A Brief History of Microbiology

First observation of cell by Hooke

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*. Although Dutch merchant and amateur scientist Anton van Leeuwenhoek was probably the first to observe live microorganisms through the magnifying lenses. Van Leeuwenhoek made detailed drawings of organisms he found in rainwater, feces, and material scraped from teeth.

The Debate over Spontaneous Generation

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 could arise from decaying corpses.

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 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

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 the following figure.

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		

First Golden

MICROBIOLOGY

Age of



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.

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. Thus 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. Some of the major events that occurred during the Second Golden Age of Microbiology are listed in the following figure.

Second Golden Age of MICROBIOLOGY	1940s 1950s	Fleming, Chain, and Florey—Penicillin 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	César Milstein (1927–) Fused cancerous cells with antibody-producing cells to produce a hybrid cell that grows continuously and produces therapeutic antibodies.
	1960s 1980s	reactions Medawar—Acquired immune tolerance Sanger and Gilbert—Techniques for sequencing DNA	
		Jerne, Köhler, and Milstein—Technique for producing monoclonal (single pure) antibodies Tonegawa—Genetics of antibody production	Françoise Barré-Sinoussi (1947–) Discovered a virus in a patient with swollen lymph nodes; the virus was human immunodeficiency virus.
Third Golden		Bishop and Varmus—Cancer-causing genes (oncogenes)	
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	Youyou Tu (1930–) Extracted artemisinin from a Chinese sage plant. Artemisinin inhibits the malaria parasite.
		Mullis—Polymerase chain reactions that amplify (make multiple copies of) DNA	A CONTRACT OF A CONTRACT.
	2000s	Doherty and Zinkernagel—Cell-mediated immunity Agre and MacKinnon—Water and ion channels in plasma membranes Marshall and Warren— <i>Helicobacter pylori</i> as the cause of peptic ulcers	
	2010s	Barré-Sinoussi and Montagnier—Discovery of HIV Ramakrishnan, Steitz, and Yonath—Detailed structure and function of ribosomes Beutler, Hoffmann, and Steinman—Innate immunity; dendritic cells in adaptive immunity	Figure 1.7 Second and Third Golden Ages of Microbiology. All researchers listed are Nobel laureates.
		Tu—Treatment for malaria	What advances occurred during the Second Golden Age of Microbiology?

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.