From a letter written on December 20, 1675, to the Royal Society of London:

“In the past summer I have made many observations upon various waters, and in almost all discovered an abundance of very little and odd animalcules, whereof some were incredibly small...”

Antonie van Leeuwenhoek
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Why is microbiology one of the most exciting disciplines of modern science? Several major developments led to its emergence as a dynamic force in both science and technology. Of particular significance was the realization that microbes provide unique experimental systems for analyzing the basic processes of all forms of life. Research with bacteria led to the important discovery, in 1944, that genes are composed of DNA. In turn, this paved the way for development of many sophisticated and powerful techniques used in current molecular biological research. These are now the major "tools" of biotechnology. The exploitation of microbes for biotechnological applications now appears to have almost unlimited horizons. In the decades ahead, we can expect that microbial-based technologies will solve problems in medicine, public health, agriculture, space exploration, environmental pollution, and industrial manufacturing.

Before 1674, no one had seen or suspected that there were living organisms invisible to the naked eye. During that year, a self-educated Dutch shop-keeper discovered the existence of "very little animalcules" in diverse places, for example, human mouths, lake water, watery suspensions of ground pepper, and sap dripping from a vine branch. Thus, using a simple microscope of his own design, Antonie van Leeuwenhoek (see photo in Chapter 1) had discovered the invisible world of microbes. Leeuwenhoek communicated his findings in letters to members of the Royal Society of London, but his discoveries disappeared into obscurity for two centuries.

During the 1870s, the French chemist Louis Pasteur turned his attention to biological problems and demonstrated that the alcoholic fermentations responsible for wine and beer production were caused by living microbes. This was an early recognition of the fact that microbes have the power to catalyze chemical transformations on a large scale.
Indeed, we now know that bacteria and other microbes are essential in the massive recycling of major chemical elements that constantly occurs in the Earth’s biosphere. If all microbes were to die suddenly due to some cataclysmic event, all life—plant and animal—would soon come to a standstill.

There are thousands of species of microbes that live and reproduce in a wide range of habitats, some quite extreme with respect to temperature and chemical conditions. Most known species are harmless to animals and plants; in fact, many are beneficial, playing important roles in symbiotic relationships with higher forms of life. During the latter part of the 19th century, however, it became clear that certain kinds of microbes cause infectious diseases of animals and plants. The isolation and study of pathogenic microbes, begun during the closing decades of the 19th century, eventually led to great improvements in combating infectious diseases, but more research is still needed in connection with a number of diseases caused by microbes and viruses.

Following Pasteur’s work, a continuing avalanche of basic discoveries in microbiology and related sciences has led to marked improvements in the quality and longevity of human life. Some of the highlights have been:

- 1880: A procedure is discovered for making a vaccine to immunize against a bacterial disease
- 1882: Proof that a bacterium, *Mycobacterium tuberculosis*, causes animal tuberculosis
- 1884: First isolation of the bacteria that cause typhoid and diphtheria
- 1885: *Escherichia coli* is found to be a normal inhabitant of the intestinal tract
- 1891: Evidence that antibodies are important in immunity against microbial diseases
- 1899: The first virus discovered is the tobacco mosaic virus, which attacks tobacco plants
- 1912: Development of an effective cure for syphilis, the first specific chemotherapeutic agent for a bacterial disease
- 1928: Discovery of the antibacterial action of penicillin, produced by the mould *Penicillium*
- 1935: For the first time, a virus is crystallized (tobacco mosaic virus)
- 1944: Experiments with the bacterium *Streptococcus pneumoniae* prove that genes are made of DNA
• 1946: Methods of studying bacterial reproduction advanced (in *Escherichia coli*); later, this led to a cornucopia of procedures essential for modern biotechnology
• 1964: With *E. coli* used as the experimental organism, it is established that the sequence of the chemical units of DNA defines the sequence of amino acids in proteins
• 1979: The disease smallpox is declared officially eliminated
• 1982: Discovery of the bacterium *Helicobacter pylori* as a primary cause of peptic ulcers
• 1983: Identification of the HIV virus, the cause of AIDS
• 1995: First description of the complete DNA genome sequence of a bacterium (*Haemophilus influenzae*)
• 1997: DNA genome sequence of *Helicobacter pylori* is completed
• 1998: DNA genome sequence of *Mycobacterium tuberculosis* is completed
• 1999: A research conference report predicts that “within the next decade, the DNA genomes of every significant bacterial pathogen of humans, animals and plants will have been sequenced” and that this vast amount of new data will provide us “with the ability to probe the inner depths of some of mankind’s oldest enemies (and some of the new ones)”
• 2002: More than 60 microbial genome sequences have been determined, and at least 100 more are being analyzed

It has been demonstrated repeatedly that applications of basic research strongly influence the course of human history. The research efforts of the pioneers of microbiology and biochemistry have had far-reaching effects on our lives. The Biographical Notes at the end of this book gives short biographies of some of the leading contributors to our understanding of the world of microbes.

In 1987, my experience in teaching a course in microbiology for nonscientists led me to write a text titled *The World of Microbes*. Since then, scientists’ understanding of the universe of microbes has expanded almost as much again as in the preceding century. *Microbes: an Invisible Universe* is a reflection of this new knowledge, but retains the same spirit as the former book: to provide a “guidebook” to the many interactions of microbes with the environment and with higher forms of life, and to introduce scientists and nonscientists alike to the pioneers of this fascinating discipline and their discoveries.
My grateful appreciation goes as always to my colleagues at Indiana University; to Dr. Thomas Brock for supplying valuable illustrative matter; and to the many people named in the Credits and Acknowledgments section who generously provided illustrations. Finally, my greatest debt is to my wife Virginia for her unfailing encouragement, patience, and support.
About the Author

Howard Gest is Distinguished Professor Emeritus of Microbiology and Adjunct Professor of History and Philosophy of Science at Indiana University, Bloomington. He received the Bachelor of Arts degree in bacteriology from the University of California, Los Angeles (U.C.L.A.) in 1942, and his Ph.D. degree from Washington University in St. Louis in 1949. During World War II, as a chemist on the Manhattan (Atomic Bomb) Project, he did basic research on the radioactive elements formed in uranium fission. He has been on the faculties of Case Western Reserve University, Washington University, and Indiana University and has been a visiting researcher at the California Institute of Technology, Dartmouth Medical School, Stanford University, Oxford University, Tokyo University, and U.C.L.A. Professor Gest has twice been named a Guggenheim Fellow and has served on a number of advisory committees of the United States government. During his second Guggenheim Fellowship, he studied problems of biochemical evolution as a member of the Precambrian Paleobiology Group. He is widely recognized for his research on microbial physiology and metabolism, especially with photosynthetic bacteria. Professor Gest is a Fellow of the American Association for the Advancement of Science, American Society for Microbiology, American Academy of Microbiology, and American Academy of Arts and Sciences.
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