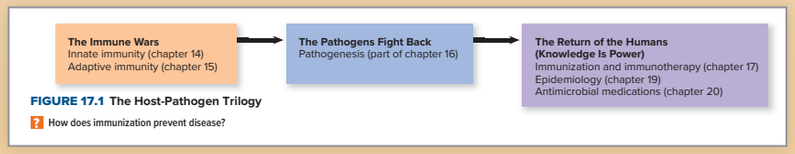

FIGURE 17.1 The Host-Pathogen Trilogy

? 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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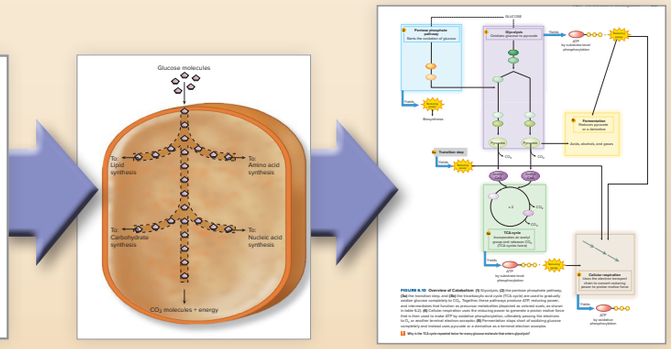
Emphasize the logic

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):***

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

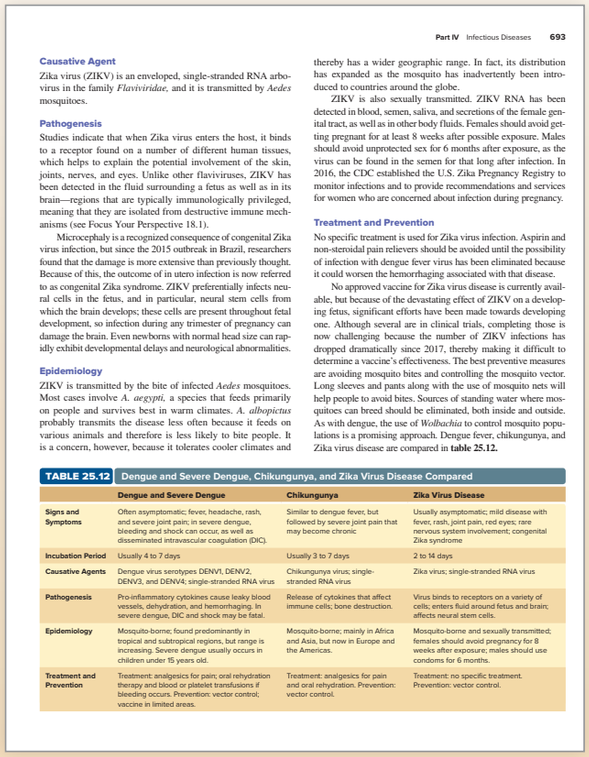
(glucose) (oxygen) (carbon dioxide) (water)

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.

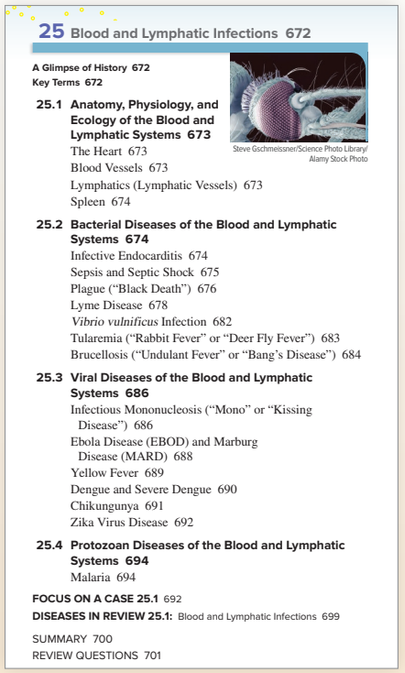
Treatment and Prevention

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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Provide a consistent conceptual framework

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

Summarize each disease's characteristics

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

Review the diseases as a group

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

Diseases in Review 21.1

Respiratory System Diseases

Disease	Causative Agent	Comment	Summary Table
BACTERIAL INFECTIONS OF THE UPPER RESPIRATORY TRACT			
Conjunctivitis (pink eye), otitis media (earache), sinus infection	Usually *Haemophilus influenzae* or *Streptococcus pneumoniae*	Often occur together; factors involved in the transmission are unknown.	
Streptococcal pharyngitis ("strep throat")	*Streptococcus pyogenes* (group A streptococcus)	Treated with antibiotics, partly to avoid sequelae; must be distinguished from viral pharyngitis, which cannot be treated with antibiotics.	Table 21.3
Diphtheria	*Corynebacterium diphtheriae*	Toxin-mediated disease characterized by pseudomembrane in the upper respiratory tract. Preventable by vaccination.	Table 21.4
VIRAL INFECTIONS OF THE UPPER RESPIRATORY TRACT			
Common cold	Rhinoviruses and other viruses	Runny nose, sore throat, and cough are due to the inflammatory response and cell destruction.	Table 21.5
Adenovirus pharyngitis	Adenoviruses	Similar to the common cold but with fever; spread to the lower respiratory tract can result in severe disease.	Table 21.6
BACTERIAL INFECTIONS OF THE LOWER RESPIRATORY TRACT			
Pneumococcal pneumonia	*Streptococcus pneumoniae*	Organism common in the throat of healthy people; causes disease when mucociliary escalator is impaired or with underlying conditions. Vaccine that protects against multiple strains is available.	Table 21.7
***Klebsiella* pneumonia**	*Klebsiella species, commonly K. pneumoniae*	Common hospital-acquired bacterium; characterized by thick, bloody, jelly-like sputum. Drug resistance is a major problem.	Table 21.7
Mycoplasmal pneumonia ("walking pneumonia")	*Mycoplasma pneumoniae*	Relatively mild pneumonia; common among college students and military recruits. Cannot be treated with medications that inhibit cell wall synthesis.	Table 21.7
Pertussis ("whooping cough")	*Bordetella pertussis*	Characterized by frequent violent coughing. Preventable by vaccination.	Table 21.8
Tuberculosis ("TB")	*Mycobacterium tuberculosis*	Most infections result in latent tuberculosis infection (LTBI), but these can reactivate to cause tuberculosis disease (TB disease). Treated using combination drug therapy, but drug resistance is an increasing problem.	Table 21.9
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

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

Acknowledgments

First and foremost, special thanks goes to Gene Nester, the leader of the team that wrote the first version of what became *Microbiology, A Human Perspective*. His efforts helped pioneer a new type of introductory microbiology textbook, designed specifically for students entering healthcare-related fields. This edition proudly builds on that original vision.

We would also like to thank the reviewers and other instructors who guided us as we developed this edition, as well as those whose input has helped the text evolve over the years. Deciding what to eliminate, what to add, and what to rearrange is always difficult, so we appreciate your suggestions.

Past students have been incredibly helpful as well. Every question helps us decide which parts of the textbook need more clarification, and every compliment lets us know when we're on the right track.

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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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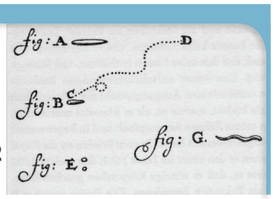

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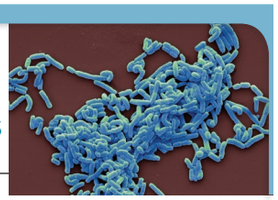
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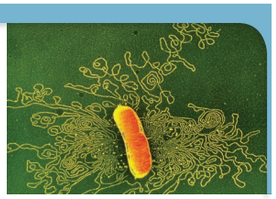
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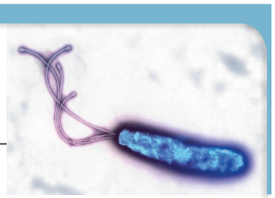
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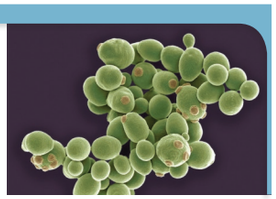
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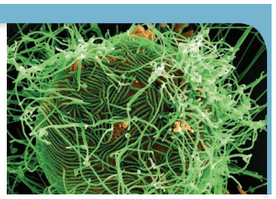
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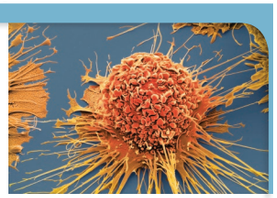
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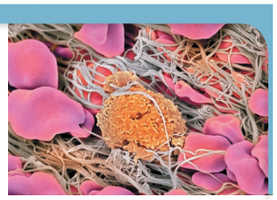
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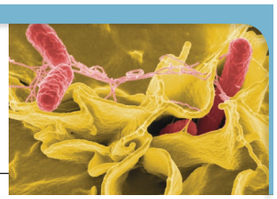
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