The Microbial World and You 1

The overall theme of this textbook is the relationship between microbes—very small organisms that usually require a microscope to be seen—and our lives. We've all heard of epidemics of infectious diseases such as plague or smallpox that wiped out populations. However, there are many positive examples of human-microbe interactions. For example, we use microbial fermentation to ensure safe food supplies, and the human microbiome, a group of microbes that lives in and on our bodies, helps keep us healthy. We begin this chapter by discussing how organisms are named and classified and then follow with a short history of microbiology. Next, we discuss the incredible diversity of microorganisms and their ecological importance, noting how they recycle chemical elements such as carbon and nitrogen among the soil, organisms, and the atmosphere. We also examine how microbes are used to treat sewage, clean pollutants, control pests, and produce foods, chemicals, and drugs. Finally, we will discuss microbes as the cause of diseases such as Zika virus disease, avian (bird) flu, Ebola virus disease, and diarrhea, and we examine the growing public health problem of antibiotic-resistant bacteria.

ASM: Microorganisms provide essential models that give us fundamental knowledge about life processes.

Shown in the photograph are *Staphylococcus aureus* (STAF-i-lō-kok'kus OR-ē-us) bacteria on human nasal epithelial cells. These bacteria generally live harmlessly on skin or inside the nose. Misuse of antibiotics, however, allows the survival of bacteria with antibiotic-resistance genes, such as methicillin-resistant *S. aureus* (MRSA). As illustrated in the Clinical Case, an infection caused by these bacteria is resistant to antibiotic treatment.

◀ ***Staphylococcus aureus*** **bacteria on skin cell culture.**

In the Clinic

As the nurse practitioner in a rural hospital, you are reviewing a microscope slide of a skin scraping from a 12-year-old girl. The slide shows branched, intertwined nucleated hyphae. The girl has dry, scaly, itchy patches on her arms. **What is causing her skin problem?**

Hint: Read about types of microorganisms (pages 4–6).

Play In the Clinic Video @ MasteringMicrobiology

Microbes in Our Lives

LEARNING OBJECTIVES

1-1 List several ways in which microbes affect our lives.

1-2 Define *microbiome*, *normal microbiota*, and *transient microbiota*.

For many people, the words *germ* and *microbe* bring to mind a group of tiny creatures that do not quite fit into any of the categories in that old question, “Is it animal, vegetable, or mineral?” *Germ* actually comes from the Latin word *germen*, meaning to spout from, or germinate. Think of wheat germ, the plant embryo from which the plant grows. It was first used in relation to microbes in the nineteenth century to explain the rapidly growing cells that caused disease. **Microbes**, also called **microorganisms**, are minute living things that individually are usually too small to be seen with the unaided eye. The group includes bacteria, fungi (yeasts and molds), protozoa, and microscopic algae. It also includes viruses, those noncellular entities sometimes regarded as straddling the border between life and nonlife (Chapters 11, 12, and 13, respectively).

We tend to associate these small organisms only with infections and inconveniences such as spoiled food. However, the majority of microorganisms actually help maintain the balance of life in our environment. Marine and freshwater microorganisms form the basis of the food chain in oceans, lakes, and rivers. Soil microbes break down wastes and incorporate nitrogen gas from the air into organic compounds, thereby recycling chemical elements among soil, water, living organisms, and air. Certain microbes play important roles in *photosynthesis*, a food- and oxygen-generating process that is critical to life on Earth.

Microorganisms also have many commercial applications. They are used in the synthesis of such chemical products as vitamins, organic acids, enzymes, alcohols, and many drugs. For example, microbes are used to produce acetone and butanol, and the vitamins B_2 (riboflavin) and B_{12} (cobalamin) are made biochemically. The process by which microbes produce acetone and butanol was discovered in 1914 by Chaim Weizmann, a Russian-born chemist working in England. With the outbreak of World War I in August of that year, the production of acetone became very important for making cordite (a smokeless form of gunpowder used in munitions). Weizmann’s discovery played a significant role in determining the outcome of the war.

The food industry also uses microbes in producing, for example, vinegar, sauerkraut, pickles, soy sauce, cheese, yogurt, bread, and alcoholic beverages. In addition, enzymes from microbes can now be manipulated to cause the microbes to produce substances they normally don’t synthesize, including cellulose, human insulin, and proteins for vaccines.

The Microbiome

An adult human is composed of about 30 trillion body cells and harbors another 40 trillion bacterial cells. Microbes that live stably in and on the human body are called the human **microbiome**, or **microbiota**. Humans and many other animals depend on these microbes to maintain good health. Bacteria in our intestines, including *E. coli*, aid digestion (see Exploring the Microbiome on page 3) and even synthesize some vitamins that our bodies require, including B vitamins for metabolism and vitamin K for blood clotting. They also prevent growth of **pathogenic** (disease-causing) species that might otherwise take up residence, and they seem to have a role in training our immune system to know which foreign invaders to attack and which to leave alone. (See Chapter 14 for more details on relationships between normal microbiota and the host.)

Even before birth, our bodies begin to be populated with bacteria. As newborns, we acquire viruses, fungi, and bacteria (**Figure 1.1**). For example, *E. coli* and other bacteria acquired from foods take residence in the large intestine. Many factors influence where and whether a microbe can indefinitely colonize the body as benign **normal microbiota** or be only a fleeting member of its community (known as **transient microbiota**). Microbes can colonize only those body sites that can supply the appropriate nutrients. Temperature, pH, and the presence or absence of chemical compounds are some factors that influence what types of microbes can flourish.

To determine the makeup of typical microbiota of various areas of the body, and to understand the relationship between changes in the microbiome and human diseases, is the goal of the **Human Microbiome Project**, which began in 2007. Likewise, the **National Microbiome Initiative (NMI)** launched in 2016 to expand our understanding of the role microbes play in different ecosystems, including soil, plants, aquatic environments, and the human body. Throughout the book, look for

Figure 1.1 Several types of bacteria found as part of the normal microbiota in an infant’s intestine.

Q **How do we benefit from the production of vitamin K by microbes?**

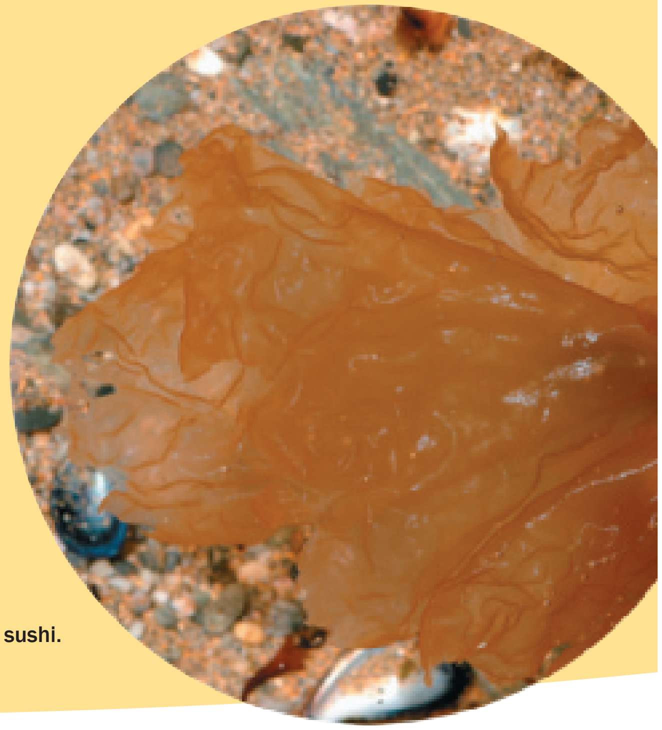
EXPLORING THE MICROBIOME How Does Your Microbiome Grow?

The specific traits of microbes that reside in human intestines can vary greatly—even within the same microbial species. Take *Bacteroides*, a bacterium commonly found in gastrointestinal tracts of humans worldwide. The strain residing in Japanese people has specialized enzymes that break down nori, the red algae used as the wrap component of sushi. These enzymes are absent from *Bacteroides* found in the gastrointestinal tracts of North Americans.

How did the Japanese *Bacteroides* acquire the ability to digest algae? It's thought the skill hails from *Zobellia galactanivorans*, a marine bacterium that lives on this alga. Not surprisingly, *Zobellia* readily breaks down the alga's main carbohydrate with enzymes. Since people living in Japan consumed algae regularly, *Zobellia* routinely met up with *Bacteroides* that lived in the human intestine. Bacteria can swap genes with other species—a process called *horizontal gene transfer*—and at some point, *Zobellia* must have given *Bacteroides* the genes to produce algae-digesting enzymes. (For more on horizontal gene transfer, see Chapter 8).

In an island nation where algae are an important diet component, the ability to extract more nutrition from algal carbohydrates would give an intestinal microbe a competitive advantage over others that couldn't use it as a food source. Over time, this *Bacteroides* strain became the dominant one found within the gastrointestinal tracts of people living in Japan.

You may be wondering whether North American sushi eaters can expect their own *Bacteroides* to shift to the algae-eating variety, too. Researchers say this is unlikely. Traditional Japanese food included raw algae, which allowed for living *Zobellia* to reach the large intestine. By contrast, the algae used in foods today is usually roasted or dried; these processes kill any bacteria that may be present on the surface.



***Porphyra*, an alga commonly used in sushi.**

stories related to the human microbiome, highlighted in the Exploring the Microbiome feature boxes.

Our realization that some microbes are not only harmless to humans, but also are actually essential, represents a large shift from the traditional view that the only good microbe was a dead one. In fact, only a minority of microorganisms are pathogenic to humans. Although anyone planning to enter a health care profession needs to know how to prevent the transmission and spread of pathogenic microbes, it's also important to know that pathogens are just one aspect of our full relationship with microbes.

Today we understand that microorganisms are found almost everywhere. Yet not long ago, before the invention of the microscope, microbes were unknown to scientists. Next we'll look at the major groups of microbes and how they are named and classified. After that, we'll examine a few historic milestones in microbiology that have changed our lives.

CHECK YOUR UNDERSTANDING

- **1-1*** Describe some of the destructive and beneficial actions of microbes.
- **1-2** What percentage of all the cells in the human body are bacterial cells?

CLINICAL CASE A Simple Spider Bite?

Andrea is a normally healthy 22-year-old college student who lives at home with her mother and younger sister, a high school gymnast. She is trying to work on a paper for her psychology class but is having a hard time because a red, swollen sore on her right wrist is making typing difficult. "Why won't this spider bite heal?" she wonders. "It's been there for days!" She makes an appointment with her doctor so she can show him the painful lesion. Although Andrea does not have a fever, she does have an elevated white blood cell count that indicates a bacterial infection. Andrea's doctor suspects that this isn't a spider bite at all, but a staph infection. He prescribes a β-lactam antibiotic, cephalosporin. Learn more about the development of Andrea's illness on the following pages.

What is staph? Read on to find out.

3 16 18 19

* The numbers preceding Check Your Understanding questions refer to the corresponding Learning Objectives.

Naming and Classifying Microorganisms

LEARNING OBJECTIVES

- **1-3** Recognize the system of scientific nomenclature that uses two names: a genus and a specific epithet.
- **1-4** Differentiate the major characteristics of each group of microorganisms.
- **1-5** List the three domains.

Nomenclature

The system of nomenclature (naming) for organisms in use today was established in 1735 by Carolus Linnaeus. Scientific names are latinized because Latin was the language traditionally used by scholars. Scientific nomenclature assigns each organism two names—the **genus** (plural: **genera**) is the first name and is always capitalized; the **specific epithet** (**species** name) follows and is not capitalized. The organism is referred to by both the genus and the specific epithet, and both names are underlined or italicized. By custom, after a scientific name has been mentioned once, it can be abbreviated with the initial of the genus followed by the specific epithet.

Scientific names can, among other things, describe an organism, honor a researcher, or identify the habitat of a species. For example, consider *Staphylococcus aureus*, a bacterium commonly found on human skin. *Staphylo-* describes the clustered arrangement of the cells; *-coccus* indicates that they are shaped like spheres. The specific epithet, *aureus*, is Latin for golden, the color of many colonies of this bacterium. The genus of the bacterium *Escherichia coli* (esh'er-IK-ē-ah KŌ-lī, or KŌ-lē) is named for a physician, Theodor Escherich, whereas its specific epithet, *coli*, reminds us that *E. coli* live in the colon, or large intestine. Table 1.1 contains more examples.

CHECK YOUR UNDERSTANDING

✓ **1-3** Distinguish a genus from a specific epithet.

Types of Microorganisms

In health care, it is very important to know the different types of microorganisms in order to treat infections. For example, antibiotics can be used to treat bacterial infections but have no effect on viruses or other microbes. Here is an overview of the main types of microorganisms. (The classification and identification of microorganisms are discussed in Chapter 10.)

Bacteria

Bacteria (singular: **bacterium**) are relatively simple, single-celled (unicellular) organisms. Because their genetic material is not enclosed in a special nuclear membrane, bacterial cells are called **prokaryotes** (prō-KAR-e-ōts), from Greek words meaning prenucleus. Prokaryotes include both bacteria and archaea.

Bacterial cells generally appear in one of several shapes. *Bacillus* (bah-SIL-lus) (rodlike), illustrated in Figure 1.2a, *coccus* (KOK-kus) (spherical or ovoid), and *spiral* (corkscrew or curved) are among the most common shapes, but some bacteria are star-shaped or square (see Figures 4.1 through 4.5, pages 74–75). Individual bacteria may form pairs, chains, clusters, or other groupings; such formations are usually characteristic of a particular genus or species of bacteria.

Bacteria are enclosed in cell walls that are largely composed of a carbohydrate and protein complex called *peptidoglycan*.

TABLE 1.1 Making Scientific Names Familiar

Use the word roots guide to find out what the name means. The name will not seem so strange if you translate it. When you encounter a new name, practice saying it out loud (guidelines for pronunciation are given in Appendix D). The exact pronunciation is not as important as the familiarity you will gain.

Following are some examples of microbial names you may encounter in the popular press as well as in the lab.

	Pronunciation	Source of Genus Name	Source of Specific Epithet
Salmonella enterica (bacterium)	sal'mō-NEL-lah en-TER-i-kah	Honors public health microbiologist Daniel Salmon	Found in the intestines (*entero-*)
Streptococcus pyogenes (bacterium)	strep'tō-KOK-kus pī-AH-jen-ēz	Appearance of cells in chains (*strepto-*)	Forms pus (*pyo-*)
Saccharomyces cerevisiae (yeast)	sak'kar-ō-MĪ-sēz se-ri-VIS-ē-ī	Fungus (*-myces*) that uses sugar (*saccharo-*)	Makes beer (*cerevisia*)
Penicillium chrysogenum (fungus)	pen'i-SIL-lē-um krī-SO-jen-um	Tuftlike or paintbrush (*penicill-*) appearance microscopically	Produces a yellow (*chryso-*) pigment
Trypanosoma cruzi (protozoan)	tri'pa-nō-SŌ-mah KROOZ-ē	Corkscrew- (*trypano-*, borer; *soma-*, body)	Honors epidemiologist Oswaldo Cruz

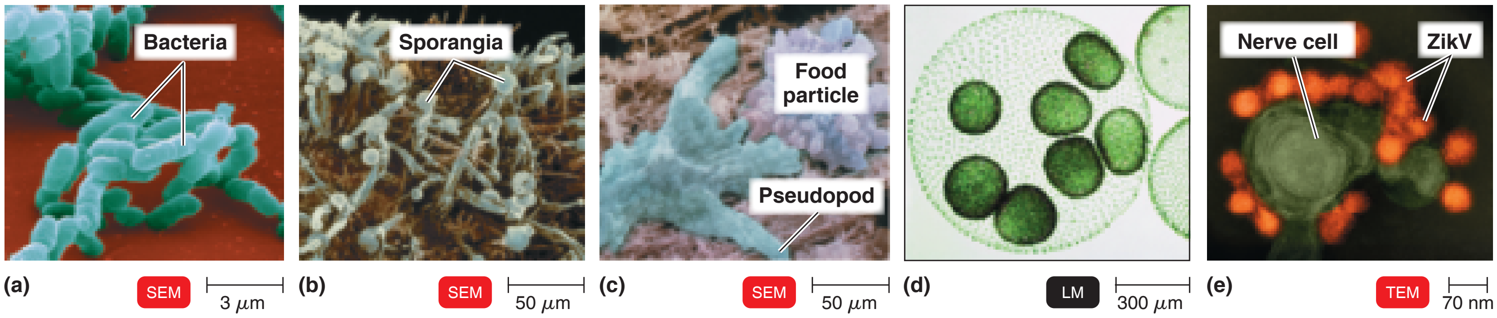


Figure 1.2 Types of microorganisms. **(a)** The rod-shaped bacterium *Haemophilus influenzae*, one of the bacterial causes of pneumonia. **(b)** *Mucor*, a common bread mold, is a type of fungus. When released from sporangia, spores that land on a favorable surface germinate into a network of hyphae (filaments) that absorb nutrients. **(c)** An ameba, a type of protozoan, approaching a food particle. **(d)** The pond alga *Volvox*. **(e)** Zika virus (ZikV). *NOTE:* Throughout the book, a red icon under a micrograph indicates that the micrograph has been artificially colored. SEM (scanning electron microscope) and LM (light microscope) are discussed in detail in Chapter 3.

Q How are bacteria, archaea, fungi, protozoa, algae, and viruses distinguished on the basis of structure?

(By contrast, cellulose is the main substance of plant and algal cell walls.) Bacteria generally reproduce by dividing into two equal cells; this process is called *binary fission*. For nutrition, most bacteria use organic chemicals, which in nature can be derived from either dead or living organisms. Some bacteria can manufacture their own food by photosynthesis, and some can derive nutrition from inorganic substances. Many bacteria can "swim" by using moving appendages called *flagella*. (For a complete discussion of bacteria, see Chapter 11.)

Archaea

Like bacteria, **archaea** (ar-KĒ-ah) consist of prokaryotic cells, but if they have cell walls, the walls lack peptidoglycan. Archaea, often found in extreme environments, are divided into three main groups. The *methanogens* produce methane as a waste product from respiration. The *extreme halophiles* (*halo* = salt; *philic* = loving) live in extremely salty environments such as the Great Salt Lake and the Dead Sea. The *extreme thermophiles* (*therm* = heat) live in hot sulfurous water, such as hot springs at Yellowstone National Park. Archaea are not known to cause disease in humans.

Fungi

Fungi (singular: **fungus**) are **eukaryotes** (ū-KAR-ē-ōts), organisms whose cells have a distinct nucleus containing the cell's genetic material (DNA), surrounded by a special envelope called the *nuclear membrane*. Organisms in the Kingdom Fungi may be unicellular or multicellular (see Chapter 12, page 324). Large multicellular fungi, such as mushrooms, may look somewhat like plants, but unlike most plants, fungi cannot carry out photosynthesis. True fungi have cell walls composed primarily of a substance called *chitin*. The unicellular forms of fungi, *yeasts*, are oval microorganisms that are larger than bacteria. The most typical fungi are *molds* (Figure 1.2b). Molds form visible masses called *mycelia*, which are composed of long filaments (*hyphae*) that branch and intertwine. The cottony growths sometimes found on bread and fruit are mold mycelia. Fungi can reproduce sexually or asexually. They obtain nourishment by absorbing organic material from their environment—whether soil, seawater, freshwater, or an animal or plant host. Organisms called *slime molds* are actually ameba-like protozoa (see Chapter 12).

Protozoa

Protozoa (singular: **protozoan**) are unicellular eukaryotic microbes (see Chapter 12, page 341). Protozoa move by pseudopods, flagella, or cilia. Amebae (Figure 1.2c) move by using extensions of their cytoplasm called *pseudopods* (false feet). Other protozoa have long *flagella* or numerous shorter appendages for locomotion called *cilia*. Protozoa have a variety of shapes and live either as free entities or as *parasites* (organisms that derive nutrients from living hosts) that absorb or ingest organic compounds from their environment. Some protozoa, such as *Euglena* (ū-GLĒ-nah), are photosynthetic. They use light as a source of energy and carbon dioxide as their chief source of carbon to produce sugars. Protozoa can reproduce sexually or asexually.

Algae

Algae (singular: **alga**) are photosynthetic eukaryotes with a wide variety of shapes and both sexual and asexual reproductive forms (Figure 1.2d). The algae of interest to microbiologists are usually unicellular (see Chapter 12, page 337). The cell walls of many algae are composed of a carbohydrate called *cellulose*. Algae are abundant in freshwater and saltwater, in soil, and in association with plants. As photosynthesizers, algae need light, water, and carbon dioxide for food production and growth, but they do not generally require organic compounds from the environment. As a result of photosynthesis, algae produce oxygen and carbohydrates that are then utilized by other organisms, including animals. Thus, they play an important role in the balance of nature.

Viruses

Viruses (Figure 1.2e) are very different from the other microbial groups mentioned here. They are so small that most can be seen only with an electron microscope, and they are acellular (that is, they are not cells). Structurally very simple, a virus particle contains a core made of only one type of nucleic acid, either DNA or RNA. This core is surrounded by a protein coat, which is sometimes encased by a lipid membrane called an *envelope*. All living cells have RNA *and* DNA, can carry out chemical reactions, and can reproduce as self-sufficient units. Viruses can reproduce only by using the cellular machinery of other organisms. Thus, on the one hand, viruses are considered to be living only when they multiply within host cells they infect. In this sense, viruses are parasites of other forms of life. On the other hand, viruses are not considered to be living because they are inert outside living hosts. (Viruses will be discussed in detail in Chapter 13.)

Multicellular Animal Parasites

Although multicellular animal parasites are not strictly microorganisms, they are of medical importance and therefore will be discussed in this text. Animal parasites are eukaryotes. The two major groups of parasitic worms are the flatworms and the roundworms, collectively called **helminths** (see Chapter 12, page 347). During some stages of their life cycle, helminths are microscopic in size. Laboratory identification of these organisms includes many of the same techniques used for identifying microbes.

CHECK YOUR UNDERSTANDING

✓ **1-4** Which groups of microbes are prokaryotes? Which are eukaryotes?

Classification of Microorganisms

Before the existence of microbes was known, all organisms were grouped into either the animal kingdom or the plant kingdom. When microscopic organisms with characteristics of animals and plants were discovered late in the seventeenth century, a new system of classification was needed. Still, biologists couldn't agree on the criteria for classifying these new organisms until the late 1970s.

In 1978, Carl Woese devised a system of classification based on the cellular organization of organisms. It groups all organisms in three domains as follows:

1. Bacteria (cell walls contain a protein–carbohydrate complex called peptidoglycan)
2. Archaea (cell walls, if present, lack peptidoglycan)
3. Eukarya, which includes the following:
   - Protists (slime molds, protozoa, and algae)
   - Fungi (unicellular yeasts, multicellular molds, and mushrooms)
   - Plants (mosses, ferns, conifers, and flowering plants)
   - Animals (sponges, worms, insects, and vertebrates)

Classification will be discussed in more detail in Chapters 10 through 12.

CHECK YOUR UNDERSTANDING

✓ **1-5** What are the three domains?

A Brief History of Microbiology

LEARNING OBJECTIVES

1-6 Explain the importance of observations made by Hooke and van Leeuwenhoek.

1-7 Compare spontaneous generation and biogenesis.

1-8 Identify the contributions to microbiology made by Needham, Spallanzani, Virchow, and Pasteur.

1-9 Explain how Pasteur's work influenced Lister and Koch.

1-10 Identify the importance of Koch's postulates.

1-11 Identify the importance of Jenner's work.

1-12 Identify the contributions to microbiology made by Ehrlich and Fleming.

1-13 Define *bacteriology*, *mycology*, *parasitology*, *immunology*, and *virology*.

1-14 Explain the importance of microbial genetics, molecular biology, and genomics.

Bacterial ancestors were the first living cells to appear on Earth. For most of human history, people knew little about the true causes, transmission, and effective treatment of disease. Let's look now at some key developments in microbiology that have spurred the field to its current technological state.

The First Observations

In 1665, after observing a thin slice of cork through a crude microscope, Englishman Robert Hooke reported that life's smallest structural units were "little boxes," or "cells." Using his improved microscope, Hooke later saw individual cells. Hooke's discovery marked the beginning of the **cell theory**—the theory that *all living things are composed of cells.*

Though Hooke's microscope was capable of showing large cells, it lacked the resolution that would have allowed him to see microbes clearly. Dutch merchant and amateur scientist Anton van Leeuwenhoek was probably the first to observe live microorganisms through the magnifying lenses of the more than

400 microscopes he constructed. Between 1673 and 1723, he wrote about the "animalcules" he saw through his simple, single-lens microscopes. Van Leeuwenhoek made detailed drawings of organisms he found in rainwater, feces, and material scraped from teeth. These drawings have since been identified as representations of bacteria and protozoa (Figure 1.3).

CHECK YOUR UNDERSTANDING

✓ **1-6** What is the cell theory?

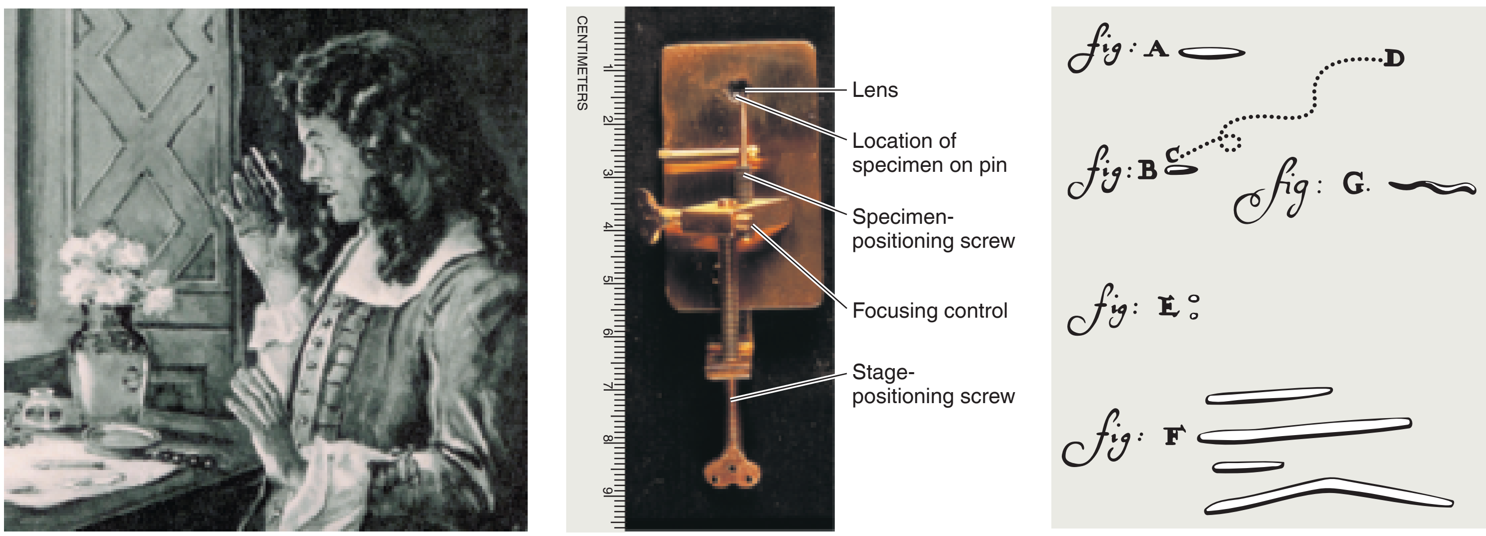
The Debate over Spontaneous Generation

After van Leeuwenhoek discovered the previously "invisible" world of microorganisms, the scientific community became interested in the origins of these tiny living things. Until the second half of the nineteenth century, many scientists and philosophers believed that some forms of life could arise spontaneously from nonliving matter; they called this hypothetical process **spontaneous generation**. Not much more than 100 years ago, people commonly believed that toads, snakes, and mice could be born of moist soil; that flies could emerge from manure; and that maggots (which we now know are the larvae of flies) could arise from decaying corpses.

Physician Francesco Redi set out in 1668 to demonstrate that maggots did not arise spontaneously. Redi filled two jars with decaying meat. The first was left unsealed, allowing flies to lay eggs on the meat, which developed into larvae. The second jar was sealed, and because the flies could not get inside, no maggots appeared. Still, Redi's antagonists were not convinced; they claimed that fresh air was needed for spontaneous generation. So Redi set up a second experiment, in which he covered a jar with a fine net instead of sealing it. No larvae appeared in the gauze-covered jar, even though air was present.

Redi's results were a serious blow to the long-held belief that large forms of life could arise from nonlife. However, many scientists still believed that small organisms, such as van Leeuwenhoek's "animalcules," were simple enough to generate from nonliving materials.

The case for spontaneous generation of microorganisms seemed to be strengthened in 1745, when John Needham found that even after he heated chicken broth and corn broth before pouring them into covered flasks, the cooled solutions were soon teeming with microorganisms. Needham claimed that microbes developed spontaneously from the fluids. Twenty years later, Lazzaro Spallanzani suggested that microorganisms from the air probably entered Needham's solutions after they were boiled. Spallanzani showed that nutrient fluids heated *after* being sealed in a flask did not develop microbial growth. Needham responded by claiming the "vital force" necessary for spontaneous generation had been destroyed by the heat and was kept out of the flasks by the seals.



(a) Van Leeuwenhoek using his microscope **(b)** Microscope replica **(c)** Drawings of bacteria

Figure 1.3 Anton van Leeuwenhoek's microscopic observations. (a) By holding his brass microscope toward a source of light, van Leeuwenhoek was able to observe living organisms too small to be seen with the unaided eye. **(b)** The specimen was placed on the tip of the adjustable point and viewed from the other side through the tiny, nearly spherical lens. The highest magnification possible with his microscopes was about 300× (times). **(c)** Some of van Leeuwenhoek's drawings of bacteria, made in 1683. The letters represent various shapes of bacteria. C–D represents a path of motion he observed.

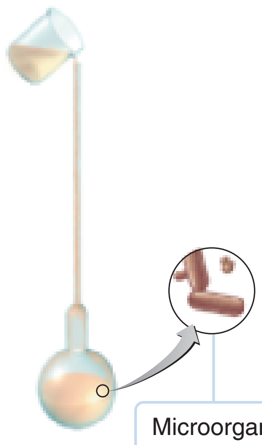
Q Why was van Leeuwenhoek's discovery so important?

FOUNDATION FIGURE 1.4

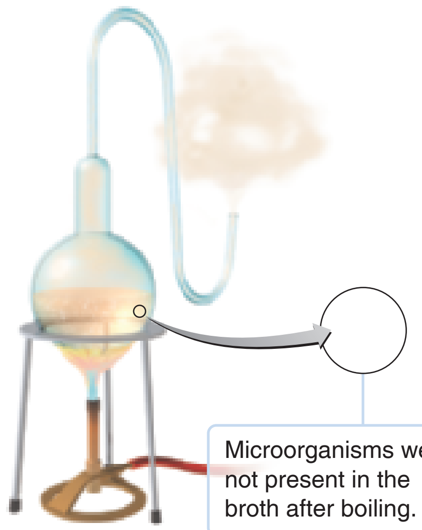
Disproving Spontaneous Generation

According to the hypothesis of spontaneous generation, life can arise spontaneously from nonliving matter, such as dead corpses and soil. Pasteur's experiment, described below, demonstrated that microbes are present in nonliving matter—air, liquids, and solids.

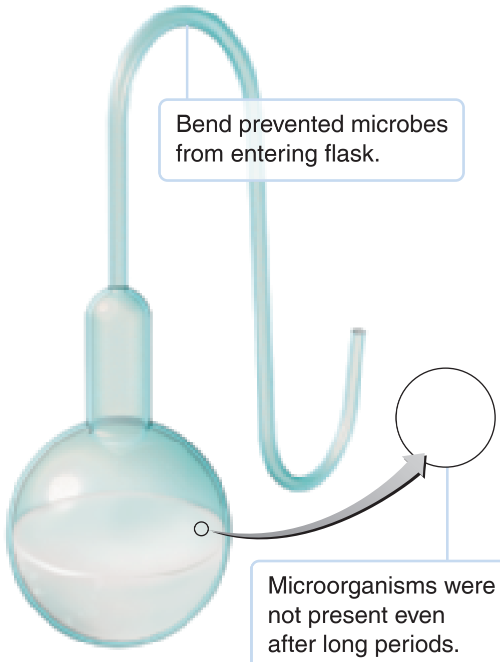
1. Pasteur first poured beef broth into a long-necked flask.



2. Next he heated the neck of the flask and bent it into an S-shape; then he boiled the broth for several minutes.



3. Microorganisms did not appear in the cooled solution, even after long periods.



Some of these original vessels are still on display at the Pasteur Institute in Paris. They have been sealed but show no sign of contamination more than 100 years later.

KEY CONCEPTS

- Pasteur demonstrated that microbes are responsible for food spoilage, leading researchers to the connection between microbes and disease.
- His experiments and observations provided the basis of aseptic techniques, which are used to prevent microbial contamination, as shown in the photo at right.

Spallanzani's observations were also criticized on the grounds that there was not enough oxygen in the sealed flasks to support microbial life.

The Theory of Biogenesis

In 1858 Rudolf Virchow challenged the case for spontaneous generation with the concept of **biogenesis**, hypothesizing that living cells arise only from preexisting living cells. Because he could offer no scientific proof, arguments about spontaneous generation continued until 1861, when the issue was finally resolved by the French scientist Louis Pasteur.

Pasteur demonstrated that microorganisms are present in the air and can contaminate sterile solutions, but that air itself does not create microbes. He filled several short-necked flasks with beef broth and then boiled their contents. Some were then left open and allowed to cool. In a few days, these flasks were found to be contaminated with microbes. The other flasks, sealed after boiling, were free of microorganisms. From these results, Pasteur reasoned that microbes in the air were the agents responsible for contaminating nonliving matter.

Pasteur next placed broth in open-ended, long-necked flasks and bent the necks into S-shaped curves (**Figure 1.4**). The contents of these flasks were then boiled and cooled. The broth in the flasks did not decay and showed no signs of life, even after months. Pasteur's unique design allowed air to pass into the flask, but the curved neck trapped any airborne micro-organisms that might contaminate the broth. (Some of these original vessels are still on display at the Pasteur Institute in

Paris. They have been sealed but, like the flask in Figure 1.4, show no sign of contamination more than 100 years later.)

Pasteur showed that microorganisms can be present in nonliving matter—on solids, in liquids, and in the air. Furthermore, he demonstrated conclusively that microbial life can be destroyed by heat and that methods can be devised to block the access of airborne microorganisms to nutrient environments. These discoveries form the basis of **aseptic techniques**, procedures that prevent contamination by unwanted microorganisms, which are now the standard practice in laboratory and many medical procedures. Modern aseptic techniques are among the first and most important concepts that a beginning microbiologist learns.

Pasteur's work provided evidence that microorganisms cannot originate from mystical forces present in nonliving materials. Rather, any appearance of "spontaneous" life in nonliving solutions can be attributed to microorganisms that were already present in the air or in the fluids themselves. Scientists now believe that a form of spontaneous generation probably did occur on the primitive Earth when life first began, but they agree that this does not happen under today's environmental conditions.

CHECK YOUR UNDERSTANDING

- 1-7 What evidence supported spontaneous generation?
- 1-8 How was spontaneous generation disproved?

The First Golden Age of Microbiology

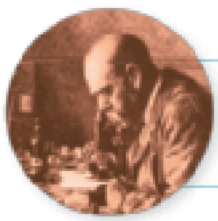
The period from 1857 to 1914 has been appropriately named the First Golden Age of Microbiology. Rapid advances, spearheaded mainly by Pasteur and Robert Koch, led to the establishment of microbiology. Discoveries included both the agents of many diseases and the role of immunity in preventing and curing disease. During this productive period, microbiologists studied the chemical activities of microorganisms, improved the techniques for performing microscopy and culturing microorganisms, and developed vaccines and surgical techniques. Some of the major events that occurred during the First Golden Age of Microbiology are listed in **Figure 1.5**.

First Golden Age of MICROBIOLOGY

1857	**Pasteur**—Fermentation
1861	**Pasteur**—Disproved spontaneous generation
1864	**Pasteur**—Pasteurization
1867	**Lister**—Aseptic surgery
1876	**Koch***—Germ theory of disease
1879	**Neisser**—*Neisseria gonorrhoeae*
1881	**Koch***—Pure cultures
	Finlay—Yellow fever
1882	**Koch***—*Mycobacterium tuberculosis*
	Hess—Agar (solid) media
1883	**Koch***—*Vibrio cholerae*
1884	**Metchnikoff***—Phagocytosis
	Gram—Gram-staining procedure
	Escherich—*Escherichia coli*
1887	**Petri**—Petri dish
1889	**Kitasato**—*Clostridium tetani*
1890	**von Bering***—Diphtheria antitoxin
	Ehrlich*—Theory of immunity
1892	**Winogradsky**—Sulfur cycle
1898	**Shiga**—*Shigella dysenteriae*
1908	**Ehrlich***—Syphilis treatment
1910	**Chagas**—*Trypanosoma cruzi*
1911	**Rous***—Tumor-causing virus (1966 Nobel Prize)

Louis Pasteur (1822–1895)
Demonstrated that life did not arise spontaneously from nonliving matter.

Joseph Lister (1827–1912)
Performed surgery under aseptic conditions using phenol. Proved that microbes caused surgical wound infections.



Robert Koch (1843–1910)
Established experimental steps for directly linking a specific microbe to a specific disease.

Figure 1.5 Milestones in the First Golden Age of Microbiology. An asterisk (*) indicates a Nobel laureate.

Q Why do you think the First Golden Age of Microbiology occurred when it did?

Fermentation and Pasteurization

One of the key steps that established the relationship between microorganisms and disease occurred when a group of French merchants asked Pasteur to find out why wine and beer soured. They hoped to develop a method that would prevent spoilage when those beverages were shipped long distances. At the time, many scientists believed that air converted the sugars in these fluids into alcohol. Pasteur found instead that microorganisms called yeasts convert the sugars to alcohol in the absence of air. This process, called **fermentation** (see Chapter 5, page 128), is used to make wine and beer. Souring and spoilage are caused by different microorganisms, called bacteria. In the presence of air, bacteria change the alcohol into vinegar (acetic acid).

Pasteur's solution to the spoilage problem was to heat the beer and wine just enough to kill most of the bacteria that caused the spoilage. The process, called **pasteurization**, is now commonly used to reduce spoilage and kill potentially harmful bacteria in milk and other beverages as well as in some alcoholic beverages.

The Germ Theory of Disease

Before the time of Pasteur, effective treatments for many diseases were discovered by trial and error, but the causes of the diseases were unknown. The realization that yeasts play a crucial role in fermentation was the first link between the activity of a microorganism and physical and chemical changes in organic materials. This discovery alerted scientists to the possibility that microorganisms might have similar relationships with plants and animals—specifically, that microorganisms might cause disease. This idea was known as the **germ theory of disease**.

The germ theory met great resistance at first—for centuries, disease was believed to be punishment for an individual's crimes or misdeeds. When the inhabitants of an entire village became ill, people often blamed the disease on demons appearing as foul odors from sewage or on poisonous vapors from swamps. Most people born in Pasteur's time found it inconceivable that "invisible" microbes could travel through the air to infect plants and animals or remain on clothing and bedding to be transmitted from one person to another. Despite these doubts, scientists gradually accumulated the information needed to support the new germ theory.

In 1865, Pasteur was called upon to help fight silkworm disease, which was ruining the silk industry in Europe. Decades earlier, amateur microscopist Agostino Bassi had proved that another silkworm disease was caused by a fungus. Using data provided by Bassi, Pasteur found that the more recent infection was caused by a protozoan, and he developed a method for recognizing afflicted silkworm moths.

In the 1860s, Joseph Lister, an English surgeon, applied the germ theory to medical procedures. Lister was aware that in the 1840s, the Hungarian physician Ignaz Semmelweis had demonstrated that physicians, who at the time did not disinfect their hands, routinely transmitted infections (puerperal, or childbirth, fever) from one obstetrical patient to another. Lister had also heard of Pasteur's work connecting microbes to animal diseases. Disinfectants were not used at the time, but Lister knew that phenol (carbolic acid) kills bacteria, so he began treating surgical wounds with a phenol solution. The practice so reduced the incidence of infections and deaths that other surgeons quickly adopted it. His findings proved that microorganisms cause surgical wound infections.

The first proof that bacteria actually cause disease came from Robert Koch (kōk) in 1876. Koch, a German physician, was Pasteur's rival in the race to discover the cause of anthrax, a disease that was destroying cattle and sheep in Europe. Koch discovered rod-shaped bacteria now known as *Bacillus anthracis* (bah-SIL-lus an-THRĀ-sis) in the blood of cattle that had died of anthrax. He cultured the bacteria on nutrients and then injected samples of the culture into healthy animals. When these animals became sick and died, Koch isolated the bacteria in their blood and compared them with the originally isolated bacteria. He found that the two sets of blood cultures contained the same bacteria.

Koch thus established **Koch's postulates**, a sequence of experimental steps for directly relating a specific microbe to a specific disease (see Figure 14.3, page 339). During the past 100 years, these same criteria have been invaluable in investigations proving that specific microorganisms cause many diseases. Koch's postulates, their limitations, and their application to disease will be discussed in greater detail in Chapter 14.

Vaccination

Often a treatment or preventive procedure is developed before scientists know why it works. The smallpox vaccine is an example. Almost 70 years before Koch established that a specific microorganism causes anthrax, Edward Jenner, a young British physician, embarked on an experiment to find a way to protect people from smallpox. The disease periodically swept through Europe, killing thousands, and it wiped out 90% of the Native Americans on the East Coast when European settlers first brought the infection to the New World.

When a young milkmaid informed Jenner that she couldn't get smallpox because she already had been sick from cowpox—a much milder disease—he decided to put the girl's story to the test. First Jenner collected scrapings from cowpox blisters. Then he inoculated a healthy 8-year-old volunteer with the cowpox material by scratching the child's arm with a pox-contaminated needle. The scratch turned into a raised bump. In a few days, the volunteer became mildly sick but recovered and never again contracted either cowpox or smallpox. The protection from disease provided by vaccination (or by recovery from the disease itself) is called **immunity**. (We will discuss the mechanisms of immunity in Chapter 17.)

Years after Jenner's experiment, Pasteur discovered why vaccinations work. He found that the bacterium that causes fowl cholera lost its ability to cause disease (lost its *virulence*, or became *avirulent*) after it was grown in the laboratory for long periods. However, it—and other microorganisms with decreased virulence—was able to induce immunity against subsequent infections by its virulent counterparts. The discovery of this phenomenon provided a clue to Jenner's successful experiment with cowpox. Both cowpox and smallpox are caused by viruses. Even though cowpox virus is not a laboratory-produced derivative of smallpox virus, it is so closely related to the smallpox virus that it can induce immunity to both viruses. Pasteur used the term *vaccine* for cultures of avirulent microorganisms used for preventive inoculation. (The Latin word *vacca* means cow—thus, the term *vaccine* honored Jenner's earlier cowpox inoculation work.)

Jenner's experiment was actually not the first time a living viral agent—in this case, the cowpox virus—was used to produce immunity. Starting in the 1500s, physicians in China had immunized patients from smallpox by removing scales from drying pustules of a person suffering from a mild case of smallpox, grinding the scales to a fine powder, and inserting the powder into the nose of the person to be protected.

Some vaccines are still produced from avirulent microbial strains that stimulate immunity to the related virulent strain. Other vaccines are made from killed virulent microbes, from isolated components of virulent microorganisms, or by genetic engineering techniques.

CHECK YOUR UNDERSTANDING

- **1-9** Summarize in your own words the germ theory of disease.
- **1-10** What is the importance of Koch's postulates?
- **1-11** What is the significance of Jenner's discovery?

The Second Golden Age of Microbiology

After the relationship between microorganisms and disease was established, medical microbiologists next focused on the search for substances that could destroy pathogenic microorganisms without damaging the infected animal or human.

Treatment of disease by using chemical substances is called **chemotherapy**. (The term also commonly refers to chemical treatment of noninfectious diseases, such as cancer.) Chemicals produced naturally by bacteria and fungi that act against other microorganisms are called **antibiotics**. Chemotherapeutic agents prepared from chemicals in the laboratory are called **synthetic drugs**. The success of chemotherapy is based on the fact that some chemicals are more poisonous to microorganisms than to the hosts infected by the microbes. Antimicrobial therapy will be discussed in further detail in Chapter 20.

The First Synthetic Drugs

Paul Ehrlich was the imaginative thinker who fired the first shot in the chemotherapy revolution. As a medical student, Ehrlich speculated about a "magic bullet" that could hunt down and destroy a pathogen without harming the infected host. In 1910, after testing hundreds of substances, he found a chemotherapeutic agent called *salvarsan*, an arsenic derivative effective against syphilis. The agent was named *salvarsan* because it was considered to offer salvation from syphilis and it contained arsenic. Before this discovery, the only known chemical in Europe's medical arsenal was an extract from the bark of a South American tree, *quinine*, which had been used by Spanish conquistadors to treat malaria.

By the late 1930s, researchers had developed several other synthetic drugs that could destroy microorganisms. Most of these drugs were derivatives of dyes. This came about because the dyes synthesized and manufactured for fabrics were routinely tested for antimicrobial qualities by microbiologists looking for a "magic bullet." In addition, *sulfonamides* (sulfa drugs) were synthesized at about the same time.

A Fortunate Accident—Antibiotics

The first antibiotic was discovered by accident. Alexander Fleming, a Scottish physician and bacteriologist, almost tossed out some culture plates that had been contaminated by mold. Fortunately, he noticed the curious pattern of growth on the plates—a clear area where bacterial growth had been inhibited encircled the mold (**Figure 1.6**). Fleming was looking at a mold that inhibited growth of a bacterium. The mold became known as *Penicillium chrysogenum* (pen'i-SIL-lē-um krī-SO-jen-um), and the mold's active inhibitor was called *penicillin*. Thus, penicillin

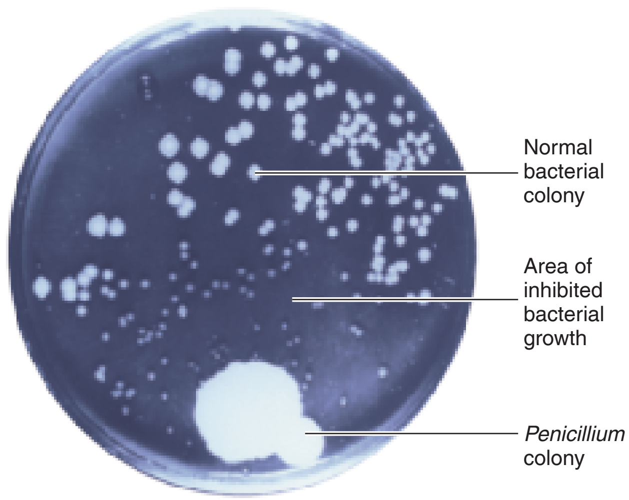


Figure 1.6 The discovery of penicillin. Alexander Fleming took this photograph in 1928. The colony of *Penicillium* mold accidentally contaminated the plate and inhibited nearby bacterial growth.

Q Why do you think penicillin is no longer as effective as it once was?

is an antibiotic produced by a fungus. The Second Golden Age of Microbiology began in the 1940s, when the enormous usefulness of penicillin became apparent and the drug came into common use.

Since these early discoveries, thousands of other antibiotics have been discovered. Unfortunately, use of antibiotics and other chemotherapeutic drugs is not without problems. Many antimicrobial chemicals kill pathogenic microbes but also damage the infected host. For reasons we will discuss later, toxicity to humans is a particular problem in the development of drugs for treating viral diseases. Viral growth depends on life processes of normal host cells. Thus, there are very few successful antiviral drugs, because a drug that would interfere with viral reproduction would also likely affect uninfected cells of the body.

Over the years, more and more microbes also developed resistance to antibiotics that were once very effective against them. Drug resistance results from genetic changes in microbes that enable them to tolerate a certain amount of an antibiotic that would normally inhibit them (see the box in Chapter 26, page 771). For example, a microbe might produce enzymes that inactivate antibiotics, or a microbe might undergo changes to its surface that prevent an antibiotic from attaching to it or entering it.

The recent appearance of vancomycin-resistant *Staphylococcus aureus* and *Enterococcus faecalis* (en'ter-ō-KOK-kus fē-KĀ-lis) has alarmed health care professionals because it indicates that some previously treatable bacterial infections may soon be impossible to treat with antibiotics.

The quest to solve drug resistance, identify viruses, and develop vaccines requires sophisticated research techniques and correlated studies that were never dreamed of in the days of Koch and Pasteur. Other microbiologists also used these

Second Golden Age of MICROBIOLOGY

- 1940s **Fleming, Chain, and Florey**—Penicillin
- 1950s **Waksman**—Streptomycin
- **H. Krebs**—Chemical steps of the Krebs cycle
- **Enders, Weller, and Robbins**—Poliovirus cultured in cell cultures
- **Beadle and Tatum**—Genetic control of biochemical reactions
- 1960s **Medawar**—Acquired immune tolerance
- 1980s **Sanger and Gilbert**—Techniques for sequencing DNA
- **Jerne, Köhler, and Milstein**—Technique for producing monoclonal (single pure) antibodies
- **Tonegawa**—Genetics of antibody production
- **Bishop and Varmus**—Cancer-causing genes (oncogenes)

Third Golden Age of MICROBIOLOGY

- 1990s **Murray and Thomas**—First successful transplants using immunosuppressive drugs
- **Fischer and E. Krebs**—Enzymes that regulate cell growth (protein kinases)
- **Roberts and Sharp**—Genes can be present in separated segments of DNA
- **Mullis**—Polymerase chain reactions that amplify (make multiple copies of) DNA
- **Doherty and Zinkernagel**—Cell-mediated immunity
- 2000s **Agre and MacKinnon**—Water and ion channels in plasma membranes
- **Marshall and Warren**—*Helicobacter pylori* as the cause of peptic ulcers
- **Barré-Sinoussi and Montagnier**—Discovery of HIV
- 2010s **Ramakrishnan, Steitz, and Yonath**—Detailed structure and function of ribosomes
- **Beutler, Hoffmann, and Steinman**—Innate immunity; dendritic cells in adaptive immunity
- **Tu**—Treatment for malaria

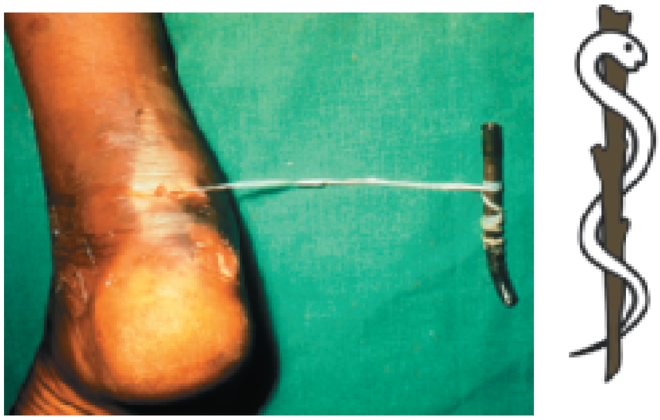
César Milstein (1927–)
Fused cancerous cells with antibody-producing cells to produce a hybrid cell that grows continuously and produces therapeutic antibodies.

Françoise Barré-Sinoussi (1947–)
Discovered a virus in a patient with swollen lymph nodes; the virus was human immunodeficiency virus.

Youyou Tu (1930–)
Extracted artemisinin from a Chinese sage plant. Artemisinin inhibits the malaria parasite.

Figure 1.7 Second and Third Golden Ages of Microbiology. All researchers listed are Nobel laureates.

Q What advances occurred during the Second Golden Age of Microbiology?



(a) A parasitic guinea worm (*Dracunculus medinensis*) is removed from the subcutaneous tissue of a patient by winding it onto a stick. This procedure may have been used for the design of the symbol in part (b).

(b) Rod of Asclepius, symbol of the medical profession

Figure 1.8 Parasitology: the study of protozoa and parasitic worms.

Q How do you think parasitic worms survive and live off a human host?

techniques to investigate industrial applications and roles of microorganisms in the environment.

Bacteriology, Mycology, and Parasitology

The groundwork laid during the First Golden Age of Microbiology provided the basis for several monumental achievements in the years following that era (Figure 1.7). New branches of microbiology were developed, including immunology and virology.

Bacteriology, the study of bacteria, began with van Leeuwenhoek's first examination of tooth scrapings. New pathogenic bacteria are still discovered regularly. Many bacteriologists, like Pasteur, look at the roles of bacteria in food and the environment. One intriguing discovery came in 1997, when Heide Schulz discovered a bacterium large enough to be seen with the unaided eye (0.2 mm wide). This bacterium, named *Thiomargarita namibiensis* (THĪ-ō-mar-gar′ē-tah nah′mib-ē-EN-sis), lives in mud on the African coast. *Thiomargarita* is unusual because of its size and its ecological niche. The bacterium consumes hydrogen sulfide, which would be toxic to mud-dwelling animals (Figure 11.28, page 320).

Mycology, the study of fungi, includes medical, agricultural, and ecological branches. Fungal infection rates have been rising during the past decade, accounting for 10% of hospital-acquired infections. Climatic and environmental changes (severe drought) are thought to account for the tenfold increase in *Coccidioides immitis* (kok′sid-ē-OID-ēz IM-mi-tis) infections in California. New techniques for diagnosing and treating fungal infections are currently being investigated.

Parasitology is the study of protozoa and parasitic worms. Because many parasitic worms are large enough to be seen with the unaided eye, they have been known for thousands of years. It has been speculated that the medical symbol, the rod of Asclepius, represents the removal of parasitic guinea worms (Figure 1.8). Asclepius was a Greek physician who practiced about 1200 B.C.E. and was deified as the god of medicine.

The clearing of rain forests has exposed laborers to previously undiscovered parasites. Parasitic diseases unknown until recently are also being found in patients whose immune systems have been suppressed by organ transplants, cancer chemotherapy, or AIDS.

Immunology

Immunology is the study of immunity. Knowledge about the immune system has accumulated steadily and expanded rapidly. Vaccines are now available for numerous diseases, including measles, rubella (German measles), mumps, chickenpox, pneumococcal pneumonia, tetanus, tuberculosis, influenza, whooping cough, polio, and hepatitis B. The smallpox vaccine was so effective that the disease has been eliminated. Public health officials estimate that polio will be eradicated within a few years because of the polio vaccine.

A major advance in immunology occurred in 1933, when Rebecca Lancefield (Figure 1.9) proposed that streptococci be classified according to serotypes (variants within a species) based on certain components in the cell walls of the bacteria. Streptococci are responsible for a variety of diseases, such as sore throat (strep throat), streptococcal toxic shock, and septicemia (blood poisoning).

In 1960, interferons, substances generated by the body's own immune system, were discovered. Interferons inhibit replication of viruses and have triggered considerable research related

Figure 1.9 Rebecca Lancefield (1895–1981), who discovered differences in the chemical composition of a polysaccharide in the cell walls of many pathogenic streptococci. Rapid laboratory tests using immunologic techniques now identify and classify streptococci into Lancefield groups based on this carbohydrate.

Q Why is it important to identify streptococci quickly?

to the treatment of viral diseases and cancer. One of today's biggest challenges for immunologists is learning how the immune system might be stimulated to ward off the virus responsible for AIDS, a disease that destroys the immune system.

Virology

The study of viruses, **virology**, originated during the First Golden Age of Microbiology. In 1892, Dmitri Iwanowski reported that the organism that caused mosaic disease of tobacco was so small that it passed through filters fine enough to stop all known bacteria. At the time, Iwanowski was not aware that the organism in question was a virus. In 1935, Wendell Stanley demonstrated that the organism, called tobacco mosaic virus (TMV), was fundamentally different from other microbes and so simple and homogeneous that it could be crystallized like a chemical compound. Stanley's work facilitated the study of viral structure and chemistry. Since the development of the electron microscope in the 1930s, microbiologists have been able to observe the structure of viruses in detail, and today much is known about their structure and activity.

Molecular Genetics

Once science turned to the study of unicellular life, rapid progress was made in genetics. **Microbial genetics** studies the mechanisms by which microorganisms inherit traits, and **molecular biology** looks at how genetic information is carried in molecules of DNA.

In the 1940s, George W. Beadle and Edward L. Tatum demonstrated the relationship between genes and enzymes; DNA was established as the hereditary material by Oswald Avery, Colin MacLeod, and Maclyn McCarty. Joshua Lederberg and Edward L. Tatum discovered that genetic material could be transferred from one bacterium to another by a process called conjugation. Then in the 1950s, James Watson and Francis Crick proposed a model for the structure and replication of DNA. In the early 1960s, François Jacob and Jacques Monod discovered messenger RNA (ribonucleic acid), a chemical involved in protein synthesis, and later they made the first major discoveries about the regulation of gene function in bacteria. During the same period, scientists were able to break the genetic code and thus understand how the information for protein synthesis in messenger RNA is translated into the amino acid sequence for making proteins.

Although molecular genetics encompasses all organisms, much of our knowledge of how genes determine specific traits has been revealed through experiments with bacteria. Unicellular organisms, primarily bacteria, have several advantages for genetic and biochemical research. Bacteria are less complex than plants and animals, and the life cycles of many bacteria last less than an hour, so scientists can cultivate very large numbers of bacteria for study in a relatively short time.

CHECK YOUR UNDERSTANDING

- **1-12** What was Ehrlich's "magic bullet"?
- **1-13** Define *bacteriology*, *mycology*, *parasitology*, *immunology*, and *virology*.

The Third Golden Age of Microbiology

Stephen Jay Gould said we now live in the "age of bacteria." The bacteria aren't new, but our understanding of their importance to the Earth and to our health is. New DNA-sequencing tools and computers allow investigators to study all the DNA in an organism, helping them to identify genes and their functions. Moreover, through **genomics**, the study of all of an organism's genes, scientists are able to classify bacteria and fungi according to their genetic relationships with other bacteria, fungi, and protozoa. These microorganisms were originally classified according to a limited number of visible characteristics. The tools of genomics are being used to identify microbes in the ocean, on leaves, and on humans, many of which are newly discovered and haven't been grown in laboratories. After microbes are discovered, the next step is to find out what they are doing. The Exploring the Microbiome boxes throughout this textbook give examples of this research.

Microorganisms can now be genetically modified to manufacture large amounts of human hormones and other urgently needed medical substances. This development had its origins in the late 1960s, when Paul Berg showed that fragments of human or animal DNA (genes) that code for important proteins can be attached to bacterial DNA. The resulting hybrid was the first example of **recombinant DNA**. **Recombinant DNA (rDNA) technology** inserts recombinant DNA into bacteria (or other microbes) to make large quantities of a desired protein. The development of recombinant DNA technology has revolutionized research and practical applications in all areas of microbiology.

CHECK YOUR UNDERSTANDING

- **1-14** Differentiate microbial genetics, molecular biology, and genomics.

Microbes and Human Welfare

LEARNING OBJECTIVES

1-15 List at least four beneficial activities of microorganisms.

1-16 Name two examples of biotechnology that use recombinant DNA technology and two examples that do not.

As mentioned earlier, only a minority of all microorganisms are pathogenic. Microbes that cause food spoilage—such as soft spots on fruits and vegetables, decomposition of meats, and rancidity of fats and oils—are also a minority. The vast majority of microbes benefit humans, other animals, and plants in many ways. For example, microbes produce methane and ethanol that can be used as alternative fuels to generate electricity and power vehicles. Biotechnology companies are using bacterial enzymes to break down plant cellulose so that yeast can metabolize the resulting simple sugars and produce ethanol. The following sections outline some of these beneficial activities. In later chapters, we will discuss these activities in greater detail.

ASM: Microbes are essential for life as we know it and the processes that support life.

ASM: Humans utilize and harness microorganisms and their products.

Recycling Vital Elements

Discoveries made by two microbiologists in the 1880s have formed the basis for today's understanding of the biogeochemical cycles that support life on Earth. Martinus Beijerinck and Sergei Winogradsky were the first to show how bacteria help recycle vital elements between the soil and the atmosphere. **Microbial ecology**, the study of the relationship between microorganisms and their environment, originated with the work of these scientists. Today, microbial ecology has branched out and includes the study of how microbial populations interact with plants and animals in various environments. Among the concerns of microbial ecologists are water pollution and toxic chemicals in the environment.

The chemical elements carbon, nitrogen, oxygen, sulfur, and phosphorus are essential for life and abundant, but not necessarily in forms that organisms can use. Microorganisms are primarily responsible for converting these elements into forms that plants and animals can use. Microorganisms, especially bacteria and fungi, return carbon dioxide to the atmosphere when they decompose organic wastes and dead plants and animals. Algae, cyanobacteria, and higher plants use the carbon dioxide during photosynthesis to produce carbohydrates for animals, fungi, and bacteria. Nitrogen is abundant in the atmosphere but in that form is not usable by plants and animals. Only bacteria can naturally convert atmospheric nitrogen to a form available to plants and animals.

Sewage Treatment: Using Microbes to Recycle Water

Our society's growing awareness of the need to preserve the environment has made people more conscious of the responsibility to recycle precious water and prevent pollution of rivers and oceans. One major pollutant is sewage, which consists of human excrement, wastewater, industrial wastes, and surface runoff. Sewage is about 99.9% water, with a few hundredths of 1% suspended solids. The remainder is a variety of dissolved materials.

Sewage treatment plants remove the undesirable materials and harmful microorganisms. Treatments combine various physical processes with the action of beneficial microbes. Large solids such as paper, wood, glass, gravel, and plastic are removed from sewage; left behind are liquid and organic materials that bacteria convert into such by-products as carbon dioxide, nitrates, phosphates, sulfates, ammonia, hydrogen sulfide, and methane. (We will discuss sewage treatment in detail in Chapter 27.)

Bioremediation: Using Microbes to Clean Up Pollutants

In 1988, scientists began using microbes to clean up pollutants and toxic wastes produced by various industrial processes. For example, some bacteria can actually use pollutants as energy sources; others produce enzymes that break down toxins into less harmful substances. By using bacteria in these ways—a process known as **bioremediation**—toxins can be removed from underground wells, chemical spills, toxic waste sites, and oil spills, such as the massive oil spill from a British Petroleum offshore drilling rig in the Gulf of Mexico in 2010. In addition, bacterial enzymes are used in drain cleaners to remove clogs without adding harmful chemicals to the environment. In some cases, microorganisms indigenous to the environment are used; in others, genetically modified microbes are used. Among the most commonly used microbes are certain species of bacteria of the genera *Pseudomonas* and *Bacillus*. *Bacillus* enzymes are also used in household detergents to remove spots from clothing.

Insect Pest Control by Microorganisms

Besides spreading diseases, insects can cause devastating crop damage. Insect pest control is therefore important for both agriculture and the prevention of human disease.

The bacterium *Bacillus thuringiensis* (ther-IN-jē-en-sis) has been used extensively in the United States to control such pests as alfalfa caterpillars, bollworms, corn borers, cabbageworms, tobacco budworms, and fruit tree leaf rollers. It is incorporated into a dusting powder that is applied to the crops these insects eat. The bacteria produce protein crystals that are toxic to the digestive systems of the insects. The toxin gene also has been inserted into some plants to make them insect resistant.

By using microbial rather than chemical insect control, farmers can avoid harming the environment. In contrast, many chemical insecticides, such as DDT, remain in the soil as toxic pollutants and are eventually incorporated into the food chain.

Biotechnology and Recombinant DNA Technology

Earlier we touched on the commercial use of microorganisms to produce some common foods and chemicals. Such practical applications of microbiology are called **biotechnology**. Although biotechnology has been used in some form for centuries, techniques have become much more sophisticated in the past few decades. In the last several years, biotechnology has undergone a revolution through the advent of recombinant DNA technology to expand the potential of bacteria, viruses, and yeast and other fungi as miniature biochemical factories. Cultured plant and animal cells, as well as intact plants and animals, are also used as recombinant cells and organisms.

The applications of recombinant DNA technology are increasing with each passing year. Recombinant DNA techniques have been used thus far to produce a number of natural proteins, vaccines, and enzymes. Such substances have great potential for medical use; some of them are described in Table 9.2 on page 256.

A very exciting and important outcome of recombinant DNA techniques is **gene therapy**—inserting a missing gene or replacing a defective one in human cells. This technique uses a harmless virus to carry the missing or new gene into certain host cells, where the gene is picked up and inserted into the appropriate chromosome. Since 1990, gene therapy has been used to treat patients with adenosine deaminase (ADA) deficiency, a cause of severe combined immunodeficiency disease (SCID), in which cells of the immune system are inactive or missing; Duchenne's muscular dystrophy, a muscle-destroying disease; cystic fibrosis, a disease of the secreting portions of the respiratory passages, pancreas, salivary glands, and sweat glands; and LDL-receptor deficiency, a condition in which low-density lipoprotein (LDL) receptors are defective and LDL cannot enter cells. The LDL remains in the blood in high concentrations and leads to fatty plaque formation in blood vessels, increasing the risk of atherosclerosis and coronary heart disease. Results of gene therapy are still being evaluated. Other genetic diseases may also be treatable by gene therapy in the future, including hemophilia, an inability of the blood to clot normally; diabetes, elevated blood sugar levels; and sickle cell disease, caused by an abnormal kind of hemoglobin.

Beyond medical applications, recombinant DNA techniques have also been applied to agriculture. For example, genetically altered strains of bacteria have been developed to protect fruit against frost damage, and bacteria are being modified to control insects that damage crops. Recombinant DNA has also been used to improve the appearance, flavor, and shelf life of fruits and vegetables. Potential agricultural uses of recombinant DNA include drought resistance, resistance to insects and microbial diseases, and increased temperature tolerance in crops.

CHECK YOUR UNDERSTANDING

- ✓ **1-15** Name two beneficial uses of bacteria.
- ✓ **1-16** Differentiate biotechnology from recombinant DNA technology.

Microbes and Human Disease

LEARNING OBJECTIVES

1-17 Define *resistance*.

1-18 Define *biofilm*.

1-19 Define *emerging infectious disease*.

When is a microbe a welcome part of a healthy human, and when is it a harbinger of disease? The distinction between health and disease is in large part a balance between the natural defenses of the body and the disease-producing properties of microorganisms. Whether our bodies overcome the offensive tactics of a particular microbe depends on our **resistance**—the ability to ward off diseases. Important resistance is provided by the barrier of the skin, mucous membranes, cilia, stomach acid, and antimicrobial chemicals such as interferons. Microbes can be destroyed by white blood cells, by the inflammatory response, by fever, and by specific responses of our immune system. Sometimes, when our natural defenses are not strong enough to overcome an invader, they have to be supplemented by antibiotics or other drugs.

Biofilms

In nature, microorganisms may exist as single cells that float or swim independently in a liquid, or they may attach to each other and/or some usually solid surface. This latter mode of behavior is called a **biofilm**, a complex aggregation of microbes. The slime covering a rock in a lake is a biofilm. Use your tongue to feel the biofilm on your teeth. Biofilms can be beneficial. They protect your mucous membranes from harmful microbes, and biofilms in lakes are an important food for aquatic animals. Biofilms can also be harmful. They can clog water pipes, and on medical implants such as joint prostheses and catheters (Figure 1.10), they can cause such infections as endocarditis (inflammation of the heart). Bacteria in biofilms are often resistant to antibiotics because the biofilm offers a protective barrier. Biofilms will be discussed in Chapter 6.

CLINICAL CASE

"Staph" is the common name for *Staphylococcus aureus* bacteria, which are carried on the skin of about 30% of the human population. Although Andrea is diligent about taking her antibiotic as prescribed, she doesn't seem to be improving. After 3 days, the lesion on her wrist is even larger than before and is now draining yellow pus. Andrea also develops a fever. Her mother insists that she call her doctor to tell him about the latest developments.

Why does Andrea's infection persist after treatment?

3 | 16 | 18 | 19

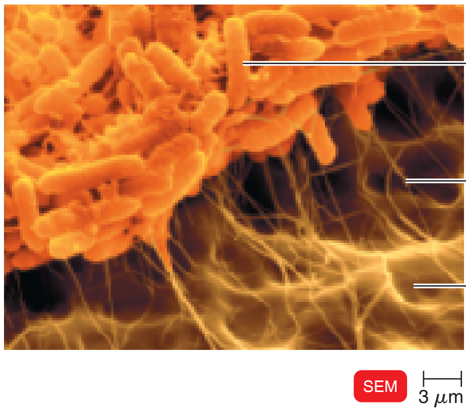


Figure 1.10 Biofilm on a piece of plastic. Bacteria stick to solid surfaces, forming a slimy layer. The filaments in the photo may be capsular material. Bacteria that break away from biofilms on medical implants can cause infections.

Q How does a biofilm's protective barrier make it resistant to antibiotics?

Infectious Diseases

An **infectious disease** is a disease in which pathogens invade a susceptible host, such as a human or an animal. In the process, the pathogen carries out at least part of its life cycle inside the host, and disease frequently results. By the end of World War II, many people believed that infectious diseases were under control. They thought malaria would be eradicated through the use of the insecticide DDT to kill mosquitoes, that a vaccine would prevent pertussis, and that improved sanitation measures would help prevent cholera transmission. Expectations did not match reality: Malaria is far from eliminated; since 1986, local outbreaks have been identified in New Jersey, California, Florida, New York, and Texas, and the disease infects over 200 million people worldwide. Pertussis is not eliminated but vaccination has decreased the incidence from 200,000 cases to 12,000 cases annually. And cholera outbreaks still occur in less-developed parts of the world.

Emerging Infectious Diseases

These recent outbreaks point to the fact that infectious diseases are not disappearing, but rather seem to be reemerging and increasing. In addition, a number of new diseases—**emerging infectious diseases (EIDs)**—have cropped up in recent years. These are diseases that are new or changing and are increasing or have the potential to increase in incidence in the near future. Some of the factors that have contributed to the development of EIDs are evolutionary changes in existing organisms (e.g., *Vibrio cholerae*; VIB-rē-ō KOL-er-ī) and the spread of known diseases to new geographic regions or populations by modern transportation. Some EIDs are the result of increased human exposure to new, unusual infectious agents in areas that are undergoing ecologic changes such as deforestation and construction (e.g., Venezuelan hemorrhagic virus). Some EIDs are due to changes in the pathogen's ecology. For example, Powassan virus (POWV) was transmitted by ticks that don't usually bite humans. However, the virus recently became established in the same deer ticks that transmit Lyme disease. An increasing number of incidents in recent years highlights the extent of the problem.

Zika Virus Disease

In 2015, the world became aware of Zika virus disease. Zika virus is spread by the bite of an infected *Aedes* mosquito; sexual transmission has also occurred. Zika is a mild disease usually presenting with fever, rash, and joint pain. However, Zika infection during pregnancy can cause severe birth defects in a fetus. The virus was discovered in 1947 in the Zika Forest of Uganda, but until 2007, only 14 cases of Zika virus disease were known. The first Zika epidemic occurred on the island of Yap in Micronesia in 2007, when 73% of the people became infected. Between 2013 and 2015, Zika epidemics occurred in French Polynesia and Brazil. Over 1600 cases of Zika have occurred in the United States. Until mid-2016, they were all acquired during travel to endemic areas (except one laboratory-acquired infection). However, the first U.S. cases of transmission by mosquitoes occurred in Florida during the summer of 2016.

Middle East Respiratory Syndrome (MERS)

Since 2014, there have been 1800 confirmed human cases and 630 deaths caused by a new virus called **Middle East respiratory syndrome coronavirus (MERS-CoV)**. The virus belongs to the same family that causes illnesses from the common cold to severe acute respiratory syndrome (SARS). Because the first reported cases were linked to the Middle East, this latest emerging infectious disease is called **Middle East respiratory syndrome (MERS)**. MERS has spread to Europe and Asia, and two travel-associated cases occurred in the United States in 2014.

Influenza

H1N1 influenza (flu), also known as *swine flu*, is a type of influenza caused by a new virus called *influenza H1N1*. H1N1 was first detected in the United States in 2009, and that same year WHO declared H1N1 flu to be a *pandemic disease* (a disease that affects large numbers of individuals in a short period of time and occurs worldwide).

Avian influenza A (H5N1), or **bird flu**, caught the attention of the public in 2003, when it killed millions of poultry and 24 people in southeast Asia. Avian influenza viruses occur in birds worldwide. In 2013, a different avian influenza, H7N9, sickened 131 people in China. In 2015, two cases of H7N9 were reported in Canada.

Influenza A viruses are found in many different animals, including ducks, chickens, pigs, whales, horses, and seals. Normally, each subtype of influenza A virus is specific to certain species. However, influenza A viruses normally seen in one species sometimes can cross over and cause illness in another species, and all subtypes of influenza A virus can infect pigs. Although it is unusual for people to get influenza infections directly from animals, sporadic human infections and outbreaks caused by certain avian influenza A viruses and pig influenza viruses have been reported. Fortunately, the virus has not yet evolved to be transmitted successfully among humans.

Human infections with avian influenza viruses detected since 1997 have not resulted in sustained human-to-human transmission. However, because influenza viruses have the potential to change and gain the ability to spread easily between people, monitoring for human infection and person-to-person transmission is important (see the box in Chapter 13 on page 367).

Antibiotic-Resistant Infections

Antibiotics are critical in treating bacterial infections. However, years of overuse and misuse of these drugs have created environments in which antibiotic-resistant bacteria thrive. Random mutations in bacterial genes can make a bacterium resistant to an antibiotic. In the presence of that antibiotic, this bacterium has an advantage over other, susceptible bacteria and is able to proliferate. Antibiotic-resistant bacteria have become a global health crisis.

Staphylococcus aureus causes a wide range of human infections from pimples and boils to pneumonia, food poisoning, and surgical wound infections, and it is a significant cause of hospital-associated infections. After penicillin's initial success in treating *S. aureus* infection, penicillin-resistant *S. aureus* became a major threat in hospitals in the 1950s, requiring the use of methicillin. In the 1980s, **methicillin-resistant *S. aureus***, called **MRSA**, emerged and became endemic in many hospitals, leading to increasing use of vancomycin. In the late 1990s, *S. aureus* infections that were less sensitive to vancomycin (**vancomycin-intermediate *S. aureus***, or **VISA**) were reported. In 2002, the first infection caused by **vancomycin-resistant *S. aureus* (VRSA)** in a patient in the United States was reported.

In 2010, the World Health Organization (WHO) reported that in Asia and eastern Europe, about 35% of all individuals with tuberculosis (TB) had the multidrug-resistant form of the disease (MDR-TB). Multidrug-resistant TB is caused by bacteria that are resistant to at least the antibiotics isoniazid and rifampicin, the most effective drugs against tuberculosis.

The antibacterial substances added to various household cleaning products inhibit bacterial growth when used correctly. However, wiping every household surface with these antibacterial agents creates an environment in which the resistant bacteria survive. Unfortunately, when you really need to disinfect your homes and hands—for example, when a family member comes home from a hospital and is still vulnerable to infection—you may encounter mainly resistant bacteria.

Routine housecleaning and handwashing are necessary, but standard soaps and detergents (without added antibacterials) are fine for these tasks. In addition, quickly evaporating chemicals, such as chlorine bleach, alcohol, ammonia, and hydrogen peroxide, remove potentially pathogenic bacteria but do not leave residues that encourage the growth of resistant bacteria.

In 2004, emergence of a new epidemic strain of *Clostridium difficile* (klo-STRID-ē-um DIF-fi-sē-il) was reported. The epidemic strain produces more toxins than others and is more resistant to antibiotics. In the United States, *C. difficile* infections kill nearly 29,000 people a year. Nearly all of the *C. difficile* infections occur in health care settings, where the infection is frequently transmitted between patients via health care personnel whose hands are contaminated after contact with infected patients or their surrounding environment.

Ebola Virus Disease

First detected in 1995, **Ebola virus disease** causes fever, hemorrhaging, and blood clotting in vessels. In the first outbreak, 315 people in the Democratic Republic of Congo contracted the disease, and over 75% of them died. The epidemic was controlled through use of protective equipment and educational measures in the community. Close personal contact with infectious blood or other body fluids or tissue (see Chapter 23) leads to human-to-human transmission.

In 2014, a new outbreak in West Africa occurred. The countries Sierra Leone, Guinea, and Liberia experienced the worst

CLINICAL CASE

The *S. aureus* bacterium responsible for Andrea's infection is resistant to the β-lactam antibiotic prescribed by Andrea's doctor. Concerned about what his patient is telling him, Andrea's doctor calls the local hospital to let them know he is sending a patient over. In the emergency department, a nurse swabs Andrea's wound and sends it to the hospital lab for culturing. The culture shows that Andrea's infection is caused by methicillin-resistant *Staphylococcus aureus* (MRSA). MRSA produces β-lactamase, an enzyme that destroys β-lactam antibiotics. The attending physician surgically drains the pus from the sore on Andrea's wrist.

How does antibiotic resistance develop?

3 | 16 | **18** | 19

CLINICAL CASE

Mutations develop randomly in bacteria; some mutations are lethal, some have no effect, and some may be beneficial. Once these mutations develop, the offspring of the mutated parent cell also carry the same mutation. Because they have an advantage in the presence of the antibiotic, bacteria that are resistant to antibiotics soon outnumber those that are susceptible to antibiotic therapy. The widespread use of antibiotics selectively allows the resistant bacteria to grow, whereas the susceptible bacteria are killed. Eventually, almost the entire population of bacteria is resistant to the antibiotic.

The emergency department physician prescribes a different antibiotic, vancomycin, which will kill the MRSA in Andrea's wrist. She also explains to Andrea what MRSA is and why it's important they find out where Andrea acquired the potentially lethal bacteria.

What can the emergency department physician tell Andrea about MRSA?

3 | 16 | 18 | **19**

impacts, with over 28,000 people infected over the next two years. Over one-third of those infected died. This time, a small number of health care workers from the United States and Europe who had been working with Ebola patients in Africa brought the disease back with them to their home countries, sparking fears that the disease would gain a foothold elsewhere in the world.

Marburg Virus

Recorded cases of **Marburg virus**, another hemorrhagic fever virus, are rare. The first cases were laboratory workers in Europe who handled African green monkeys from Uganda. Thirteen outbreaks were identified in Africa between 1975 and 2016, involving 1 to 252 people, with 57% mortality. African fruit bats are the natural reservoir for the Marburg virus, and microbiologists suspect that bats are also the reservoir for Ebola.

Just as microbiological techniques helped researchers in the fight against syphilis and smallpox, they will help scientists discover the causes of new emerging infectious diseases in the twenty-first century. Undoubtedly there will be new diseases. *Ebolavirus* and *Influenzavirus* are examples of viruses that may be changing their abilities to infect different host species. Emerging infectious diseases will be discussed further in Chapter 14 on page 411.

Infectious diseases may reemerge because of antibiotic resistance and through the use of microorganisms as weapons. (See the Clinical Focus box in Chapter 26 on page 771.) The breakdown of public health measures for previously controlled infections has resulted in unexpected cases of tuberculosis, whooping cough, and measles (see Chapter 24).

CHECK YOUR UNDERSTANDING

- **1-17** Differentiate normal microbiota and infectious disease.
- **1-18** Why are biofilms important?
- **1-19** What factors contribute to the emergence of an infectious disease?

* * *

The diseases we have mentioned are caused by viruses, bacteria, and protozoa—types of microorganisms. This book introduces you to the enormous variety of microscopic organisms. It shows you how microbiologists use specific techniques and procedures to study the microbes that cause such diseases as AIDS and diarrhea—and diseases that have yet to be discovered. You will also learn how the body responds to microbial infection and how certain drugs combat microbial diseases. Finally, you will learn about the many beneficial roles that microbes play in the world around us.

CLINICAL CASE Resolved

The first MRSA was healthcare–associated MRSA (HA-MRSA), transmitted between staff and patients in health care settings. In the 1990s, infections by a genetically different strain, community-associated MRSA (CA-MRSA), emerged as a major cause of skin disease in the United States. CA-MRSA enters skin abrasions from environmental surfaces or other people. Andrea has never been hospitalized before now, so they are able to rule out the hospital as the source of infection. Her college courses are all online, so she didn't contract MRSA at the university, either. The local health department sends someone to her family home to swab for the bacteria there.

MRSA is isolated from Andrea's living room sofa, but how did it get there? A representative from the health department, knowing that clusters of CA-MRSA infections have been seen among athletes, suggests swabbing the mats used by the gymnasts at the school Andrea's sister attends. The cultures come back positive for MRSA. Andrea's sister, although not infected, transferred the bacteria from her skin to the sofa, where Andrea laid her arm. (A person can carry MRSA on the skin without becoming infected.) The bacteria entered through a scratch on Andrea's wrist.

3 | 16 | 18 | **19**

Study Outline

Microbes in Our Lives (pp. 2–3)

1. Living things too small to be seen with the unaided eye are called microorganisms.
2. Microorganisms are important in maintaining Earth's ecological balance.
3. Everyone has microorganisms in and on the body; these make up the normal microbiota or human microbiome. The normal microbiota are needed to maintain good health.
4. Some microorganisms are used to produce foods and chemicals.
5. Some microorganisms cause disease.

Naming and Classifying Microorganisms (pp. 4–6)

Nomenclature (p. 4)

1. In a nomenclature system designed by Carolus Linnaeus (1735), each living organism is assigned two names.
2. The two names consist of a genus and a specific epithet, both of which are underlined or italicized.

Types of Microorganisms (pp. 4–6)

3. Bacteria are unicellular organisms. Because they have no nucleus, the cells are described as prokaryotic.
4. Most bacteria have a peptidoglycan cell wall; they divide by binary fission, and they may possess flagella.
5. Bacteria can use a wide range of chemical substances for their nutrition.
6. Archaea consist of prokaryotic cells; they lack peptidoglycan in their cell walls.
7. Archaea include methanogens, extreme halophiles, and extreme thermophiles.
8. Fungi (mushrooms, molds, and yeasts) have eukaryotic cells (cells with a true nucleus). Most fungi are multicellular.
9. Fungi obtain nutrients by absorbing organic material from their environment.
10. Protozoa are unicellular eukaryotes.
11. Protozoa obtain nourishment by absorption or ingestion through specialized structures.
12. Algae are unicellular or multicellular eukaryotes that obtain nourishment by photosynthesis.
13. Algae produce oxygen and carbohydrates that are used by other organisms.
14. Viruses are noncellular entities that are parasites of cells.
15. Viruses consist of a nucleic acid core (DNA or RNA) surrounded by a protein coat. An envelope may surround the coat.
16. The principal groups of multicellular animal parasites are flatworms and roundworms, collectively called helminths.
17. The microscopic stages in the life cycle of helminths are identified by traditional microbiological procedures.

Classification of Microorganisms (p. 6)

18. All organisms are classified into one of three domains: Bacteria, Archaea, and Eukarya. Eukarya include protists, fungi, plants, and animals.

A Brief History of Microbiology (pp. 6–14)

The First Observations (pp. 6–7)

1. Hooke's observations laid the groundwork for development of the cell theory, the concept that all living things are composed of cells.
2. Anton van Leeuwenhoek, using a simple microscope, was the first to observe microorganisms (1673).

The Debate over Spontaneous Generation (pp. 7–9)

3. Until the mid-1880s, many people believed in spontaneous generation, the idea that living organisms could arise from nonliving matter.
4. Francesco Redi demonstrated that maggots appear on decaying meat only when flies are able to lay eggs on the meat (1668).
5. John Needham claimed that microorganisms could arise spontaneously from heated nutrient broth (1745).
6. Lazzaro Spallanzani repeated Needham's experiments and suggested that Needham's results were due to microorganisms in the air entering his broth (1765).
7. Rudolf Virchow introduced the concept of biogenesis: living cells can arise only from preexisting cells (1858).
8. Louis Pasteur demonstrated that microorganisms are in the air everywhere and offered proof of biogenesis (1861).
9. Pasteur's discoveries led to the development of aseptic techniques used in laboratory and medical procedures to prevent contamination by microorganisms.

The First Golden Age of Microbiology (pp. 9–11)

10. The science of microbiology advanced rapidly between 1857 and 1914.
11. Pasteur found that yeasts ferment sugars to alcohol and that bacteria can oxidize the alcohol to acetic acid.
12. A heating process called pasteurization is used to kill bacteria in some alcoholic beverages and milk.
13. Agostino Bassi (1835) and Pasteur (1865) showed a causal relationship between microorganisms and disease.
14. Joseph Lister introduced the use of a disinfectant to clean surgical wounds in order to control infections in humans (1860s).
15. Robert Koch proved that microorganisms cause disease. He used a sequence of procedures, now called Koch's postulates (1876), that are used today to prove that a particular microorganism causes a particular disease.
16. In 1798, Edward Jenner demonstrated that inoculation with cowpox material provides humans with immunity to smallpox.
17. About 1880, Pasteur discovered that avirulent bacteria could be used as a vaccine for fowl cholera.
18. Modern vaccines are prepared from living avirulent microorganisms or killed pathogens, from isolated components of pathogens, and by recombinant DNA techniques.

The Second Golden Age of Microbiology (pp. 11–14)

19. The Second Golden Age began with the discovery of penicillin's effectiveness against infections.

20. Two types of chemotherapeutic agents are synthetic drugs (chemically prepared in the laboratory) and antibiotics (substances produced naturally by bacteria and fungi that inhibit the growth of bacteria).
21. Paul Ehrlich introduced an arsenic-containing chemical called salvarsan to treat syphilis (1910).
22. Alexander Fleming observed that the *Penicillium* fungus inhibited the growth of a bacterial culture. He named the active ingredient penicillin (1928).
23. Researchers are tackling the problem of drug-resistant microbes.
24. Bacteriology is the study of bacteria, mycology is the study of fungi, and parasitology is the study of parasitic protozoa and worms.
25. The study of AIDS and analysis of the action of interferons are among the current research interests in immunology.
26. New techniques in molecular biology and electron microscopy have provided tools for advancing our knowledge of virology.
27. The development of recombinant DNA technology has helped advance all areas of microbiology.

The Third Golden Age of Microbiology (p. 14)

28. Microbiologists are using genomics, the study of all of an organism's genes, to study microbiomes in different environments.

Microbes and Human Welfare (pp. 14–16)

1. Microorganisms degrade dead plants and animals and recycle chemical elements to be used by living plants and animals.
2. Bacteria are used to decompose organic matter in sewage.
3. Bioremediation processes use bacteria to clean up toxic wastes.
4. Bacteria that cause diseases in insects are being used as biological controls of insect pests. Biological controls are specific for the pest and do not harm the environment.
5. Using microbes to make products such as foods and chemicals is called biotechnology.
6. Using recombinant DNA, bacteria can produce important substances such as proteins, vaccines, and enzymes.
7. In gene therapy, viruses are used to carry replacements for defective or missing genes into human cells.
8. Genetically modified bacteria are used in agriculture to protect plants from frost and insects and to improve the shelf life of produce.

Microbes and Human Disease (pp. 16–19)

1. The disease-producing properties of a species of microbe and the host's resistance are important factors in determining whether a person will contract a disease.
2. Bacterial communities that form slimy layers on surfaces are called biofilms.
3. An infectious disease is one in which pathogens invade a susceptible host.
4. An emerging infectious disease (EID) is a new or changing disease showing an increase in incidence in the recent past or a potential to increase in the near future.

Study Questions

For answers to the Knowledge and Comprehension questions, turn to the Answers tab at the back of the textbook.

Knowledge and Comprehension

Review

1. How did the idea of spontaneous generation come about?
2. Briefly state the role microorganisms play in each of the following:
   a. biological control of pests
   b. recycling of elements
   c. normal microbiota
   d. sewage treatment
   e. human insulin production
   f. vaccine production
   g. biofilms
3. Into which field of microbiology would the following scientists best fit?

Researcher Who	Field
____ **a.** Studies biodegradation of toxic wastes	**1.** Biotechnology
____ **b.** Studies the causative agent of Ebola virus disease	**2.** Immunology
____ **c.** Studies the production of human proteins by bacteria	**3.** Microbial ecology
____ **d.** Studies the symptoms of AIDS	**4.** Microbial genetics
____ **e.** Studies the production of toxin by *E. coli*	**5.** Microbial physiology
____ **f.** Studies biodegradation of pollutants	**6.** Molecular biology
____ **g.** Develops gene therapy for a disease	**7.** Mycology
____ **h.** Studies the fungus *Candida albicans*	**8.** Virology

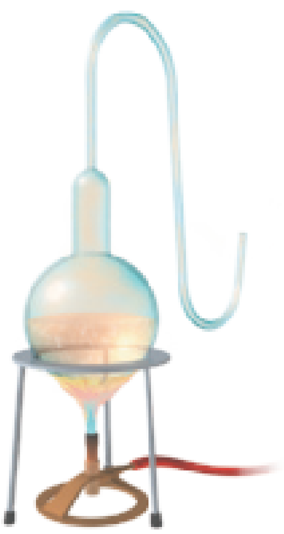
4. Match the microorganisms in column A to their descriptions in column B.

Column A	Column B
____ **a.** Archaea	**1.** Not composed of cells
____ **b.** Algae	**2.** Cell wall made of chitin
____ **c.** Bacteria	**3.** Cell wall made of peptidoglycan
____ **d.** Fungi	**4.** Cell wall made of cellulose; photosynthetic
____ **e.** Helminths	**5.** Unicellular, complex cell structure lacking a cell wall
____ **f.** Protozoa	**6.** Multicellular animals
____ **g.** Viruses	**7.** Prokaryote without peptidoglycan cell wall

5. Match the people in column A to their contribution toward the advancement of microbiology, in column B.

Column A	Column B
______ **a.** Avery, MacLeod, and McCarty	**1.** Developed vaccine against smallpox
______ **b.** Beadle and Tatum	**2.** Discovered how DNA controls protein synthesis in a cell
______ **c.** Berg	**3.** Discovered penicillin
______ **d.** Ehrlich	**4.** Discovered that DNA can be transferred from one bacterium to another
______ **e.** Fleming	**5.** Disproved spontaneous generation
______ **f.** Hooke	**6.** First to characterize a virus
______ **g.** Iwanowski	**7.** First to use disinfectants in surgical procedures
______ **h.** Jacob and Monod	**8.** First to observe bacteria
______ **i.** Jenner	**9.** First to observe cells in plant material and name them
______ **j.** Koch	**10.** Observed that viruses are filterable material
______ **k.** Lancefield	**11.** Proved that DNA is the hereditary material
______ **l.** Lederberg and Tatum	**12.** Proved that microorganisms can cause disease
______ **m.** Lister	**13.** Said living cells arise from preexisting living cells
______ **n.** Pasteur	**14.** Showed that genes code for enzymes
______ **o.** Stanley	**15.** Spliced animal DNA to bacterial DNA
______ **p.** van Leeuwenhoek	**16.** Used bacteria to produce acetone
______ **q.** Virchow	**17.** Used the first synthetic chemotherapeutic agent
______ **r.** Weizmann	**18.** Proposed a classification system for streptococci based on antigens in their cell walls

6. It is possible to purchase the following microorganisms in a retail store. Provide a reason for buying each.
   a. *Bacillus thuringiensis*
   b. *Saccharomyces*
7. NAME IT What type of microorganism has a peptidoglycan cell wall, has DNA that is not contained in a nucleus, and has flagella?
8. DRAW IT Show where airborne microbes ended up in Pasteur's experiment.



Multiple Choice

1. Which of the following is a scientific name?
   a. *Mycobacterium tuberculosis*
   b. Tubercle bacillus
2. Which of the following is *not* a characteristic of bacteria?
   a. are prokaryotic
   b. have peptidoglycan cell walls
   c. have the same shape
   d. grow by binary fission
   e. have the ability to move
3. Which of the following is the most important element of Koch's germ theory of disease? The animal shows disease symptoms when
   a. the animal has been in contact with a sick animal.
   b. the animal has a lowered resistance.
   c. a microorganism is observed in the animal.
   d. a microorganism is inoculated into the animal.
   e. microorganisms can be cultured from the animal.
4. Recombinant DNA is
   a. DNA in bacteria.
   b. the study of how genes work.
   c. the DNA resulting when genes of two different organisms are mixed.
   d. the use of bacteria in the production of foods.
   e. the production of proteins by genes.
5. Which of the following statements is the best definition of *biogenesis*?
   a. Nonliving matter gives rise to living organisms.
   b. Living cells can only arise from preexisting cells.
   c. A vital force is necessary for life.
   d. Air is necessary for living organisms.
   e. Microorganisms can be generated from nonliving matter.
6. Which of the following is a beneficial activity of microorganisms?
   a. Some microorganisms are used as food for humans.
   b. Some microorganisms use carbon dioxide.
   c. Some microorganisms provide nitrogen for plant growth.
   d. Some microorganisms are used in sewage treatment processes.
   e. all of the above
7. It has been said that bacteria are essential for the existence of life on Earth. Which of the following is the essential function performed by bacteria?
   a. control insect populations
   b. directly provide food for humans
   c. decompose organic material and recycle elements
   d. cause disease
   e. produce human hormones such as insulin
8. Which of the following is an example of bioremediation?
   a. application of oil-degrading bacteria to an oil spill
   b. application of bacteria to a crop to prevent frost damage
   c. fixation of gaseous nitrogen into usable nitrogen
   d. production by bacteria of a human protein such as interferon
   e. all of the above
9. Spallanzani's conclusion about spontaneous generation was challenged because Antoine Lavoisier had just shown that oxygen was the vital component of air. Which of the following statements is true?
   a. All life requires air.
   b. Only disease-causing organisms require air.
   c. Some microbes do not require air.
   d. Pasteur kept air out of his biogenesis experiments.
   e. Lavoisier was mistaken.

10. Which of the following statements about *E. coli* is *false*?
    - **a.** *E. coli* was the first disease-causing bacterium identified by Koch.
    - **b.** *E. coli* is part of the normal microbiome of humans.
    - **c.** *E. coli* is beneficial in human intestines.
    - **d.** *E. coli* gets nutrients from intestinal contents.
    - **e.** None of the above; all the statements are true.

Analysis

1. How did the theory of biogenesis lead the way for the germ theory of disease?
2. Even though the germ theory of disease was not demonstrated until 1876, why did Semmelweis (1840) and Lister (1867) argue for the use of aseptic techniques?
3. The genus name of a bacterium is "erwinia," and the specific epithet is "amylovora." Write the scientific name of this organism correctly. Using this name as an example, explain how scientific names are chosen.
4. Find at least three supermarket products made by microorganisms. (*Hint:* The label will state the scientific name of the organism or include the word *culture*, *fermented*, or *brewed*.)
5. In the 1960s, many physicians and the public believed that infectious diseases were retreating and would be fully conquered. Discuss why this didn't happen. Is it possible?

Clinical Applications and Evaluation

1. The prevalence of arthritis in the United States is 1 in 100,000 children. However, 1 in 10 children in Lyme, Connecticut, developed arthritis between June and September 1973. Allen Steere, a rheumatologist at Yale University, investigated the cases in Lyme and found that 25% of the patients remembered having a skin rash during their arthritic episode and that the disease was treatable with penicillin. Steere concluded that this was a new infectious disease and did not have an environmental, genetic, or immunologic cause.
    - **a.** What was the factor that caused Steere to reach his conclusion?
    - **b.** What is the disease?
    - **c.** Why was the disease more prevalent between June and September?
2. In 1864, Lister observed that patients recovered completely from simple fractures but that compound fractures had "disastrous consequences." He knew that the application of phenol (carbolic acid) to fields in the town of Carlisle prevented cattle disease. Lister treated compound fractures with phenol, and his patients recovered without complications. How was Lister influenced by Pasteur's work? Why was Koch's work still needed?
3. Discuss whether antibacterial soaps and detergents should be used in the home.