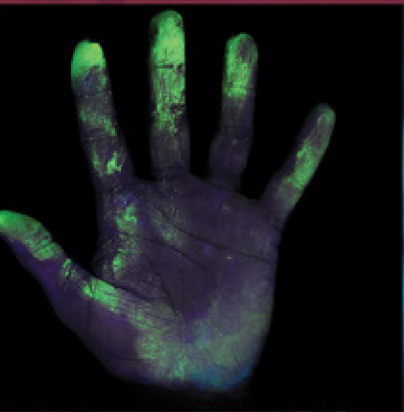
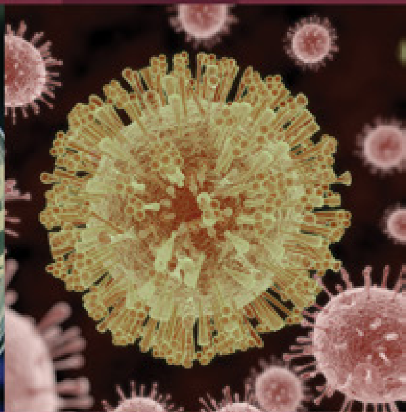
FOURTH EDITION

KRASNER'S MICROBIAL CHALLENGE

A PUBLIC HEALTH PERSPECTIVE




TERI SHORS

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A PUBLIC HEALTH PERSPECTIVE

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DEDICATIONS

This edition of *The Microbial Challenge* is dedicated to Robert I. Krasner. The publishing team at Jones & Bartlett Learning has chosen to honor his memory and passion for lifelong learning by updating the title of this edition to *Krasner's Microbial Challenge*. It is our hope that students and instructors using this book will continue to be inspired by Dr. Krasner's enthusiasm for new discoveries, connecting with the world around us, and learning both inside and outside the classroom.

From Teri Shors

To the late Elaine (Motschke) Gross, my mother, *Ich vermisse dich jeden Tag.*

To John Cronn, my undergraduate microbiology mentor, colleague, and friend who opened my eyes to the invisible world of microbes and viruses.

To the hundreds of students I have taught, past and present.

"We know nothing of what will happen in the future, but by the analogy of experience."
—Abraham Lincoln

BRIEF TABLE OF CONTENTS

TABLE OF CONTENTS

PREFACE

Birth and Development of *The Microbial Challenge*

After 50 years in the classroom at Providence College in Rhode Island teaching microbiology to biology majors, Dr. Robert Krasner decided to develop a microbiology course for nonbiology majors. Outbreaks of disease were in the news frequently, and, judging by the questions students in a nonmajors, general biology course asked, it was apparent that they, too, needed to know more about microbes and human–microbe interactions. Actually, he had been thinking about teaching a nonmajors course for a number of years, but to his surprise there was no text available. Hence, he used handouts, online resources, magazine and newspaper articles, and videos. He even called in a few speakers to supplement his lectures. This strategy worked, but it was cumbersome, required too many handouts, and resulted in confusion; so he decided to write his own text.

At about that time, Dr. Krasner decided to study public health microbiology and was accepted into the Harvard School of Public Health for the 1999–2000 academic year, 41 years after he had completed his PhD. He had wanted to do this for many years, but raising a family and educating his children were his top priority. Now it was his turn! As far as he was able to determine, Dr. Krasner was the oldest student on a full-time basis to earn the Master of Public Health (MPH) degree at Harvard. His classmates were primarily young medical students who had postponed their fourth year of medical school to earn a MPH before completing medical school. His Harvard studies included 6 weeks in a tropical disease laboratory in Brazil culminating in a 2-week field trip to Manaus in the Amazon.

While at Harvard's School of Public Health, every day Dr. Krasner passed by an inscription that reads, in several languages, "*The highest attainable standard of health is one of the fundamental rights of every human being*." This inscription, his studies at Harvard, and his travel experiences were major factors in the birth and in the public health perspective of his text, *The Microbial Challenge*.

During the development of the third edition, Dr. Teri Shors, Professor in the Department of Biology and Microbiology at the University of Wisconsin Oshkosh, signed on as a coauthor. Her creativity, judgment, and knowledge resulted in a text Dr. Krasner continued to be proud of. Her specialty is virology, and together the two of them brought many years of teaching experience to this text. Dr. Krasner passed away in 2014 at the age of 84. Dr. Shors has taken up the torch to carry on Dr. Krasner's vision to provide nonmajors with a better understanding of the microbial world we live in. For this Fourth Edition she enlisted the help of two contributors: Dr. Terri Hamrick of Campbell University to assist with updating the chapters on immunity and microbial control and Dr. Nancy Boury of Iowa State University to assist with the chapter on biological weapons, innovations, and technology.

Text Overview

Microbes are as much a part of our biological world as are the more familiar plants, animals, and insects. They are an extremely diverse group, consisting of thousands of species, including viruses, which are not even considered to be "alive." Most microbes are not pathogens that cause infections. The majority are necessary for the maintenance of all life. A number of species have been exploited in the food industry, in genetic engineering, in the research and development of pharmaceuticals to treat infections and vaccines to prevent them, environmental applications, and in many areas of research. This book focuses on the relative "handful" of microbes that cause infectious diseases in humans.

Annihilation of microbes is not a possibility, a goal, or a desirable outcome, but learning to live in harmony with microbes is realistic and necessary. All students, not only biology or microbiology majors, will benefit from understanding microbes and those factors that lead to collisions between microbes and humans. As a potential parent, you will deal with immunizations and the rashes, fevers, ear infections, and sore throats that your child will develop. Further, as history has shown, epidemics and pandemics are a constant threat, and prevention utilizes knowledge-based preparation. Your generation has not known a world without HIV/AIDS, avian influenza, Zika virus disease, Ebola virus disease, Middle East respiratory syndrome, Nipah encephalitis, multidrug-resistant tuberculosis, healthcare-associated infections, Powassan encephalitis, and many other infectious diseases that remain a source of great concern throughout the world.

The following are just a few microbe-related news stories that were making headlines at the time of this writing (2018):

- An epidemic of Ebola virus disease in the Democratic Republic of Congo (DRC) was continuing to slow but had not stopped.
- More than 2,173 laboratory-confirmed cases of cyclosporiasis tied to contaminated romaine lettuce, basil, and cilantro present in store-bought premade salads and an unknown source associated with trays of vegetables in 33 states were reported from May through August 2018.

- The United Kingdom reported its first human case of monkeypox in September 2018. The patient was infected by monkeypox virus while in Nigeria before traveling to the United Kingdom.
- Centers for Disease Control and Prevention (CDC) experts expressed concerns over the prevalence of the increasing number of infections caused by the multidrug-resistant fungus *Candida auris* in New York City hospitals. *C. auris* cases continue to spread, causing large outbreaks in Europe.
- Rare *Capnocytophaga canimorsus* infections transmitted through a dog lick caused flesh-eating disease in three Wisconsinites (including one death) in September 2018.
- During fall, 2018, the CDC was investigating cases involving nearly 200 young children located in 24 states across the U.S. suffering from acute flaccid paralysis (AFP). The likely culprit in a non-poliovirus strain of enterovirus that commonly circulates in summer and fall. It is a rare disease that has devastating effects on families.

At the time of this writing, ecological disturbances could potentially facilitate infectious disease outbreaks. In mid-September 2018, Hurricane Florence ravaged North and South Carolina. Flooding caused more than 100 pig farm lagoons to overflow, contaminating shallow groundwater sources and crops with pig manure. More than 900,000 households get their drinking water from a private well supplied by the contaminated groundwater. Approximately two dozen drinking water systems were forced to halt operations, and an additional two dozen facilities were given "boil water" advisories. Any crops exposed to floodwaters were considered contaminated and could not be sold or enter the food supply. More than 5,500 pigs and 3.4 million chickens or turkeys were killed by flooding. North Carolina was labeled a cesspool of pig feces and urine; displaced native species, such as poisonous snakes; chicken waste; animal corpses; toxic chemicals, such as coal ash containing mercury and arsenic; and fecal pathogens, such as *E. coli, Salmonella, Campylobacter, Vibrio*, noroviruses, and adenoviruses. CDC experts warned hurricane survivors to avoid walking in flooded areas. As the floodwaters recede, North and South Carolina residents will face germinating fungal spores and deadly pathogens in the mud. Researchers have detected high levels of *E. coli* from samples of sediments collected in streets and homes. The post-Florence cleanup will be challenging.

Text Format

The chapters are arranged into five logical and sequential parts:

Part 1: Discovery of Microbes and the History of Public Health (Chapters 1–3)

Part 2: The Microbial Challenge (Chapters 4–9)

Part 3: Microbial Disease (Chapters 10–14)

Part 4: Meeting the Microbial Challenge (Chapters 15–16)

Part 5: Current Microbial Challenges (Chapters 17–18)

Taken as a whole, the dynamics of the interactions between microbes and humans unfold. Per recommendations by reviewers of this text, chapters containing the history of microbes in health and disease were added. Part 1 (Chapters 1–3) addresses the discovery of microbes and healthcare practices before and after the medical community accepted the germ theory of disease. It dissects the reasoning and situations in history that resulted in the development of strategies used in microbial disease control based on sanitation and clean water.

Part 2 (Chapters 4–9) considers the appearance of new (or emerging) and reemerging infectious diseases and factors that contribute to their presence, including world population growth, technological advances, human behavior, and ecological disturbances. The array of microbes that constitute the microbial world and their distinctive properties are introduced. Lest students think that all microbes are "bad guys and out to get us," the emphasis here is on "the other side of the coin"—the beneficial aspects of microbial life in health and biogeochemical cycles. The concept of the human microbiome and the biology of bacteria, viruses, and prions are described, as well as basic aspects of microbial genetics, with an emphasis on mechanisms of genetic exchange in bacteria that contribute to pathogenicity or antibiotic resistance of bacterial pathogens. It is stressed that microbes do not "seek us out," but that the association between microbes and their hosts is accidental—a chance collision that may result in harm to the host. Further, the mechanisms of virulence and the stages of disease are discussed.

Part 3 (Chapters 10–14) focuses on the concepts of microbial disease; epidemiology; the cycle of microbial disease; and healthcare-associated infections (HAIs), an increasing worldwide problem. Chapters 12, 13, and 14 present a sample of "the challengers"—namely, bacteria (Chapter 12), viruses and prions (Chapter 13), and protozoans, helminths, and fungi (Chapter 14)—and the infectious diseases they cause. These chapters focus on modes of transmission; each chapter is divided into foodborne and waterborne, airborne, sexually transmitted, contact, soilborne, and arthropodborne infectious diseases.

Part 4 (Chapters 15 and 16) embellishes how microbial challenges are met. Chapter 15 considers the strategies of microbial disease control based on technologies used to prevent contamination, including disinfection methods, the importance of handwashing, and treatment of microbial infections with antibiotics and antiviral agents. The development of antibiotic resistance is also discussed. The immune system is the topic of Chapter 16; the chapter describes the anatomy and physiology of the body's defenses, including the mechanisms by which molecules embedded in microbes or released (toxins) by microbes, seen by the host immune system as "foreign," are targeted for elimination.

Immunization and examples of microbes or treatments that impair the body's defenses are also fodder for discussion.

Part 5 (Chapters 17 and 18) portrays the current challenges faced in public health. Chapter 17 describes the power and peril of microbes, the promising use of microbial processes in genetic engineering, and the ethical dilemmas scientists and policymakers must consider as new discoveries bring both new opportunities and new challenges. Chapter 18 recognizes the burden of disease and the future of public health. Epidemics and pandemics are most effectively prevented and controlled by partnerships at all levels, ranging from the local level to the national level, to the international level, and to the private sector.

New to the Fourth Edition

Care was taken to preserve Robert I. Krasner's voice, tone, and level of this text. The inside cover of *Krasner's Microbial Challenge, Fourth Edition* contains a listing of World Health Days to raise global awareness of specific health themes related to microbiology that are of concern to the World Health Organization (WHO). The number of parts in this edition have been updated to five and are sequentially presented to assist the student in following the logic of the narrative. All of the examples that illustrate key principles in the chapters have been updated, and the art, photos, and overall design have been improved throughout the text.

New to this text is the opening of each chapter with a case study that includes questions and activities and a set of learning objectives that spans the entire chapter. Nearly all case studies are based on case reports in the primary literature. References are included with each case study. Sometimes fictitious names have been used to improve the reading comprehension of students. Topics of case studies focus on contemporary examples that will pique the interest of both nonmajor biology students and students preparing for healthcare-related careers. Examples of case studies are:

- Wounded Civil War Soldiers That Glowed in the Dark
- Saved by a Syringe Full of Dodge Pond Bacteriophages
- Take Two Fecal Pills and Call Me in the Morning
- Don't Touch That Armadillo!
- From Sea to Sepsis
- Surviving Ebola
- Killer Bagpipes
- A Pain in the Back
- Fighting the World's Deadliest Animal

The text was revised to address feedback from instructors and students. Accordingly, Part 1 is new to this edition, per the request of reviewers. In contrast to other microbiology texts, this text did not contain a stand-alone chapter pertaining to the history of microbiology pioneers and their discoveries. Historical perspectives were intertwined throughout various chapters as microbiology concepts and microbial diseases were discussed. Toward this end, many historical accounts scattered throughout the text have been removed and combined into Part 1 of this revised edition. Emphasis has been placed on the discovery of "germs," or microbes, and their role as causative agents in disease; how battlefield medicine led to innovations in medicine and public health practices; the birth of nursing; the construction of hospitals in the 18th and 19th centuries; the role of the scientific method in proving disease causation; the modern era of microbiology; improved sanitation, water quality, and food safety; and infectious disease surveillance.

Part 2, "The Microbial Challenge" (Chapters 4–9), is consistent with the prior edition of this text. It discusses the beneficial aspects of microbes as well as the worldwide challenge posed by the different types of microbes, including viruses. Quorum sensing, fecal microbiota transplants, probiotics, prebiotics, metagenomics, engineering probiotic bacteria, and dysbiosis have been introduced in this edition, with detailed examples provided in Chapters 4, 7, and 9. A number of new boxes have also been incorporated into Part 2, such as:

- The Mystery of the *Elizabethkingia* Outbreak in Wisconsin
- Talking Starter Cultures and Sourdough Bread
- Microbes Clean Up Lead, South Dakota
- Claimed Medical Benefits of Good Gut Microbiota
- Killing Cancer with Oncolytic Viruses
- Promiscuous Bubonic Plague Bacteria
- Engineering Live Microbes as Therapies

Part 3, "Microbial Disease," was updated to reflect more information on the human microbiome and healthcare-associated infections. Box 10.1, "You Need Guts to Survive," was expanded upon to discuss bacterial diversity and the influences of the composition of gut microbiota on health and disease. Chapters 11 and 12 describe the hospital environment as a source for bacterial pathogens causing healthcare-associated infections. The One Health concept, introduced in Chapter 11, is also new to this edition of the text.

The chapters in Part 3 underwent several rearrangements. In prior editions, tuberculosis, anthrax, smallpox, HIV/AIDS, and influenza were discussed as "Current Challenges." These infectious diseases have been moved into their associated microbial disease chapters in Part 3 of this edition. For example, Chapter 12, "Bacterial Diseases," discusses bacterial diseases (tuberculosis and anthrax were moved into Chapter 12). The rationale behind this rearrangement was to aid instructors who preferred to teach infectious diseases by microbial groups (e.g., bacterial diseases or viral diseases and prions). In prior editions, instructors using this strategy would be required to use sections of two or three different chapters to cover bacterial diseases or viral diseases.

New information in Chapters 12, 13, and 14 addresses the impact of climate change on pathogenic microbes and viruses and their distribution in the environment, in addition to emerging and reemerging infectious diseases. Examples include new topics such as healthcare-associated infections caused by bacteria; noroviruses; cytomegalovirus infections; Ebola virus disease; Middle East respiratory syndrome; Chikungunya virus disease; Zika virus disease; measles virus outbreaks; Powassan encephalitis; monkeypox; increases in sexually transmitted infections; hypersensitivity pneumonitis; *Candida auris* infections; and prevention of HIV infections in light of recent complacency regarding the disease. Box 12.3, "1979: The Year of the Biological Chernobyl!"; Box 13.1, "The Coming Flu Pandemic?"; and updated Box 14.2, "Sushi Eaters Beware!" represent new content in the microbial disease chapters.

Part 4, "Meeting the Challenge" (Chapters 15 and 16), was strengthened in content by inviting Dr. Terri Hamrick to revise and contribute within her expertise and teaching experiences. Chapter 15, which covers the immune system, includes new content pertaining to the body's recognition of foreignness (e.g., invading microbes) at a molecular level, the variations of immune status within an individual and between individuals, the role of normal microbiota as protection from microbial infections, and vaccinations. Chapter 15 includes a new box, "Send in the Monoclonal Search Team." Topics were removed from Chapter 15 (Third Edition) to create Chapter 3, which is now focused on the achievements made toward sanitation, clean water, hand hygiene, food safety, and infectious disease surveillance.

Chapter 16 was redesigned to expand upon topics in the previous edition and to provide new content. It is focused on disinfection and disease control, antibiotics and the development of antibiotic resistance, antibiotic-resistance mechanisms, the clinical challenges of biofilms and antibiotic treatment, possible solutions to antibiotic resistance, and antivirals. Chapter 16 contains two new boxes, "MRSA, VRE, CRE, and Others: A Very Dangerous Alphabet Soup" and "Drug Development."

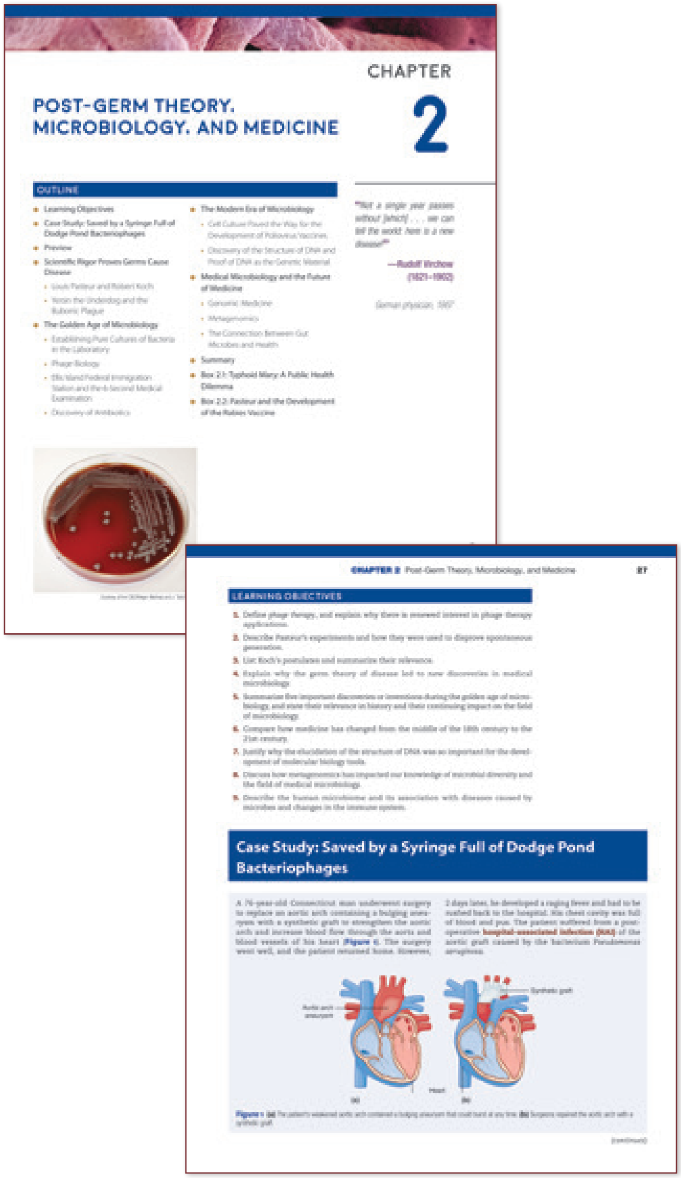
Part 5, "Current Microbial Challenges," consists of the final two chapters (Chapters 17 and 18). Dr. Nancy Boury revised and updated Chapter 17, "Harnessing the Power of Microbes: Peril and Promise." This chapter introduces new topics such as past and future influenza threats and topics that expose the controversies around genetically modified microbes, including CRISPR/Cas technology and bioethics catching up with technology. It includes new Box 17.3, "Sulfanilamide and the Birth of the Modern FDA."

Chapter 18 is a recombination of Chapters 14 and 17 from the Third Edition of this text, now titled "Partnerships in the Control of Infectious Diseases: The Future of Public Health." New topics include the WHO's Blueprint Priority Disease list, the Global Virome Project, zoonotic diseases, the species barrier and spillover, infectious disease hotspots, syndrome/symptom surveillance, real-time surveillance, mobile health, updated information about the CDC's Vessel Sanitation Program, mosquito control, FEMA responses to catastrophic events, and the One Health initiative.

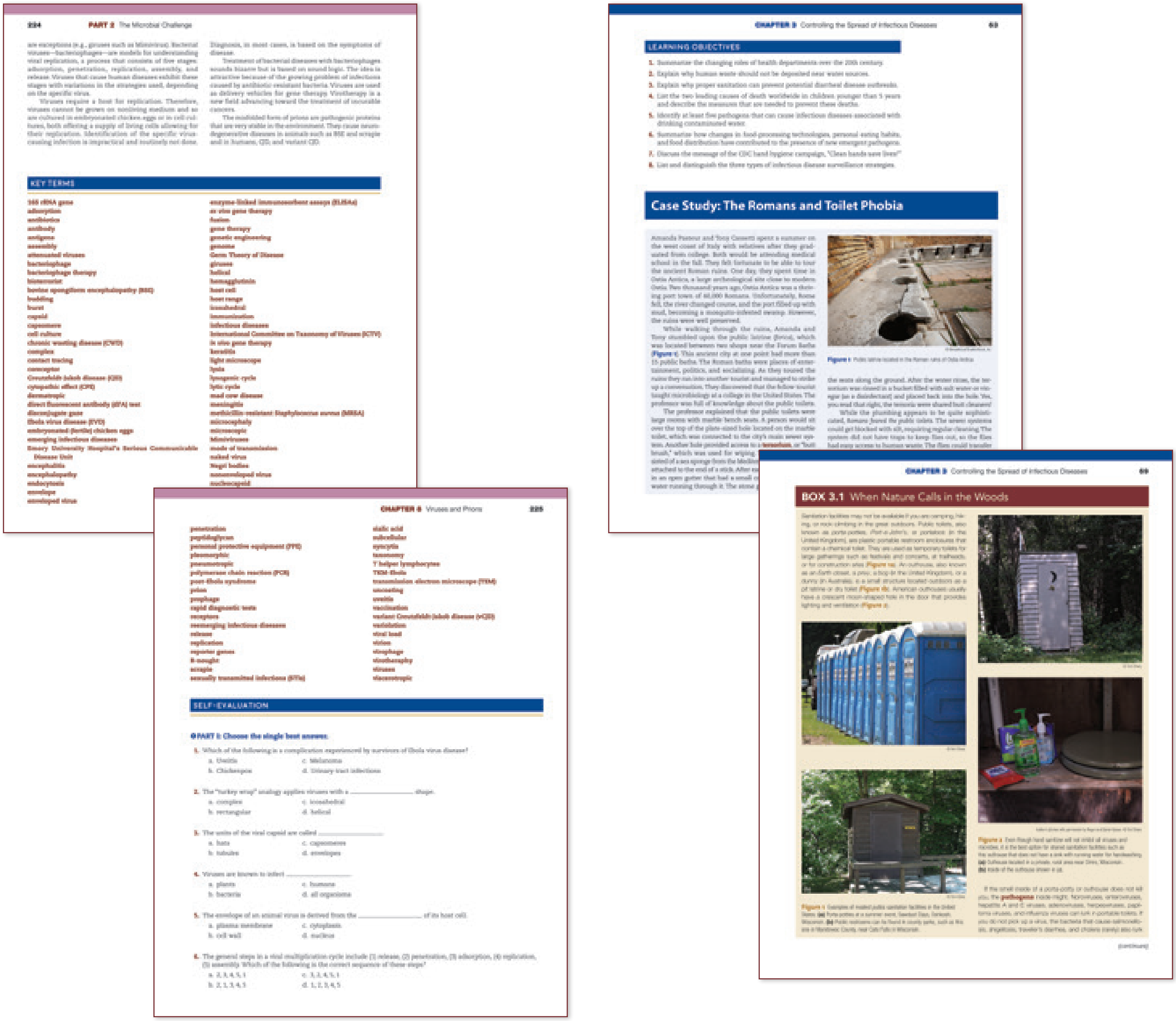
The text underwent a modest facelift with a new interior design and updated and new tables, illustrations, photos, and self-evaluation questions at the end of each chapter.

The Student Experience

Learning is a difficult, time-consuming, and often tedious task that justifies the inclusion of strategies to help the student; therefore, we include a variety of "assists" in this Fourth Edition. Each chapter begins with a **content outline**; a **case study** followed by references, questions, and activities; **learning objectives**; and a **chapter preview**, allowing students to look ahead and to stay focused on the material; and each is concluded with a broad summary and a sampling of questions for self-evaluation. Website URLs are provided throughout the text to support content. The list of World Health Days located in the inside cover of the text may be used as a way to involve students in global awareness activities.



Key terms are highlighted in bold within the chapters and defined in a glossary at the back of the book. The design of the book has also been changed to make the combination of art and text more user-friendly. Numerous feature boxes with human-interest items, **author notes**, and boxes containing microbiology-related information are scattered throughout the text to pique student interest, and we use humor to break the monotony of study. A number of unique photographs were taken by Robert I. Krasner over the years to depict the microbial diseases described in the text, in particular, many photographs in Chapter 14 ("Protozoan, Helminthic, and Fungal Diseases") were taken by Dr. Krasner. He was provided support in 1999 to study neglected tropical diseases in developing countries. Some of the microbial disease photographs are unpleasant to look at, but they are included to let readers know that Robert I. Krasner had "been there." The Author's Notebook replaced the Author's Note which provides annectodes written by all of the authors of the text as another means to reinforce that they have "been there."



Krasner's Notebook

In writing this text the original author was initially in a dilemma. Should the discussion of the microbes and their virulence mechanisms precede explanation of the body's immune defense, or the other way around? It is the "what came first, the chicken or the egg?" puzzle. Because a strong focus in this text is on disease prevention, it seemed to him more logical to first present what it is that the immune system is combating. It makes sense to me, and I hope you agree!

Krasner's Notebook

The photo in Figure 14.10b is of a row of traditional huts in Botswana, Africa, which has a high incidence of Chagas disease and kissing bugs. In a similar village, more than 50 bugs were isolated from a wooden bed frame, the only piece of "furniture" in the one-room hut. The bugs were examined for the presence of trypanosomes, and most of the insects were positive.

Krasner's Notebook

Frequently, to make a point, the authors have asked in their respective classes for a show of hands as to "Who feels tired and not so great?" Just about every hand goes up (including the author's). Is this the beginning of an infectious disease or conditions related to academic life, including preparing papers, studying (or lack of it), boredom, lack of sleep, and . . . (you can fill in the rest)?

Online Resources

A student companion website has been developed exclusively for this text and is accessible at go.jblearning.com/MicrobialChallengeCWS. The site includes robust practice quizzes, web links, and flashcards.

Note to the Student

During our many years of teaching (70+ years of experience among the authors), we have witnessed that the lack of frequent study, combined with the lack of organizational and time management skills, are the primary cause of academic disappointment. College students face many distractions (e.g., social media, jobs) and more types of technology (e.g., PCs, smartphones, tablets, and smartwatches).

Cramming a few days before an exam will not earn you the best grade you can achieve. Perhaps an analogy will help illustrate what we believe to be the best strategy of action for success. Maybe in your younger years you took music lessons. If so, you would have learned quickly that the time spent practicing between lessons was at least as important as the lessons themselves; the key to improvement and accomplishment was the frequent repetition of the musical exercises assigned. And so it is in handling your college coursework. Studies demonstrate that those students who review course material within 24 hours of a class lecture have higher test scores.

Regular lecture attendance is imperative, but equally so is the effort spent between lectures. More and more students today are working while going to school. Jobs take up study time and time away from social interactions with other students. We encourage you to form study groups as you prepare for exams. Quizzing each other will help to identify which material may need more attention and effort. Some students may understand certain concepts better than others. Studying in groups allows students to help each other learn the material. Lasting friendships will also form and may continue past graduation and many years into the future. After college, networking will play an important role as you seek employment. Studying in groups is how networking begins.

First and foremost, it is important that you get plenty of rest, eat healthy foods (fruits and vegetables!), exercise, and take time to laugh (it can boost your immune system). Handwashing is one of the best ways to prevent the spread of infectious diseases. Developing health-conscious habits (many of which are emphasized in this text) can extend your life and the lives of others. Beyond college, you may have to make decisions about your health. This text provides you with information and points you to some of the resources you can use in making certain decisions and encourages you to be a lifelong learner. Always remember, most microbes are good. You need them to remain healthy. Very few microbes cause disease. Best wishes to you!

Note to the Instructor

The organization of *Krasner's Microbial Challenge: A Public Health Perspective* allows for flexibility in course design. This text, unlike many on the market today, is not intended to be encyclopedic, but to allow coverage of most of the material in a one-semester nonmajors biology or microbiology course. Because this text provides contemporary examples of how microbes impact our daily lives, it has been well received by students who are not biology majors. It can be used for pre-nursing majors or students interested in careers related to health care, but overall it serves as a lab-science general education course. Chapters 4 through 11 make up the core content, but even here there is room for flexibility. Chapters 12, 13, and 14 present approximately 60 diseases: some instructors assign them all, while others pick and choose representative diseases for each mode of transmission or choose those diseases in which students express the most interest.

Instructors can streamline content to fit the needs of the student population in their courses. For example, if the text is used for nonbiology majors who are not healthcare oriented, many topics in Part 1 of the text can be omitted from the course and the core chapters would be the focus for this group. For instructors teaching courses in which the majority of the students are pre-nursing majors, Chapters 6, 12, and 17 may be covered more quickly, with more time being spent on Parts 3 and 4 of the text (microbial diseases and meeting the challenge of microbial diseases). Instructors teaching an honors-level general biology course may spend more time on content related to bacterial genetics, the mechanisms of antibiotics, and the power and peril of microbes in applications and bioethics (e.g., development of vaccines, therapeutics, or food microbiology applications).

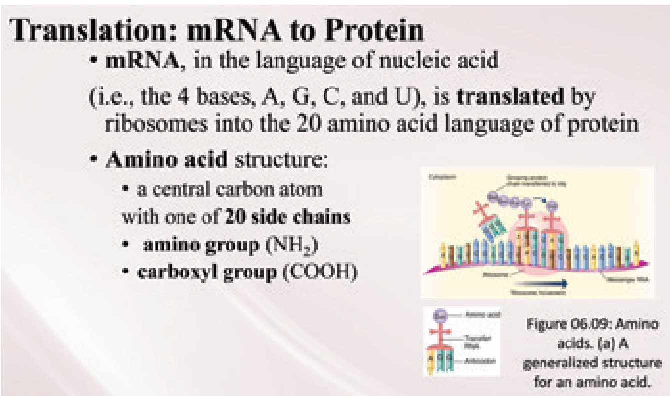
Depending on the class size and backgrounds of students in the course, the case studies can be used in group exercises or assigned separately. Instructors can pick and choose which questions students should answer. References to primary literature and URLs are provided for instructors but will be useful to students interested in more details about the subject matter.

The text uses a global approach with examples of disease outbreaks that occur in other parts of the world besides the United States. Those infectious diseases that might be endemic to the area where your students live would be of particular interest. Semester time restraints may dictate that a few chapters, or parts of chapters, be eliminated or assigned as self-study, depending on your own course design. This text can be easily adapted to a two-semester course by the addition of scientific papers, class discussion and debates, digital resources, demonstrations, and "hands-on" exercises that can be performed in the classroom or in the laboratory. Case studies in the primary literature, daily news broadcasts, and Internet resources, including relevant podcasts and YouTube content, can serve as excellent and timely supplements to the text.

Teaching Tools

We are pleased to offer a number of Teaching Tools to instructors using this book to help them prepare for their courses. These were updated for the Fourth Edition by Dr. Kathleen Seiler of Champlain College. All are available for digital download by contacting your Jones & Bartlett Learning Account Manager at go.jblearning.com/findmyrep.

- **Lecture Outlines in PowerPoint format** provides outline summaries of each chapter. The slide set can be customized to meet your classroom needs.
- The **Image Bank in PowerPoint format** provides all the illustrations and photos (to which Jones & Bartlett Learning owns the copyright or has permission to reprint digitally) inserted into PowerPoint slides. With the Microsoft® PowerPoint program you can quickly and easily copy individual image slides into your existing lecture slides.



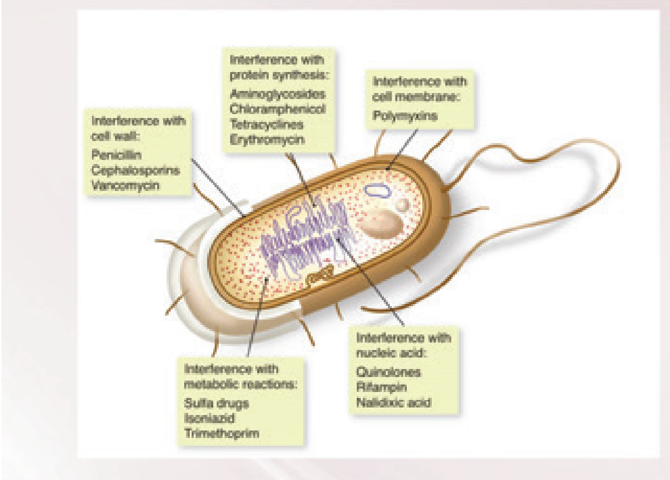


Figure 13.F16: Mechanisms of antimicrobial activity.

- The **Test Bank** contains more than 650 test items. A typical chapter file contains 15 multiple-choice objective questions, 15 short-answer questions, and 5 essay questions.
- A complete **Instructor's Manual** includes the Learning Objectives from the text for easy reference, a detailed Chapter Outline, Key Terms list, and a number of suggested In-Class Discussions and Activities for every chapter.
- A **Transition Guide** has been prepared to assist instructors who have used previous editions of the text with conversion to this new edition.
- Hand-selected lists of **Web Links** for each chapter will direct students and instructors to relevant Internet resources
- An **Answer Key to the Self-Evaluation Questions** has been prepared by the author and contributors.

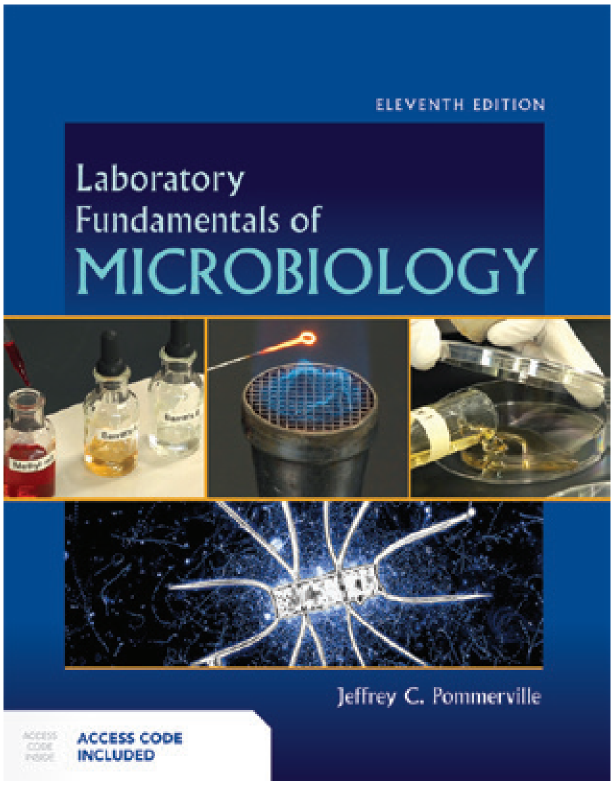
Laboratory Component

Most likely, this text will be used in courses that do not have a scheduled laboratory session. Nevertheless, you may be able to squeeze in some exercises that can be done as a demonstration or as a "hands-on" exercise in the classroom or in the laboratory. For example, you could use antibiotic disks to demonstrate antibiotic activity; you can even use prestreaked plates. The presence of bacteria in the environment and on and in the body can be shown by swabbing the floor, desk, a doorknob, and body parts (skin, throat, ear) and streaking the swabs on agar plates. Exercises using market-purchased yeasts are safe and inexpensive and can be used to demonstrate fermentation or disease transmission and other principles.

If your course does include a lab component or you are interested in more hands-on activities, Jones & Bartlett Learning has both print and digital resources to help you and your students succeed:

- ***Laboratory Fundamentals of Microbiology*** has been the trusted resource for providing undergraduate students a solid foundation of microbiology laboratory skills. Now, the completely modernized Eleventh Edition represents a lab manual revolution built for today's learners, focusing on the student's experience in the lab. Access to more than 100 minutes of 34 instructor-chosen, high-quality videos of actual students performing the most common lab skills, procedures, and techniques provides a seamless experience for the user. Within the manual, Sections and Exercises open with a list of relevant videos, and icons identify where students should refer to them to best prepare for each exercise. This encourages students to read, see, do, and connect with the material.

  In addition to the integration of videos, other significant updates to the Eleventh Edition include the new, full-color, easy-to-navigate interior design, with images from the videos found throughout the manual. Labs have been expanded and reorganized into new sections, such as "Laboratory Safety," "Population Growth," and "Immunology." The all-new Laboratory Safety section emphasizes a "culture of safety" approach to the microbiology lab. *Laboratory Fundamentals of Microbiology, Eleventh Edition* is the perfect companion to any modern microbiology course.



- If you don't need a printed lab manual for your course but still want to expose students to key laboratory skills, our ***Fundamentals of Microbiology Laboratory Video Series*** is available as a stand-alone product. In addition to 110 minutes of high-quality videos showing real students performing the most common lab skills, procedures, and techniques, Skills Checklists are available to record progress and assignability.

Acknowledgments

Writing and revising a textbook requires much focus and energy. Without the support of people in our daily lives, it would be nearly impossible to remain focused during the toughest of times. A few kind words of encouragement are what authors draw upon when their reserve energies are low. I especially acknowledge Sami Saydjari for his support of this writing project, enthusiasm for the impact of microbes and viruses on life (especially humans), and his willingness to critically review case studies and boxes from another textbook author's perspective outside of the field of microbiology despite his busy schedule. The support of this text and communications pertaining to microbiology-related topics and life in general with my former undergraduate mentor, colleague, and friend John Cronn were precious. It kept me grounded.

Developing a textbook is a daunting task requiring a harmonious partnership between authors and a publisher. Each has particular ideas, and there is no one right way to go about producing the best text possible. Ultimately, in a spirit of compromise, a book comes together of which all involved can be proud and that will enhance the college experience of the students who read it. In the preparation and publication of this text, Drs. Terri Hamrick and Nancy Boury were invited to revise and update chapters in the text. They breathed new life and content into this text, and I especially thank them for all of their hard work and efforts that extended during production of the book.

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ABOUT THE AUTHORS

Robert I. Krasner

Professor Emeritus Robert I. Krasner, a member of the Department of Biology at Providence College (PC) in Rhode Island, retired after 50 years of teaching and research starting in 1958. During his tenure, he developed new courses and mentored many students in research, many of whom went on to graduate and medical schools. Dr. Krasner's courses were popular, demanding, and embellished with humor. He was recognized on several occasions for excellence in teaching. The Robert I. Krasner Teaching Award was established upon his retirement at PC to recognize outstanding graduating seniors. He is the author of *20th Century Microbe Hunters*, many scientific papers, and a contributor to other scholarly works.

Dr. Krasner's love for travel was sparked by his service as a young army medical officer in Japan. He has spent sabbaticals and leaves of absence from PC at numerous domestic and foreign institutions, including Fort Detrick Army Biological Laboratories, Georgetown University School of Medicine, and those in Israel, Paris, Brazil, and London. At 69 years of age, he was accepted into the Harvard School of Public Health and earned a Master of Public Health (MPH) degree and is the oldest full-time student to have accomplished this.

Dr. Krasner founded and directed the Summer Science Program for high school students at PC from 1975 to 2006; the program hosted approximately 1,000 students in its 31 years of operation. During this time he also developed and directed several grant-funded microbiology and biotechnology workshops for high school teachers.

Over the years, Dr. Krasner presented over 60 research papers in the United States and abroad, including at numerous annual meetings of the American Society for Microbiology (ASM). Teaching remained his major interest, and when asked by colleagues "what (research) he was working on," his favorite reply was "students." His initiative in 1980 led to the establishment of the Division for Microbiology Educators within the ASM. After retirement he continued to lecture occasionally and enjoyed gardening, pet therapy, studio art, and playing the harmonica. Dr. Krasner passed away in 2014.

Teri Shors

Teri Shors has been a member of the Department of Biology and Microbiology at the University of Wisconsin–Oshkosh since 1997; she was promoted to the rank of Professor in 2010. Dr. Shors is a devoted teacher and researcher at the primarily undergraduate level and has been a recipient of university awards, including a distinguished teaching award and two endowed professorships. She has taught a variety of courses and laboratories and has made a strong contribution to the development of new courses in microbiology and molecular biology.

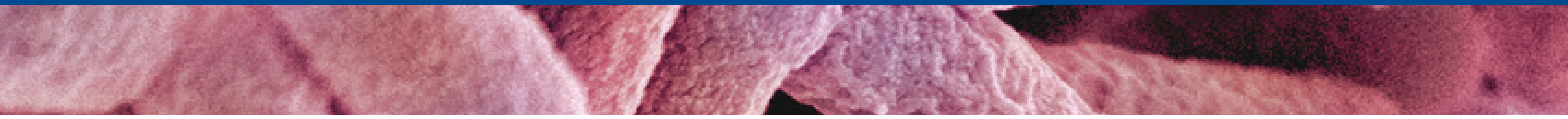
Dr. Shors' graduate and postgraduate education is virology based and is reflected in her research. Before teaching at University of Wisconsin–Oshkosh, she was a postdoctoral fellow in the Laboratory of Viral Diseases under the direction of Dr. Bernard Moss in the National Institute of Allergies and Infectious Diseases (NIAID) at the National Institutes of Health (NIH). While her expertise centers upon the expression of vaccinia virus genes, she was involved with research investigating cranberries and other fruits for the presence of antiviral compounds. This antiviral research was funded by a variety of granting agencies, including a prestigious Merck/AAAS award. She has mentored many students engaged in independent research and related readings projects.

Dr. Shors was the major contributor to the Fourth Edition of *Krasner's The Microbial Challenge*. She is also the author of *Understanding Viruses* (2013), now in its third edition, and *Encounters in Virology* (2012). She was a coauthor of *AIDS: The Biological Basis* (2015). Dr. Shors has contributed to and authored a variety of other texts and scientific papers.

Initiative, creativity, humor, networking, using current events and the latest technology in her courses, and leading collaborative, cross-disciplinary studies are hallmarks of Dr. Shors' talents and makes her popular among students in the classroom. She has recently developed and taught an online virology course for undergraduates.

PART 1

Discovery of Microbes and the History of Public Health



CHAPTER

PRE-GERM THEORY, MICROBIOLOGY, AND MEDICINE 1

OUTLINE

"The rapidly evolving outbreak of Zika warns us that an old disease that slumbered for 6 decades in Africa and Asia can suddenly wake up on a new continent to cause a global health emergency."

—World Health Organization (WHO)

Director-General Dr. Margaret Chan, May 23, 2016

Visualizing stained bacteria through a light microscope remains a common practice in clinical microbiology laboratories today.

LEARNING OBJECTIVES

1. Explain why it is important to know that microbes can cause infectious diseases.
2. Identify why it was necessary to visualize microbes with a microscope.
3. Summarize changes that occurred in hygiene practices during the Crimean War and the American Civil War.
4. Describe the barriers that female nurses encountered in the field of health care during the 19th century.
5. List at least three pioneers in medical microbiology and describe their contributions toward creating safer hospitals, obstetrics and neonatal care, and surgery practices before the germ theory of disease was established.
6. Summarize the history of hospitals and nursing in the United States and England in the 19th century.
7. Compare and contrast the organization of hospitals in the 19th century with that of hospitals today.
8. Describe the significance of the introduction of handwashing and antisepsis for wound treatment, surgical procedures, and management of childbirth.

Case Study: Wounded Civil War Soldiers Who Glowed in the Dark

The American Civil War (1861–1865) was the bloodiest war in U.S. history. Twice as many soldiers died of **infectious diseases** (diseases caused by **microorganisms** that can be transmitted to others) during the war than of battlefield injuries. Approximately 752,000 soldiers died, and countless others were left disabled. After the war ended, the state of Mississippi spent 20% of its annual budget on artificial limbs for its veteran soldiers.

The war was fought in over 10,000 locations. The Battle of Shiloh (also called the Battle of Pittsburg Landing) was fought April 6th and 7th, 1862, in Hardin County, Tennessee. Hardin County is located in the southwestern part of the state. The Confederate Army was defeated even though the Union Army had more casualties. Both sides were shocked at the carnage; the number of deaths was four times higher than it was at the Battle of Bull Run, just 10 months prior.

According to Confederate military records, at the Battle of Shiloh 1,728 were killed, 8,012 wounded, and 959 missing or captured, for a combined total of 10,699 Confederate casualties. Tragically, the cries of wounded and dying soldiers lying on the battlefield could be heard for days (**Figure 1**). Ulysses S. Grant wrote in his memoirs that:

> *I saw an open field, in our possession on the second day, over which the Confederates had made repeated charges the day before, so covered with dead that it would have been possible to walk across the clearing, in any direction, stepping on dead bodies, without a foot touching the ground.*

An unusual phenomenon was observed among the wounded soldiers that was not witnessed among those injured in other battles. It was referred to as the **Angel's Glow**. As soldiers lied on the battlefield waiting for treatment, their wounds glowed faintly blue at night. Interestingly, the wounds that glowed in the dark healed more quickly than those wounds that did not glow. Hence, the term *Angel's Glow* to describe the wounds. The cause of these glow-in-the-dark wounds was a mystery until 17-year-old Bowie High School student Bill Martin and his family visited the Tennessee Civil War battlefield in 2001. As soon as he heard the tales of the enigmatic glowing wounds, he immediately thought about his mother's research on a glowing, or **bioluminescent**, bacterium, *Photorhabdus luminescens*. Bill's mother was a microbiologist at the Agricultural Research Service (ARS) Plant Science Institute in Beltsville, Maryland. He asked his mother if *Photorhabdus* could have caused the soldiers wounds to glow (because *Photorhabdus* emits light) and heal more quickly. His mother suggested that Bill, along with his friend Jonathon Curtis, collect soil from

(*continues*)

Case Study: Wounded Civil War Soldiers Who Glowed in the Dark (continued)

Library of Congress Civil War Collection.

Figure 1 Casualties at Shiloh. Watercolor by artist Adolph Metzner, dated April 7, 1862, illustrating the bloodshed of this battle.

the battlefield and try to isolate bioluminescent bacteria in the research laboratory.

Bill and Jonathon isolated three different strains of *P. luminescens* from the swampy Tennessee battlefield soil. However, because *Photorhabdus* is a soil **bacterium**, the two high school seniors wondered if the bacteria could multiply in the wounds of soldiers at body temperature (37°C or 98.6°F). Experiments in which they incubated the bacterial cultures at 37°C (98.6°F) resulted in no colonies on bacteriological media. While this seemed to put a damper on their hypothesis that *Photorhabdus* was multiplying in the wounds of the soldiers, they decided to further research the weather and temperature conditions during and after the Battle of Shiloh. They learned that there was a thunderstorm on the eve of the first day of battle. Wounded soldiers were stuck in the cold muck for a day or longer as they waited for medics to carry them off the battlefield and attend their wounds. They developed **hypothermia**. Hypothermia occurs when the body rapidly loses heat, causing the body temperature to deteriorate below 35°C (95°F). Therefore, the idea emerged that *Photorhabdus* could possibly multiply in the wounds of cold, hypothermic soldiers.

As they continued their research, Bill was curious if and how *Photorhabdus* could be involved in the healing process of battle wounds. First, they gathered research to learn more about the traits of *P. luminescens* and what is known about its role in the soil ecosystem. Typically, bioluminescent bacteria such as *Vibrio*, *Shewanella*, and *Photobacterium* live in the guts of marine animals, whereas *P. luminescens* is a terrestrial (soil) bacterium.

P. luminescens lives in the midgut of a species of **nematodes**, *Heterorhabditis bacteriophora* (**Figure 2**). The two organisms maintain a mutualistic relationship. A **mutualism** is a form of **symbiosis** in which both organisms benefit by living together. The bacteria infect and colonize the midgut of nematodes present in the soil. The nematode serves as a **host** for the symbiont bacteria to multiply when the appropriate nutrients are available. The nematodes infect insect larvae present in the soil and subsequently regurgitate the *P. luminescens* bacteria. The bacteria release insecticidal **crystal toxins** into the hemolymph (similar to the bloodstream in humans) of the larvae, killing the larvae but not harming their nematode host (therefore, the nematodes benefit from hosting the bacteria). At the same time, the bacteria produce antibiotics that kill or inhibit scavengers and competing bacteria, preventing them from colonizing the nematode host. The regurgitated *Photorhabdus* bacteria secrete **exoenzymes** (**proteases** and **lipases**) that convert the carcass of the larvae into nutrients that both the nematode and bacteria can utilize, allowing both to grow and multiply. The nematodes reproduce inside of the dead larvae, and as adults search for more prey. The life cycle illustrating the symbiotic phase and insect pathogenic phase is shown in **Figure 3**.

Bill and Jonathon were excited to learn that *P. luminescens* produces antibiotics in order to deter other scavenger and insect microbes from colonizing the nematodes or stealing nutrients from the dead insect carcass. One of the main antibiotics produced by *P. luminescens* are **carbapenems**, **broad-spectrum antibiotics** that kill both **Gram (+)** and **Gram (–) bacteria**.

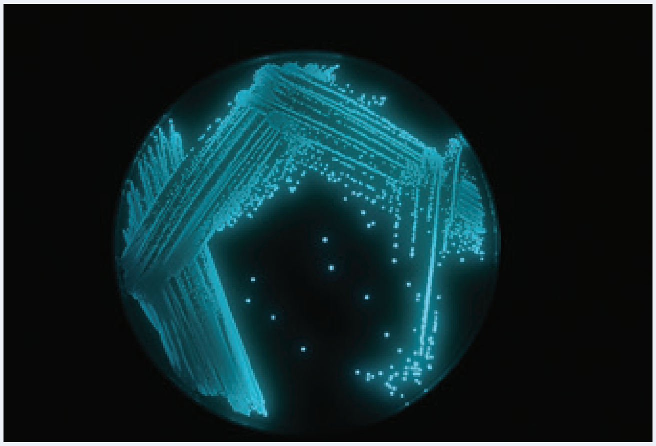


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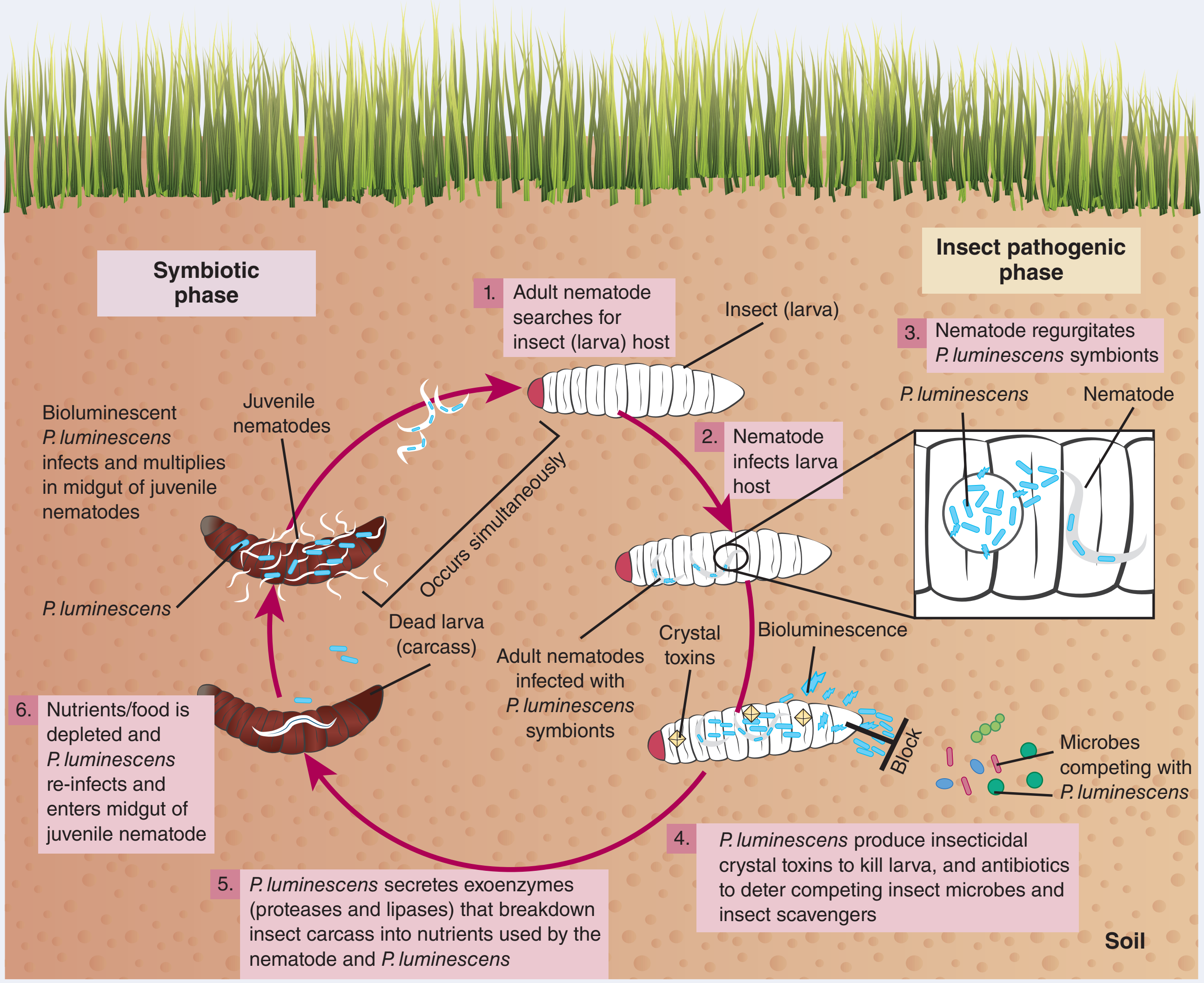
Figure 2 These colonies of bioluminescent bacteria growing on the solid media in the petri plate glow light blue, similar to the bioluminescence emanating from the wounds of soldiers at the Battle of Shiloh.



Information from M. E. Hoinville & A. C. Wollenberg. (2018). Changes in *Caenorhabditis elegans* gene expression following exposure to *Photorhabdus luminescens* strain TT01. *Developmental and Comparative Immunology, 82*, 165–176.

Figure 3 Illustration of the life cycle between *Heterorhabditis bacteriophora* nematodes and *Photorhabdus luminescens* that depicts their mutualistic relationship. Bioluminescence is most intense when *P. luminescens* is free-living (due to being regurgitated from the nematode inside of a larval host) outside of its host during the insect-pathogenic phase. The insecticidal insoluble crystal toxin complexes produced by *P. luminescens* are similar to toxins produced by *Yersinia pestis*, the bacterium that caused the **plague**, or **Black Death**, that swept through Asia and Europe during the mid-1300s, killing 25 million people.

Bill and Jonathon believed it was highly likely that the antibiotics produced by *P. luminescens* could kill bacteria causing infections in the wounds of soldiers. They performed experiments to demonstrate that their isolated strains of *P. luminescens* also produced antibiotics. The mystery of the Angel's Glow had been solved. Bill Martin and Jonathon Curtis entered their research into the 2001 Intel International Science and Engineering Fair, an annual science fair competition for innovative high school students around the world. They won first prize!

Questions and Activities

1. Define *symbiosis*. Describe the symbiotic relationship between *P. luminescens* and *H. bacteriophora*.
2. What happens if *H. bacteriophora* nematodes are not infected with *P. luminescens*? Can the nematodes survive without the bacteria? What challenges do the nematodes face if they can survive without it? Explain.
3. *P. luminescens* cannot be directly isolated from soil. How were the students able to isolate and identify three different strains of this bacterium from the Civil War battlefield in Tennessee? (Hint: think about symbiosis.)
4. What is bioluminescence? List four bacterial genera that produce bioluminescence and identify their hosts.

(*continues*)

Case Study: Wounded Civil War Soldiers Who Glowed in the Dark (continued)

5. Why did the glowing wounds of soldiers heal faster than the wounds that did not glow?
6. Is it possible that *P. luminescens* could be used as an insecticide to kill crop pests in agricultural applications? Explain.
7. In the laboratory, *P. luminescens* multiplies best at 30ºC (86ºF). Explain why there was the possibility that these bacteria could multiply in the wounds of the soldiers given the fact that normal body temperature is 37ºC (98.6ºF).
8. *P. luminescens* colonies produce red pigments and emit blue light (bioluminescence). Hypothesize the role these traits may play in their relationship with nematodes. What role might they play with competing microbes in the environment? How could you test for this in the laboratory?
9. Some bacteria communicate with each other through **quorum sensing (QS)**. When present in high density, or a *quorum*, quorum-sensing bacteria perform group behavior(s) or metabolic activities. What group activities are *P. luminescens* bacteria involved in after being regurgitated from their nematode hosts? (See Figure 3.)

Information based on F. L. Inman III, S. Singh, & L. D. Holmes. (2012). Mass production of the beneficial nematode *Heterorhabditis bacteriophora* and its bacterial symbiont *Photorhabdus luminescens. Indian Journal of Microbiology, 52*, 316 -324; Glowing wounds, Science NetLinks. Retrieved from http://sciencenetlinks.com/science-news/science-updates/glowing-wounds/

Preview

At one time or another, everyone has been reminded to wash their hands in order to prevent the spread of germs that can cause disease. It may be hard to imagine that it took centuries to debunk the theory of **spontaneous generation** or dispel the belief that "bad air" or **miasmas** were the main source of sickness and death in hospitals.

This chapter retraces some of the earliest insights into the prevention of infectious diseases before the **germ theory of disease** and **Koch's postulates** were established within the medical community. The notion that microbes can cause infectious diseases did not come with the invention of the microscope, but instead was based on critical observations of hospital infection-control practices used in surgery and delivering babies. The attempts to solve the problem of infections were unrelenting. Medicine remains an experimental science that takes dedication, persistence, and the willingness to make changes in patient care and hygiene practices in order to prevent infections and their spread.

The Origin of Life and Spontaneous Generation

The origin of life was a subject of debate for early thinkers. Two trains of thought predominated: (1) all life was derived from preexisting life and (2) living things emerge from nonliving things, also known as *spontaneous generation*. According to spontaneous generation, plants, insects, and animals emerged from nonliving objects. This was the generally accepted view for centuries. People based beliefs on their interpretations of untested observations of the world around them. They did not use the **scientific method**. For example, it was believed that frogs and salamanders spontaneously arose from mud. This is because people observed that in the springtime rivers would flood certain locations. When the floodwaters receded, large numbers of frogs and salamanders were observed in the mud. Scholars such as Aristotle rationalized that the mud must have given rise to the frogs and salamanders. Of course, today, we know this is not the case.

Other beliefs were that sewage and dirty rags gave rise to rats, fireflies came from morning dew, rotting meat was a source of flies, oysters materialized from the sea, and fish and eels came from riverbeds and sand. These beliefs became fodder for recipes to create life. In the 17th century, Belgian physician and chemist Johannes (also spelled Jean or Johann) Baptiste van Helmont (1579–1644) devised recipes for producing mice, bees, and scorpions (**FIGURE 1.1A–C**) and set up a 5-year willow tree experiment in which he justified that water created the wood, bark, and leaves of the willow tree (**FIGURE 1.1D**). His experiments at the time seemed to reinforce support for the belief in spontaneous generation. The view that spontaneous generation explained the origin of life was generally believed for more than 2,000 years, from 340 B.C. to approximately 1870 A.D.

Visualizing Germs

Even though there were observations and reports of microorganisms by individuals in the 1600s, the accounts were ignored for about 200 years. Robert Hooke and Anton van Leeuwenhoek are credited with developing the first instruments for biological investigations in which one could observe and document microorganisms that were too small to be seen by the naked eye. However, neither Hooke nor van Leeuwenhoek made the

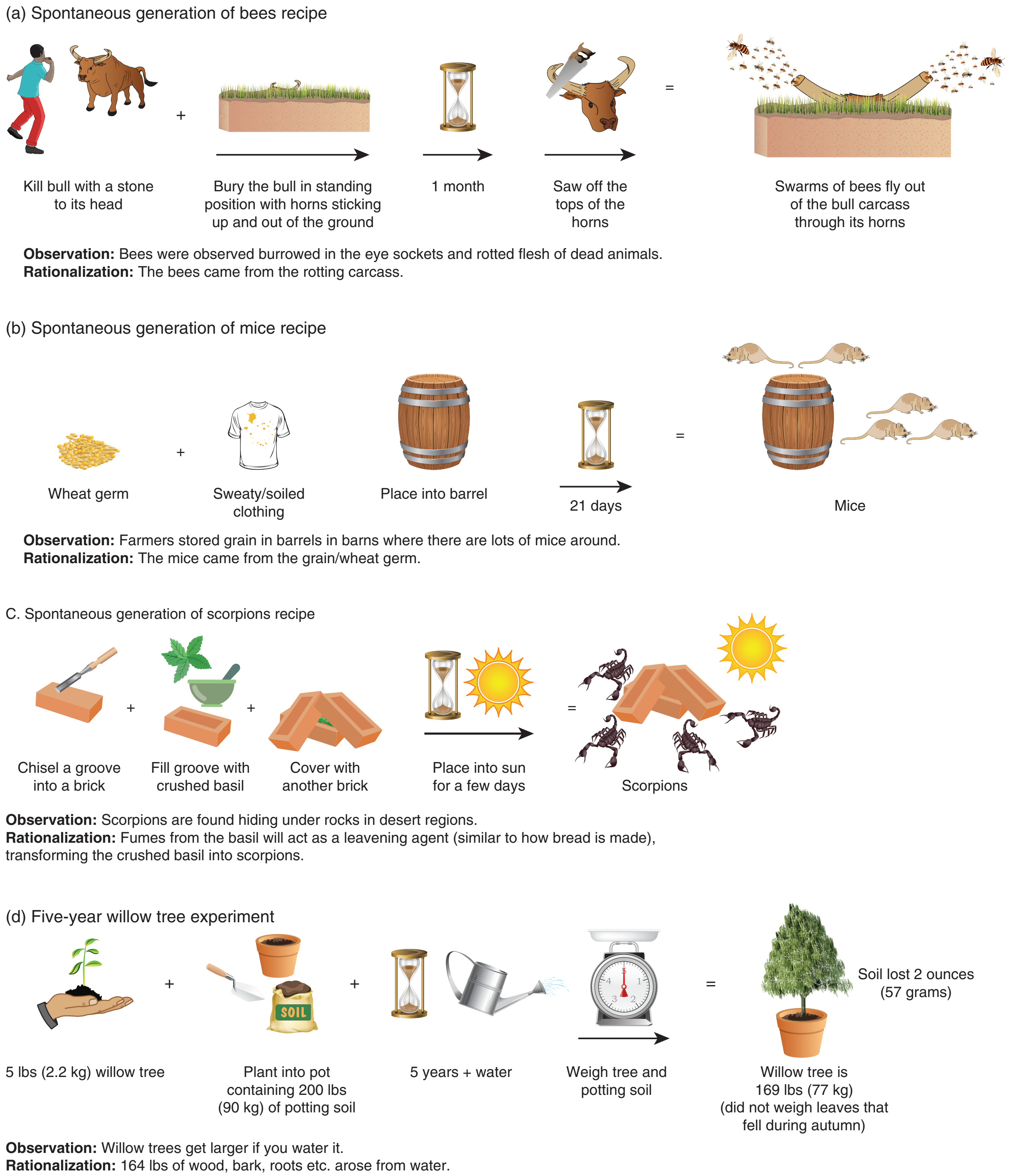


FIGURE 1.1 Van Helmont's spontaneous generation recipes and experiments during the 1600s. His conclusions were based on superficial observations. **(a)** Recipe for bees. **(b)** Recipe for mice. **(c)** Recipe for scorpions. **(d)** Five-year willow tree experiment.

connection that microorganisms play a role in causing infectious diseases.

Robert Hooke

Robert Hooke (1635–1703) wore many different hats. He was a curator and fellow of the Royal Society in London, a natural philosopher (today the term used would be scientist), an architect, an astronomer, surveyor of the City of London, and an inventor. He is credited with coining the term *cell*, which is still used in biology today. Hooke was one of the inventors of the first **compound microscope**, which he used to magnify and resolve living things

© The Royal Society.

FIGURE 1.2 Copperplate engraving of an illustration based on the microscopic observation of blue mold growing on leather in Micrographica as Figure Schem XII. It is the first published image of a microorganism. The mold is likely of the genus Mucor. Sporangia, reproductive structures, are identified by letters A–D.

35 times their normal size. He examined thin slices of cork from the bark of an oak tree, bones, insects, plants, and mold. He published his observations in his book, *Micrographica: or Some Physiological Descriptions of Minute Bodies Made by Magnifying Glasses with Observations and Inquiries Thereupon*, published in 1665. Because of the limitations of magnification at 35×, it was difficult for Hooke to learn much about the internal structures and organization of cells. **FIGURE 1.2** is Hooke's illustration of the microscopic view of blue mold growing on leather.

Anton van Leeuwenhoek

"I'm well aware that my writings will not be accepted by some, as they judge it to be impossible to make such discoveries. . . . [but] I will say once more that 'tis my habit to hold fast to my notions only until I'm better informed or till my observations make me go over to others."

—Anton van Leeuwenhoek, amateur microbiologist (excerpt taken from English translations given by Dobell, 1932)

Anton van Leeuwenhoek (1632–1702; also spelled Antoni, Antonie, and Antony) was born into a large family in Delft, Holland. Like Hooke, van Leeuwenhoek also wore many hats. At the age of 15 or 16, he was sent to school in Amsterdam to learn how to master the linen-draper trade (wholesaler of linen goods and related items). After completing school, he set up his own drapery business in Delft, married twice, had children, and remained there his entire life. He also became the town surveyor, an honorary sheriff, the executor of an artist's estate, and the official wine gauger. The wine gauger tasted and measured all wine and spirits entering Delft. Van Leeuwenhoek lived to be 91 years old. Is it possible that his position as the wine gauger contributed to his longevity?

At the age of 36, during a trip to London, van Leeuwenhoek was given a copy of *Micrographia*, which he read with the help of English friends who acted as translators. He was literally "hooked"! van Leeuwenhoek began his journey as an amateur microbiologist. He ground and polished lenses made from glass, sand, and rock crystal and built **simple microscopes**. In his lifetime, he made about 500 simple microscopes and lenses that could magnify specimens from 32× to 266×. The microscopes were tiny handheld devices like the one illustrated in **FIGURE 1.3**. A lens was mounted between two brass plates and was held close to the eye. He also held it up toward the bright light while observing samples.

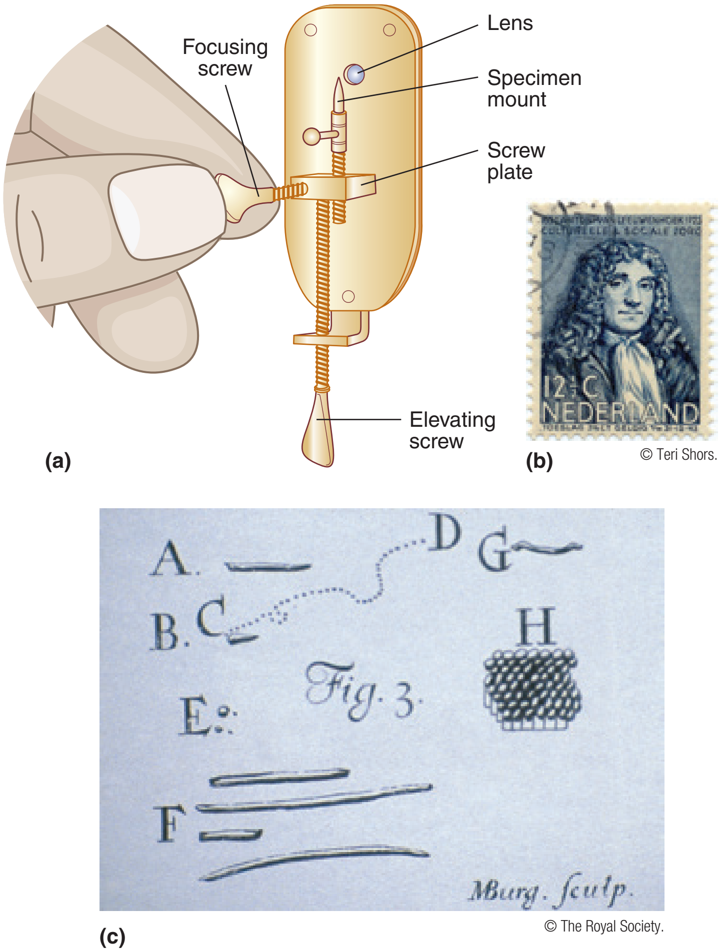


FIGURE 1.3 **(a)** Illustration of a replica of van Leeuwenhoek's simple microscope being held by a human hand. Observations of specimens were made by applying the eye at a distance of 1 centimeter (0.4 inches) or less. Note that it is so small (the entire instrument was less than 50 millimeters, or 2.2 inches, in length) that the brass body of the instrument was the size of a postage stamp! **(b)** 1937 Anton van Leeuwenhoek Nederland Commemorative Postage Stamp. **(c)** Anton van Leeuwenhoek sketched bacteria from his mouth, which are shown here. The dotted lines from the letter C to D in the illustration represent movement.

van Leeuwenhoek discovered the invisible world. Even though he had no medical or anatomy training, his record keeping was exceptional. He kept detailed sketches and notes describing everything he observed microscopically (Figure 1.3C). He is credited with reporting the first known descriptions of microorganisms. Many of his discoveries were communicated by letter to the Royal Society of London, of which he became a non-British member. The letters were published in the most prestigious scientific publication at the time, *Philosophical Transactions of the Royal Society*. It was the first journal in the world dedicated solely to science.

For over 60 years, as an amateur microbiologist, van Leeuwenhoek described freshwater samples that had hundreds of tiny moving particles, which he thought were small, living animals, which he called **animalcules**. He also observed samples that included teeth scrapings, saliva, soil, rainwater, well water, seawater, spices, mold, algae, wine, blood, rabbit feces, plant matter, food, millet seeds, bone, teeth, vinegar eels (nematodes), lice, frog eggs, and even the sperm of rabbits, lambs, and codfish. His passion for microscopy was indefatigable. He was able to observe a wide variety of microorganisms, including bacteria. At the time of his discoveries, van Leeuwenhoek did not make the connection that the animalcules, or **microbes**, also caused disease. For this reason, even though his scientific contributions to society were impressive at the time of his work, very little was known about them until 200 years after his death.

Battlefield Medicine

The Crimean War of 1853–1856 and the American Civil War of 1861–1865 were two of the bloodiest wars in human history. It is estimated that more than 1 million soldiers died during the Crimean War and about 752,000 during the American Civil War. Countless soldiers were left disabled after the wars ended. Not enough doctors were available to handle battlefield injuries and disease. The doctors themselves were woefully unprepared. Medical training was not standardized. Surgeons were inexperienced. Doctors were practicing before the germ theory of disease (the recognition that microbes caused infectious diseases that could spread from person to person) was established. Few medicines were available. Knowledge of sterile technique or the use of antiseptics was nonexistent. Poor sanitation and overcrowding in camps contributed to deaths from wound infections and noncombat diseases.

Despite this, many medical innovations occurred as a result of dedicated medical staff. *Both wars gave birth to the modern nursing profession*. Capable nurses were needed to care for large numbers of sick and wounded soldiers. Before this time, nurses in the United States cared for the sick within the home, which usually occurred when epidemics swept through towns and cities.

The Crimean War and Florence Nightingale, the Sanitarian

In 1853, the Russian military invaded Turkey. Out of concern over Russia's growing power, Britain and France deployed troops to support the Turkish military. Most of the war was fought on the Crimean Peninsula. The most famous engagement of the Crimean War, known as the Charge of the Light Brigade, took place on October 25, 1854, at the Battle of Balaclava (also spelled Balaklava). The British, led by Lord Cardigan, along with allied soldiers from Turkey and France, fought against the Russians.

Approximately 670 British soldiers on horses were armed with sabers and ordered (through a miscommunication blunder) to proceed down the valley to capture Russian guns in the surrounding hills. Alfred Lord Tennyson wrote the poem titled "*The Charge of the Light Brigade*" to memorialize the event. He wrote: "*Theirs not to reason why, theirs but to do and die, into the valley of Death rode the six hundred*." The British were forced to retreat. Hundreds of soldiers and horses were wounded and killed by Russian cannon and rifle fire or captured as they charged to bottom of the valley in a mere 7.5 minutes of battle.

The Turks offered the British the use of their army barrack hospital located in Scutari (now Uskudar, Turkey) to care for the wounded and sick soldiers of the Light Brigade. Florence Nightingale (1820–1910) was asked by the head of Britain's War Office, Sydney Herbert, to be the superintendent of all female nurses in the British military hospitals in Turkey. She was to train female nurses to care for the soldiers in Scutari. Prior to this, she was the superintendent at the Institute for the Care of Sick Gentlewomen on Upper Harley Street, London, and a volunteer nurse to cholera patients at the Middlesex Hospital during the epidemic of 1854. Each volunteer nurse was offered a uniform, free meals, weekly wages, and a bed for her work. Nightingale was also provided with food and supplies, and she brought with her a sizeable amount of funding collected through her personal efforts.

Florence Nightingale arrived at Scutari 5 days after the Battle of Balaclava with a group of 38 voluntary nurses from England. They went directly to the Selimiye Barrack Hospital. Prejudiced surgeons who believed female nurses were risqué and drank too much alcohol did not welcome them and prevented them from caring for the wounded and sick soldiers. (There were British male nurses at the time, but their numbers were few and their work was limited to British insane asylums because of their superior strength to restrain violent patients.)

Nightingale immediately tasked the nurses with preparing meals using portable stoves. She delegated the nurses to sew large bags together and fill them with straw to use as beds, and to wash and mend the tattered bed linens. The men were lacking basic needs such as cutlery