

## 22.4 Bacterial Diseases in Humans

*By the end of this section, you will be able to do the following:*

- Identify bacterial diseases that caused historically important plagues and epidemics
- Describe the link between biofilms and foodborne diseases
- Explain how overuse of antibiotics may be creating “super bugs”
- Explain the importance of MRSA with respect to the problems of antibiotic resistance

To a prokaryote, humans may be just another housing opportunity. Unfortunately, the tenancy of some species can have harmful effects and cause disease. Bacteria or other infectious agents that cause harm to their human hosts are called **pathogens**. Devastating pathogen-borne diseases and plagues, both viral and bacterial in nature, have affected humans and their ancestors for millions of years. The true cause of these diseases was not understood until modern scientific thought developed, and many people thought that diseases were a “spiritual punishment.” Only within the past several centuries have people understood that staying away from afflicted persons, disposing of the corpses and personal belongings of victims of illness, and sanitation practices reduced their own chances of getting sick.

Epidemiologists study how diseases are transmitted and how they affect a population. Often, they must follow the course of an **epidemic**—a disease that occurs in an unusually high number of individuals in a population at the same time. In contrast, a **pandemic** is a widespread, and usually worldwide, epidemic. An **endemic disease** is a disease that is always present, usually at low incidence, in a population.

### Long History of Bacterial Disease

There are records about infectious diseases as far back as 3000 B.C. A number of significant pandemics caused by bacteria have been documented over several hundred years. Some of the most memorable pandemics led to the decline of cities and entire nations.

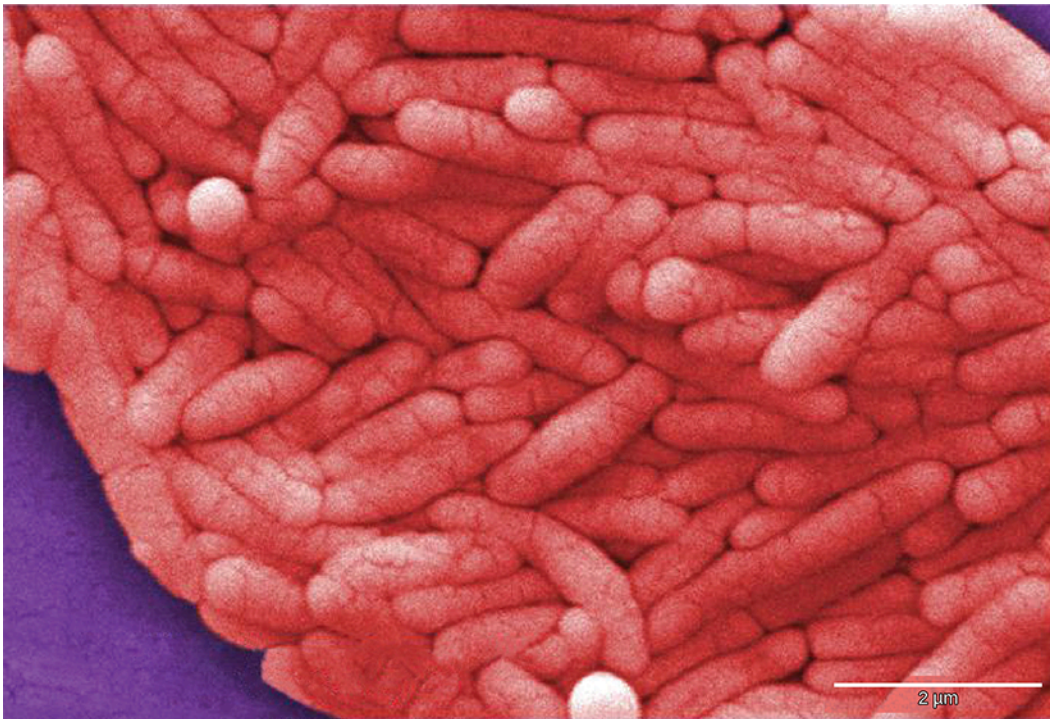
In the 21<sup>st</sup> century, infectious diseases remain among the leading causes of death worldwide, despite advances made in medical research and treatments in recent decades. A disease *spreads* when the pathogen that causes it is passed from one person to another. For a pathogen to cause disease, it must be able to reproduce in the host’s body and damage the host in some way.

### The Plague of Athens

In 430 B.C., the Plague of Athens killed one-quarter of the Athenian troops who were fighting in the great Peloponnesian War and weakened Athens’s dominance and power. The plague impacted people living in overcrowded Athens as well as troops aboard ships that had to return to Athens. The source of the plague may have been identified recently when researchers from the University of Athens were able to use DNA from teeth recovered from a mass grave. The scientists identified nucleotide sequences from a pathogenic bacterium, *Salmonella enterica* serovar Typhi (Figure 22.20), which causes *typhoid fever*.<sup>3</sup> This disease is commonly seen in overcrowded areas and has caused epidemics throughout recorded history.

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<sup>3</sup>Papagrigoriakis MJ, Synodinos PN, and Yapijakis C. Ancient typhoid epidemic reveals possible ancestral strain of *Salmonella enterica* serovar Typhi. *Infect Genet Evol* 7 (2007): 126–7, Epub 2006 Jun.

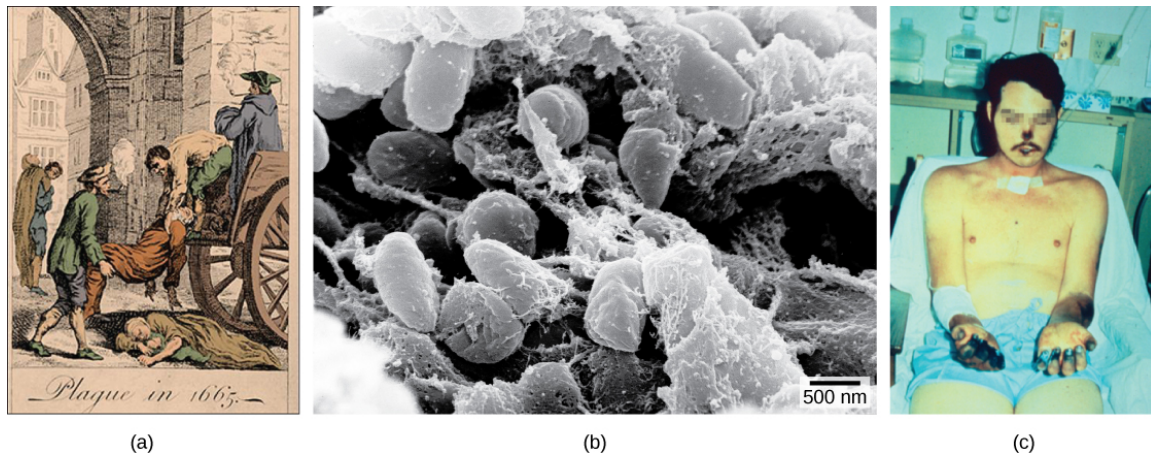


**Figure 22.20** *Salmonella enterica*. *Salmonella enterica* serovar Typhi, the causative agent of Typhoid fever, is a Gram-negative, rod-shaped gamma proteobacterium. Typhoid fever, which is spread through feces, causes intestinal hemorrhage, high fever, delirium, and dehydration. Today, between 16 and 33 million cases of this re-emerging disease occur annually, resulting in over 200,000 deaths. Carriers of the disease can be asymptomatic. In a famous case in the early 1900s, a cook named Mary Mallon (“Typhoid Mary”) unknowingly spread the disease to over fifty people, three of whom died. Other serotypes of *Salmonella* cause food poisoning. (credit: modification of work by NCI, CDC)

### Bubonic Plagues

From 541 to 750, the Plague of Justinian, an outbreak of what was likely *bubonic plague*, eliminated one-quarter to one-half of the human population in the eastern Mediterranean region. The population in Europe dropped by 50 percent during this outbreak. Astoundingly, bubonic plague would strike Europe more than once!

Bubonic plague is caused by the bacterium *Yersinia pestis*. One of the most devastating pandemics attributed to bubonic plague was the **Black Death** (1346 to 1361). It is thought to have originated in China and spread along the Silk Road, a network of land and sea trade routes, to the Mediterranean region and Europe, carried by fleas living on black rats that were always present on ships. The Black Death was probably named for the tissue necrosis ([Figure 22.21c](#)) that can be one of the symptoms. The “buboes” of bubonic plague were painfully swollen areas of lymphatic tissue. A *pneumonic form* of the plague, spread by the coughing and sneezing of infected individuals, spreads directly from human to human and can cause death within a week. The pneumonic form was responsible for the rapid spread of the Black Death in Europe. The Black Death reduced the world’s population from an estimated 450 million to about 350 to 375 million. Bubonic plague struck London yet again in the mid-1600s ([Figure 22.21](#)). In modern times, approximately 1,000 to 3,000 cases of plague arise globally each year, and a “sylvatic” form of plague, carried by fleas living on rodents such as prairie dogs and black footed ferrets, infects 10 to 20 people annually in the American Southwest. Although contracting bubonic plague before antibiotics meant almost certain death, the bacterium responds to several types of modern antibiotics, and mortality rates from plague are now very low.



**Figure 22.21** The Black Death. The (a) Great Plague of London killed an estimated 200,000 people, or about 20 percent of the city's population. The causative agent, the (b) bacterium *Yersinia pestis*, is a Gram-negative, rod-shaped bacterium from the class Gammaproteobacteria. The disease is transmitted through the bite of an infected flea, which is carried on a rodent. Symptoms include swollen lymph nodes, fever, seizure, vomiting of blood, and (c) gangrene. (credit b: Rocky Mountain Laboratories, NIAID, NIH; scale-bar data from Matt Russell; credit c: Textbook of Military Medicine, Washington, D.C., U.S. Dept. of the Army, Office of the Surgeon General, Borden Institute)

### LINK TO LEARNING

Watch a [video \(http://openstax.org/l/black\\_death\)](http://openstax.org/l/black_death) on the modern understanding of the Black Death—bubonic plague in Europe during the 14<sup>th</sup> century.

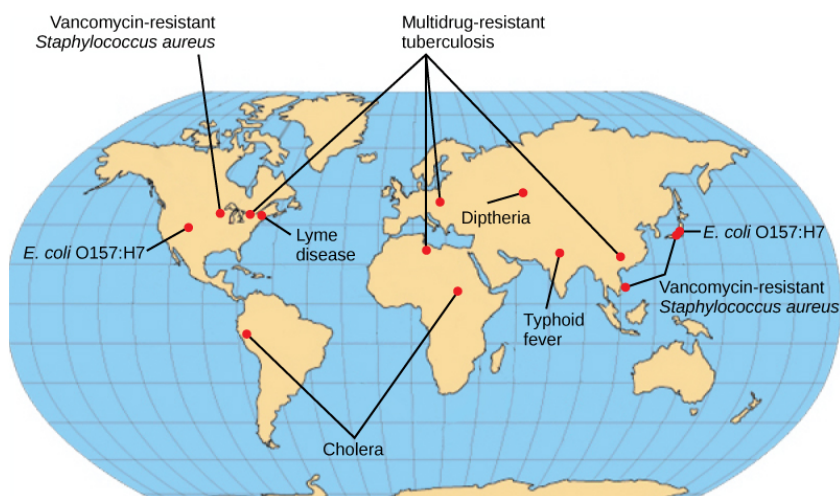
## Migration of Diseases to New Populations

One of the negative consequences of human exploration was the accidental “biological warfare” that resulted from the transport of a pathogen into a population that had not previously been exposed to it. Over the centuries, Europeans tended to develop genetic immunity to endemic infectious diseases, but when European conquerors reached the western hemisphere, they brought with them disease-causing bacteria and viruses, which triggered epidemics that completely devastated many diverse populations of Native Americans, who had no natural resistance to many European diseases. It has been estimated that up to 90 percent of Native Americans died from infectious diseases after the arrival of Europeans, making conquest of the New World a foregone conclusion.

## Emerging and Re-emerging Diseases

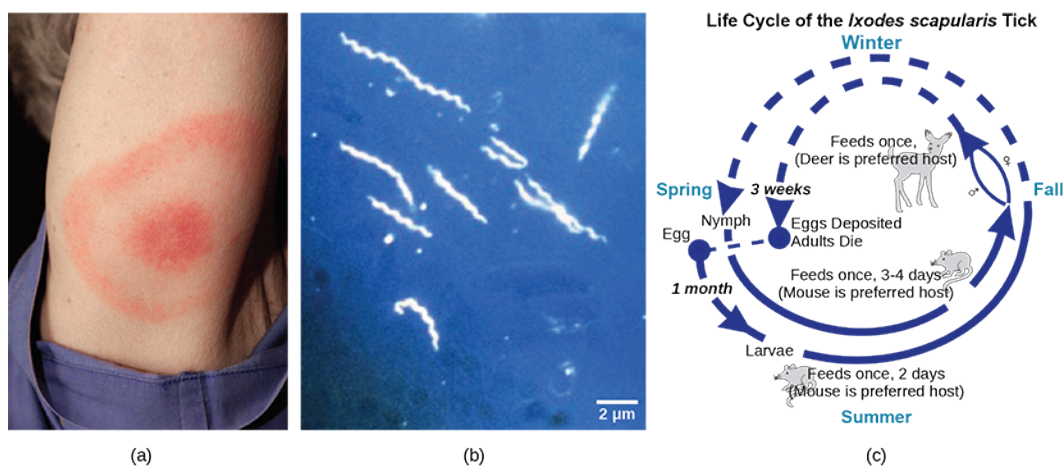
The distribution of a particular disease is *dynamic*. Changes in the environment, the pathogen, or the host population can dramatically impact the spread of a disease. According to the World Health Organization (WHO), an **emerging disease** ([Figure 22.22](#)) is one that has appeared in a population for the first time, or that may have existed previously but is rapidly increasing in incidence or geographic range. This definition also includes *re-emerging diseases* that were previously under control. Approximately 75 percent of recently emerging infectious diseases affecting humans are zoonotic diseases. **Zoonoses** are diseases that primarily infect animals but can be transmitted to humans; some are of viral origin and some are of bacterial origin. Brucellosis is an example of a prokaryotic zoonosis that is re-emerging in some regions, and *necrotizing fasciitis* (commonly known as flesh-eating bacteria) has been increasing in virulence for the last 80 years for unknown reasons.





**Figure 22.22** Emerging diseases. The map shows regions where bacterial diseases are emerging or re-emerging. (credit: modification of work by NIH)

Some of the present emerging diseases are not actually new, but are diseases that were catastrophic in the past (Figure 22.23). They devastated populations and became dormant for a while, just to come back, sometimes more virulent than before, as was the case with bubonic plague. Other diseases, like tuberculosis, were never eradicated but were under control in some regions of the world until coming back, mostly in urban centers with high concentrations of immunocompromised people. WHO has identified certain diseases whose worldwide re-emergence should be monitored. Among these are three viral diseases (dengue fever, yellow fever, and Zika), and three bacterial diseases (diphtheria, cholera, and bubonic plague). The war against infectious diseases has no foreseeable end.



**Figure 22.23** Lyme Disease. Lyme disease often, but not always, results in (a) a characteristic bullseye rash. The disease is caused by a (b) Gram-negative spirochete bacterium of the genus *Borrelia*. The bacteria (c) infect ticks, which in turn infect mice. Deer are the preferred secondary host, but the ticks also may feed on humans. Untreated, the disease causes chronic disorders in the nervous system, eyes, joints, and heart. The disease is named after Lyme, Connecticut, where an outbreak occurred in 1995 and has subsequently spread. The disease is not new, however. Genetic evidence suggests that Ötzi the Iceman, a 5,300-year-old mummy found in the Alps, was infected with *Borrelia*. (credit a: James Gathany, CDC; credit b: CDC; scale-bar data from Matt Russell)

## Foodborne Diseases

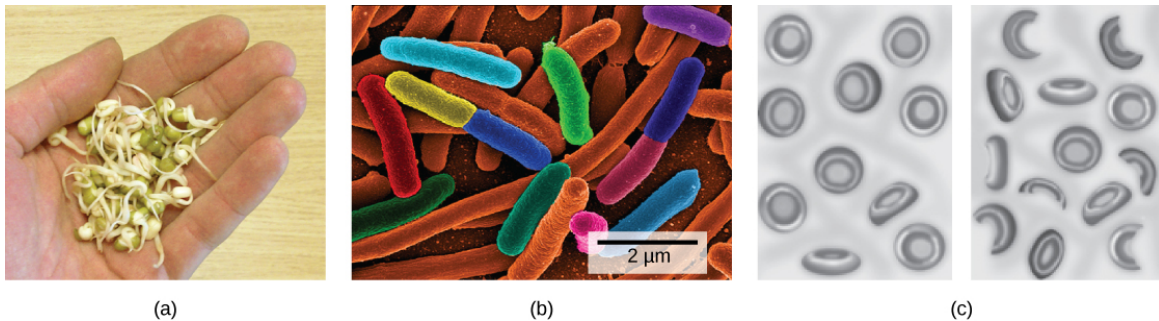
Prokaryotes are everywhere: They readily colonize the surface of any type of material, and food is not an exception. Most of the time, prokaryotes colonize food and food-processing equipment in the form of a *biofilm*, as we have discussed earlier. Outbreaks of bacterial infection related to food consumption are common. A foodborne disease (commonly called “food poisoning”) is an illness resulting from the consumption the pathogenic bacteria, viruses, or other parasites that contaminate food. Although the United States has one of the safest food supplies in the world, the U.S. Centers for Disease Control and Prevention (CDC) has reported that “76 million people get sick, more than 300,000 are hospitalized, and 5,000 Americans die

each year from foodborne illness.”

The characteristics of foodborne illnesses have changed over time. In the past, it was relatively common to hear about sporadic cases of botulism, the potentially fatal disease produced by a toxin from the anaerobic bacterium *Clostridium botulinum*. Some of the most common sources for this bacterium were non-acidic canned foods, homemade pickles, and processed meat and sausages. The can, jar, or package created a suitable anaerobic environment where *Clostridium* could grow. Proper sterilization and canning procedures have reduced the incidence of this disease.

While people may tend to think of foodborne illnesses as associated with animal-based foods, most cases are now linked to produce. There have been serious, produce-related outbreaks associated with raw spinach in the United States and with vegetable sprouts in Germany, and these types of outbreaks have become more common. The raw spinach outbreak in 2006 was produced by the bacterium *E. coli* serotype O157:H7. A serotype is a strain of bacteria that carries a set of similar antigens on its cell surface, and there are often many different serotypes of a bacterial species. Most *E. coli* are not particularly dangerous to humans, but serotype O157:H7 can cause bloody diarrhea and is potentially fatal.

All types of food can potentially be contaminated with bacteria. Recent outbreaks of *Salmonella* reported by the CDC occurred in foods as diverse as peanut butter, alfalfa sprouts, and eggs. A deadly outbreak in Germany in 2010 was caused by *E. coli* contamination of vegetable sprouts (Figure 22.24). The strain that caused the outbreak was found to be a new serotype not previously involved in other outbreaks, which indicates that *E. coli* is continuously evolving. Outbreaks of listeriosis, due to contamination of meats, raw cheeses, and frozen or fresh vegetables with *Listeria monocytogenes*, are becoming more frequent.



**Figure 22.24** Foodborne pathogens. (a) Vegetable sprouts grown at an organic farm were the cause of an (b) *E. coli* outbreak that killed 32 people and sickened 3,800 in Germany in 2011. The strain responsible, *E. coli* O104:H4, produces Shiga toxin, a substance that inhibits protein synthesis in the host cell. The toxin (c) destroys red blood cells resulting in bloody diarrhea. Deformed red blood cells clog the capillaries of the kidney, which can lead to kidney failure, as happened to 845 patients in the 2011 outbreak. Kidney failure is usually reversible, but some patients experience kidney problems years later. (credit c: NIDDK, NIH)

## Biofilms and Disease

Recall that biofilms are microbial communities that are very difficult to destroy. They are responsible for diseases such as Legionnaires' disease, otitis media (ear infections), and various infections in patients with cystic fibrosis. They produce dental plaque and colonize catheters, prostheses, transcutaneous and orthopedic devices, contact lenses, and internal devices such as pacemakers. They also form in open wounds and burned tissue. In healthcare environments, biofilms grow on hemodialysis machines, mechanical ventilators, shunts, and other medical equipment. In fact, 65 percent of all infections acquired in the hospital (nosocomial infections) are attributed to biofilms. Biofilms are also related to diseases contracted from food because they colonize the surfaces of vegetable leaves and meat, as well as food-processing equipment that isn't adequately cleaned.

Biofilm infections develop gradually and may not cause immediate symptoms. They are rarely resolved by host defense mechanisms. Once an infection by a biofilm is established, it is very difficult to eradicate, because biofilms tend to be resistant to most methods used to control microbial growth, including antibiotics. The matrix that attaches the cells to a substrate and to other another protects the cells from antibiotics or drugs. In addition, since biofilms grow slowly, they are less responsive to agents that interfere with cell growth. It has been reported that biofilms can resist up to 1,000 times the antibiotic concentrations used to kill the same bacteria when they are free-living or planktonic. An antibiotic dose that large would harm the patient; therefore, scientists are working on new ways to get rid of biofilms.

## Antibiotics: Are We Facing a Crisis?

The word *antibiotic* comes from the Greek *anti* meaning “against” and *bios* meaning “life.” An **antibiotic** is a chemical, produced either by microbes or synthetically, that is hostile to or prevents the growth of other organisms. Today’s media often address concerns about an antibiotic crisis. Are the antibiotics that easily treated bacterial infections in the past becoming obsolete? Are there new “superbugs”—bacteria that have evolved to become more resistant to our arsenal of antibiotics? Is this the beginning of the end of antibiotics? All these questions challenge the healthcare community.

One of the main causes of antibiotic resistance in bacteria is overexposure to antibiotics. The imprudent and excessive use of antibiotics has resulted in the natural selection of resistant forms of bacteria. The antibiotic kills most of the infecting bacteria, and therefore only the resistant forms remain. These resistant forms reproduce, resulting in an increase in the proportion of resistant forms over non-resistant ones. In addition to transmission of resistance genes to progeny, lateral transfer of resistance genes on plasmids can rapidly spread these genes through a bacterial population. A major misuse of antibiotics is in patients with viral infections like colds or the flu, against which antibiotics are useless. Another problem is the excessive use of antibiotics in livestock. The routine use of antibiotics in animal feed promotes bacterial resistance as well. In the United States, 70 percent of the antibiotics produced are fed to animals. These antibiotics are given to livestock in low doses, which maximize the probability of resistance developing, and these resistant bacteria are readily transferred to humans.

### LINK TO LEARNING

Watch a recent news [report \(http://openstax.org/l/antibiotics\)](http://openstax.org/l/antibiotics) on the problem of routine antibiotic administration to livestock and antibiotic-resistant bacteria.

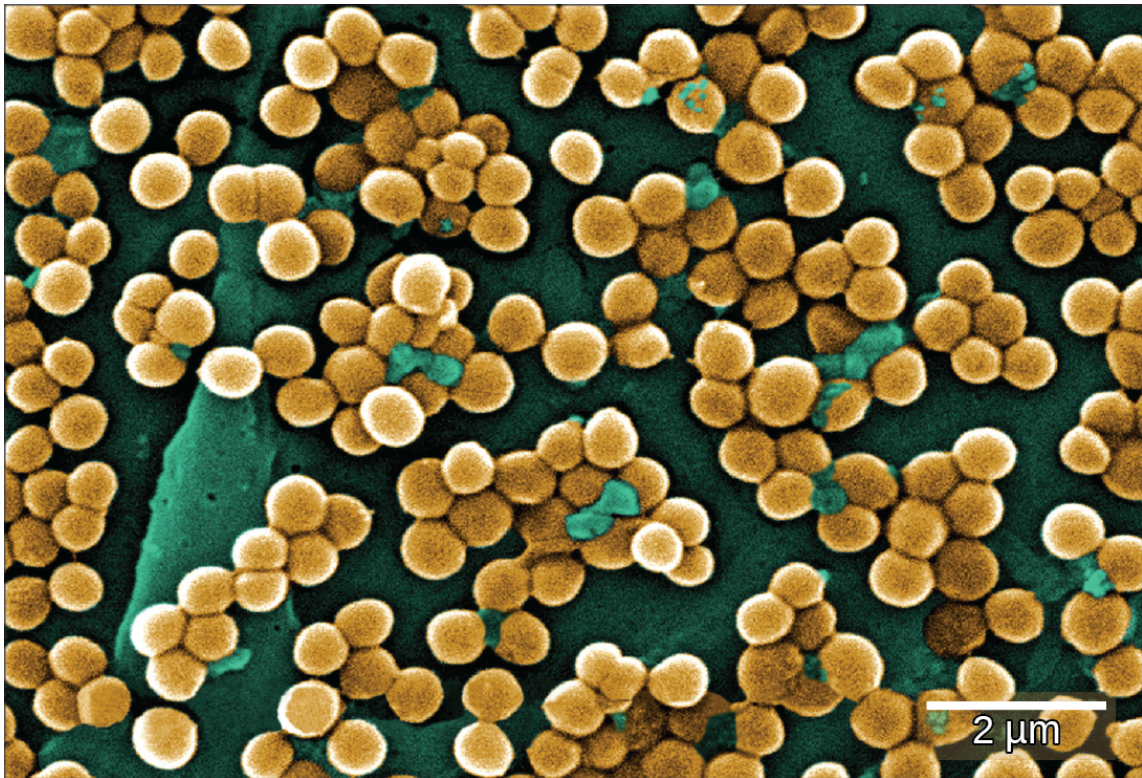
### One of the Superbugs: MRSA

The imprudent use of antibiotics has paved the way for the expansion of resistant bacterial populations. For example, *Staphylococcus aureus*, often called “staph,” is a common bacterium that can live in the human body and is usually easily treated with antibiotics. However, a very dangerous strain, **methicillin-resistant *Staphylococcus aureus* (MRSA)** has made the news over the past few years ([Figure 22.25](#)). This strain is resistant to many commonly used antibiotics, including methicillin, amoxicillin, penicillin, and oxacillin. MRSA can cause infections of the skin, but it can also infect the bloodstream, lungs, urinary tract, or sites of injury. While MRSA infections are common among people in healthcare facilities, they have also appeared in healthy people who haven’t been hospitalized, but who live or work in tight populations (like military personnel and prisoners). Researchers have expressed concern about the way this latter source of MRSA targets a much younger population than those residing in care facilities. *The Journal of the American Medical Association* reported that, among MRSA-afflicted persons in healthcare facilities, the average age is 68, whereas people with “community-associated MRSA” (**CA-MRSA**) have an average age of 23.<sup>4</sup>

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<sup>4</sup>Naimi, TS, LeDell, KH, Como-Sabetti, K, et al. Comparison of community- and health care-associated methicillin-resistant *Staphylococcus aureus* infection. *JAMA* 290 (2003): 2976–84, doi:10.1001/jama.290.22.2976.





**Figure 22.25** MRSA. This scanning electron micrograph shows methicillin-resistant *Staphylococcus aureus* bacteria, commonly known as MRSA. *S. aureus* is not always pathogenic, but can cause diseases such as food poisoning and skin and respiratory infections. (credit: modification of work by Janice Haney Carr; scale-bar data from Matt Russell)

In summary, the medical community is facing an antibiotic crisis. Some scientists believe that after years of being protected from bacterial infections by antibiotics, we may be returning to a time in which a simple bacterial infection could again devastate the human population. Researchers are developing new antibiotics, but it takes many years of research and clinical trials, plus financial investments in the millions of dollars, to generate an effective and approved drug.



## CAREER CONNECTION

### Epidemiologist

Epidemiology is the study of the occurrence, distribution, and determinants of health and disease in a population. It is, therefore, part of public health. An epidemiologist studies the frequency and distribution of diseases within human populations and environments.

Epidemiologists collect data about a particular disease and track its spread to identify the original mode of transmission. They sometimes work in close collaboration with historians to try to understand the way a disease evolved geographically and over time, tracking the natural history of pathogens. They gather information from clinical records, patient interviews, surveillance, and any other available means. That information is used to develop strategies, such as vaccinations ([Figure 22.26](#)), and design public health policies to reduce the incidence of a disease or to prevent its spread. Epidemiologists also conduct rapid investigations in case of an outbreak to recommend immediate measures to control it.

An epidemiologist has a bachelor's degree, plus a master's degree in public health (MPH). Many epidemiologists are also physicians (and have an M.D. or D.O degree), or they have a Ph.D. in an associated field, such as biology or microbiology.



**Figure 22.26** Vaccination. Vaccinations can slow the spread of communicable diseases. (credit: modification of work by Daniel Paquet)

## 22.5 Beneficial Prokaryotes

*By the end of this section, you will be able to do the following:*

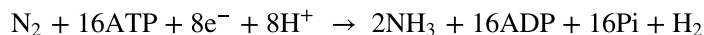
- Explain the need for nitrogen fixation and how it is accomplished
- Describe the beneficial effects of bacteria that colonize our skin and digestive tracts
- Identify prokaryotes used during the processing of food
- Describe the use of prokaryotes in bioremediation

Fortunately, only a few species of prokaryotes are pathogenic! Prokaryotes also interact with humans and other organisms in a number of ways that are beneficial. For example, prokaryotes are major participants in the carbon and nitrogen cycles. They produce or process nutrients in the digestive tracts of humans and other animals. Prokaryotes are used in the production of some human foods, and also have been recruited for the degradation of hazardous materials. In fact, our life would not be possible without prokaryotes!

### Cooperation between Bacteria and Eukaryotes: Nitrogen Fixation

Nitrogen is a very important element to living things, because it is part of nucleotides and amino acids that are the building blocks of nucleic acids and proteins, respectively. Nitrogen is usually the most limiting element in terrestrial ecosystems, with atmospheric nitrogen,  $N_2$ , providing the largest pool of available nitrogen. However, eukaryotes cannot use atmospheric, gaseous nitrogen to synthesize macromolecules. Fortunately, nitrogen can be “fixed,” meaning it is converted into a more accessible form—ammonia ( $NH_3$ )—either biologically or abiotically.

Abiotic nitrogen fixation occurs as a result of physical processes such as lightning or by industrial processes. **Biological nitrogen fixation** (BNF) is exclusively carried out by prokaryotes: soil bacteria, cyanobacteria, and *Frankia* spp. (filamentous bacteria interacting with actinorhizal plants such as alder, bayberry, and sweet fern). After photosynthesis, BNF is the most important biological process on Earth. The overall nitrogen fixation equation below represents a series of *redox reactions* (Pi stands for inorganic phosphate).



The total fixed nitrogen through BNF is about 100 to 180 million metric tons per year, which contributes about 65 percent of the nitrogen used in agriculture.

Cyanobacteria are the most important nitrogen fixers in aquatic environments. In soil, members of the genera *Clostridium* and *Azotobacter* are examples of free-living, nitrogen-fixing bacteria. Other bacteria live symbiotically with legume plants, providing the most important source of fixed nitrogen. Symbionts may fix more nitrogen in soils than free-living organisms by a factor of 10. Soil bacteria, collectively called rhizobia, are able to symbiotically interact with legumes to form **nodules**, specialized structures where nitrogen fixation occurs (Figure 22.27). *Nitrogenase*, the enzyme that fixes nitrogen, is inactivated by oxygen, so the nodule provides an oxygen-free area for nitrogen fixation to take place. The oxygen is sequestered by a form of