

Marjorie Kelly Cowan

with Jennifer Bunn, RN

Microbiology FUNDAMENTALS

Second Edition

A Clinical Approach

Clinical Insights

Tips and stories from a practicing nurse

Digital Tools

Focused on learning outcomes to help you achieve your goals

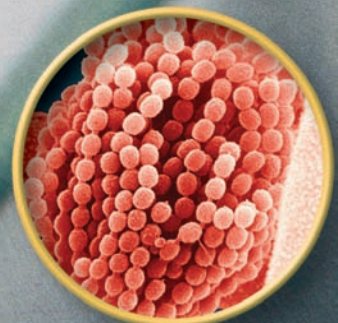
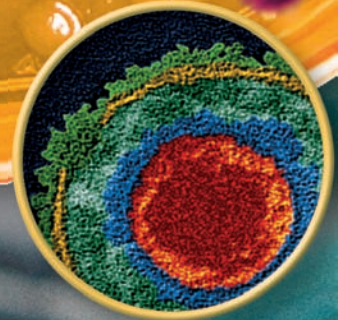
NCLEX®-Style Questions

Inside & Online!

New Chapter: *One Health* by Ronald M. Atlas

The Interconnected Health of the Environment, Humans, and Other Animals

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A close-up photograph of a petri dish containing a bacterial culture. The medium is a light orange color, and there are numerous small, yellowish, circular colonies scattered across the surface. Some colonies are larger and more distinct, while others are smaller and more numerous. The petri dish is shown from a slightly elevated angle, with the lid partially visible at the top.

Microbiology

FUNDAMENTALS

A Clinical Approach

SECOND EDITION

Marjorie Kelly Cowan

Miami University Middletown

WITH

Jennifer Bunn

RN, Clinical Advisor

Ronald M. Atlas

University of Louisville
Contributor

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Digital Author

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Contributed by Ronald M. Atlas

About the Authors



Kelly Cowan, PhD, has been a microbiologist at Miami University since 1993, where she teaches microbiology for pre-nursing/allied health students at the university's Middletown campus, a regional commuter campus that accepts first-time college students with a high school diploma or GED, at any age. She started life as a dental hygienist. She then went on to attain her PhD at the University of Louisville, and later worked at the University of Maryland's Center of Marine Biotechnology and the University of Groningen in The Netherlands. Kelly has published (with her students) 24 research articles stemming from her work on bacterial adhesion mechanisms and plant-derived antimicrobial compounds. But her first love is teaching—both doing it and studying how to do it better. She is past chair of the Undergraduate Education Committee of the American Society for Microbiology (ASM). When she is not teaching or writing, Kelly hikes, reads, and still tries to (s)mother her three grown kids.

Jennifer Bunn, RN, is a registered nurse, having spent most of her career in rural medicine, where she has had the opportunity to interact with patients of all ages. Her experience includes emergency medicine and critical care, pediatrics, acute care, long-term care, and labor and delivery. Currently, Jennifer works on an acute care unit. Over the span of her career, she has enjoyed mentoring and precepting LPN and RN students. Jennifer writes medical content for websites, apps, and blogs.



Ronald M. Atlas is Professor of Biology at the University of Louisville. He was a postdoctoral fellow at the Jet Propulsion Laboratory where he worked on Mars Life Detection. He has served as President of the American Society for Microbiology, as cochair of the American Society for Microbiology Biodefense Committee, as a member of the DHS Homeland Security Science and Technology Advisory Committee, and as chair of the Board of Directors of the One Health Commission. He is author of nearly 300 manuscripts and 20 books. His research on hydrocarbon biodegradation has helped pioneer the field of petroleum bioremediation. He has performed extensive studies on oil biodegradation and has worked for both Exxon and the U.S. EPA as a consultant on the *Exxon Valdez* spill and for BP on the *Deepwater Horizon* spill in the Gulf of Mexico.



Heidi Smith leads the microbiology department at Front Range Community College, Fort Collins, Colorado. Student success is a strategic priority at FRCC and a personal passion of Heidi's. Collaboration with other faculty across the nation, the development and implementation of new digital learning tools, and her focus on student learning outcomes have revolutionized her face-to-face and online teaching approaches and student performance in her classes. Outside of the classroom, Heidi served as the director of the FRCC Honors Program for six years, working with other faculty to build the program from the ground up. She is also an active member of the American Society for Microbiology and participated as a task force member for the development of their Curriculum Guidelines for Undergraduate Microbiology Education. Off campus, Heidi spends as much time as she can enjoying the beautiful Colorado outdoors with her husband and three young children.



Preface

Students:

Welcome! I am so glad you are here. I am very excited for you to try this book. I wrote it after years of frustration, teaching from books that didn't focus on the right things that my students needed. My students (and, I think, you) need a solid but not overwhelming introduction to microbiology and infectious diseases. I asked myself: What are the major concepts I want my students to remember 5 years from now? And then I worked backward from there, making sure everything pointed to the big picture.

While this book has enough detail to give you context, there is not so much detail that you will lose sight of the major principles. Biological processes are described right next to the illustrations that illustrate them. The format is easier to read than most books, because there is only one column of text on a page and wider margins. The margins gave me space to add interesting illustrations and clinical content. My coauthor, Jennifer Bunn, is a nurse who brings her years of experience to life on the page and shows you how this information will matter to you when you are working as a health care provider. We have interesting and up-to-the-moment Case Files, Medical Moments, Inside the Clinic selections, and NCLEX® questions in every chapter. Also be sure to use the Connect content—this is where you can really take control of your success in the class by making use of as many of the tools as you need.

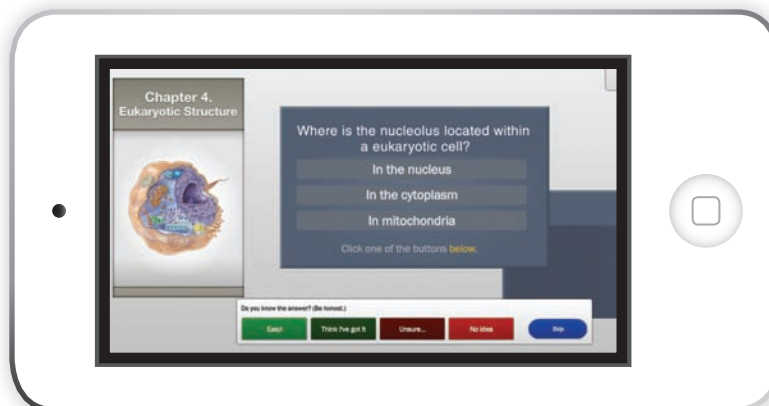
I really wanted this to be a different kind of book. I started using it in my own classes and my students love it! Well, maybe they have to say that, but I hope that you truly do enjoy it and find that it is a refreshing kind of science book.

—Kelly Cowan

I dedicate this book to Ted.

McGraw-Hill LearnSmart® is one of the most effective and successful adaptive learning resources available on the market today. More than 2 million students have answered more than 1.3 billion questions in LearnSmart since 2009, making it the most widely used and intelligent adaptive study tool that's proven to strengthen memory recall, keep students in class, and boost grades. Students using LearnSmart are 13% more likely to pass their classes, and 35% less likely to drop out.

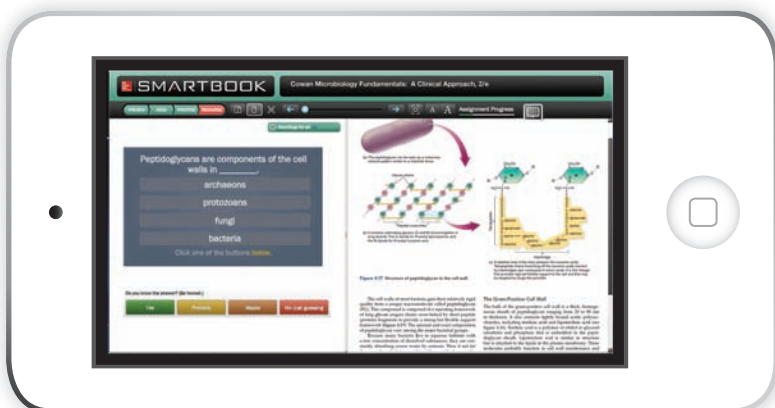
LearnSmart continuously adapts to each student's needs by building an individual learning path so students study smarter and retain more knowledge. Turnkey reports provide valuable insight to instructors, so precious class time can be spent on higher-level concepts and discussion.



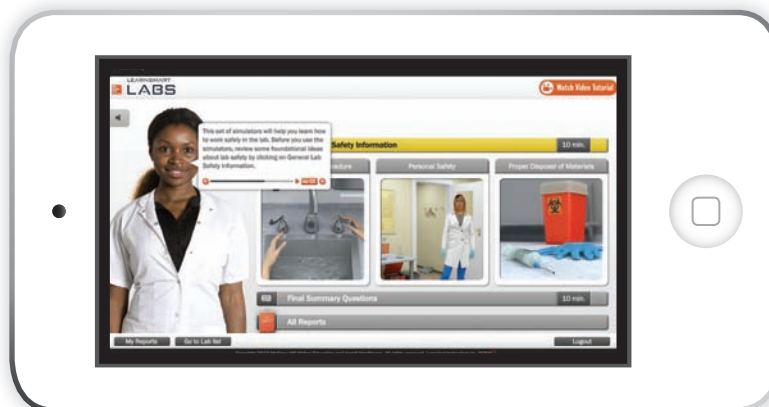
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As a result of the adaptive reading experience found in SmartBook, students are more likely to retain knowledge, stay in class, and get better grades.



LearnSmart Labs® is an adaptive simulated lab experience that brings meaningful scientific exploration to students. Through a series of adaptive questions, LearnSmart Labs identifies a student's knowledge gaps and provides resources to quickly and efficiently close those gaps. Once students have mastered the necessary basic skills and concepts, they engage in a highly realistic simulated lab experience that allows for mistakes and the execution of the scientific method.



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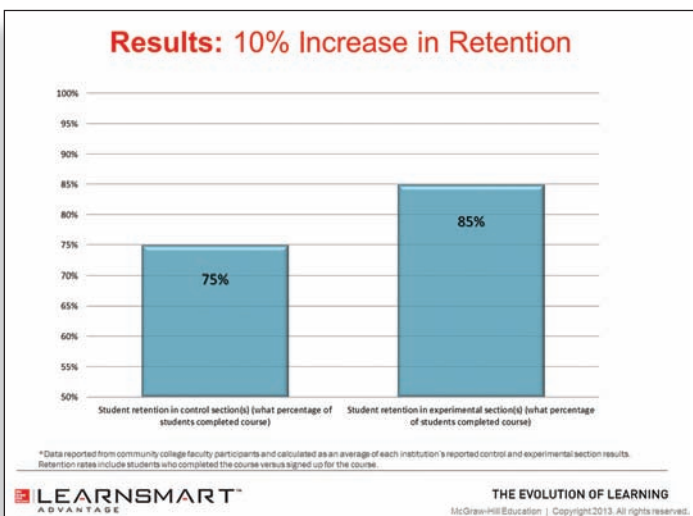
Digital efficacy study shows results!

Digital efficacy study final analysis shows students experience higher success rates when required to use LearnSmart.

- Passing rates increased by an average of **11.5%** across the schools and by a weighted average of **7%** across all students.
- Retention rates increased an average of **10%** across the schools and by a weighted average of **8%** across all students.

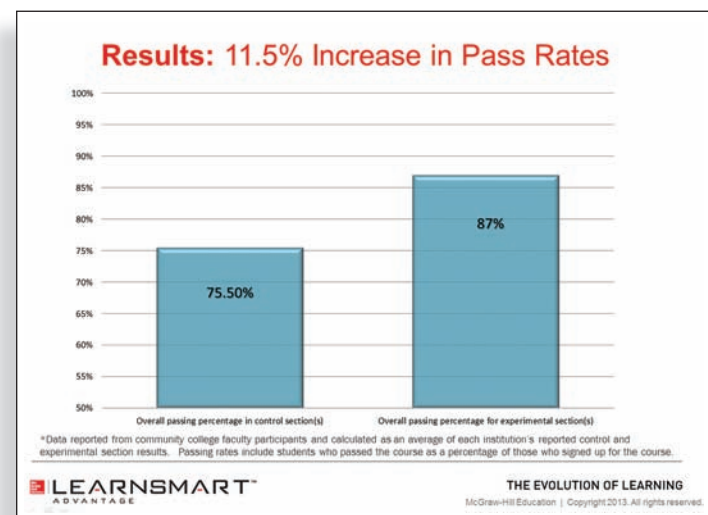
Study details:

- Included two state universities and four community colleges.
- Control sections assigned chapter assignments consisting of testbank questions and the experimental sections assigned LearnSmart, both through McGraw-Hill Connect®.
- Both types of assignments were counted as a portion of the grade, and all other course materials and assessments were consistent.
- 358 students opted into the LearnSmart sections and 332 into the sections where testbank questions were assigned.



"Use of technology, especially LearnSmart, assisted greatly in keeping on track and keeping up with the material."

—student, Triton College



"LearnSmart has helped me to understand exactly what concepts I do not yet understand. I feel like after I complete a module I have a deeper understanding of the material and a stronger base to then build on to apply the material to more challenging concepts."

—Student

"After collecting data for five semesters, including two 8-week intensive courses, the trend was very clear: students who used LearnSmart scored higher on exams and tended to achieve a letter grade higher than those who did not."

—Gabriel Guzman, Triton College

"This textbook was selected due to the LearnSmart online content as well as the fact that it is geared for an allied health student. This textbook has certainly enhanced the classroom experience and I see that my students are better prepared for class after they have worked within LearnSmart."

—Jennifer Bess, Hillsborough Community College

Connecting Instructors to Students

McGraw-Hill Connect® Microbiology



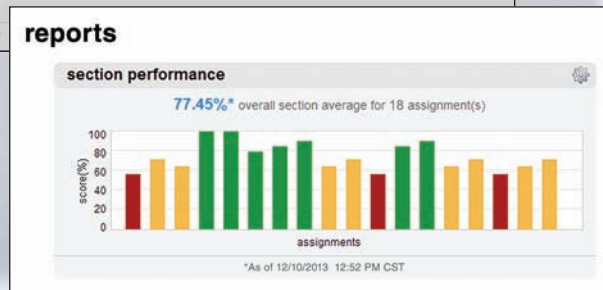
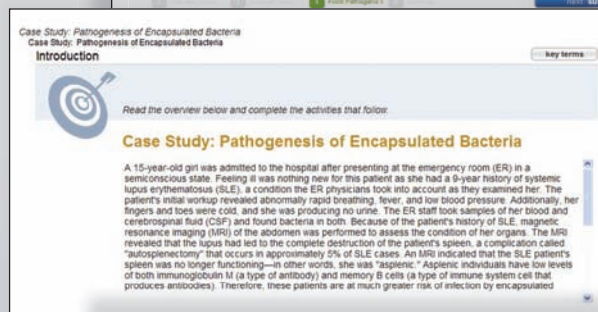
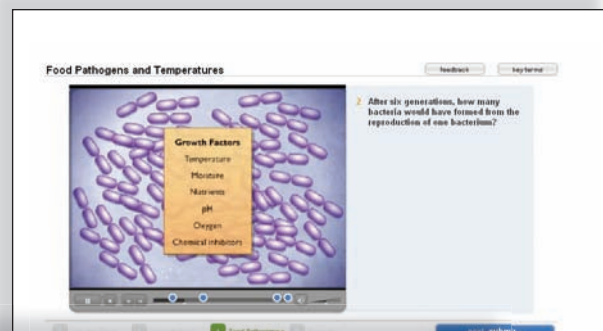
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MICROBIOLOGY

McGraw-Hill Connect Microbiology is a digital teaching and learning environment that saves students and instructors time while improving performance over a variety of critical outcomes.

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- Digital images, PowerPoint® lecture outlines, and instructor resources are also available through Connect.
- All Connect questions are tagged to a learning outcome, specific section and topic, ASM topics and curriculum guidelines, and Bloom's level for easy tracking of assessment data.

Visit www.mcgrawhillconnect.com.



connect

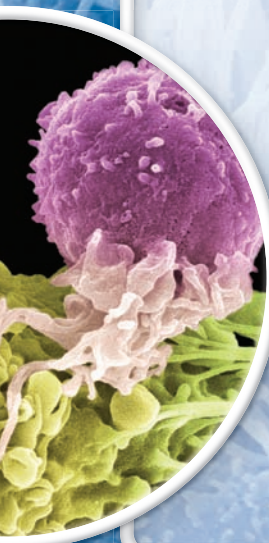
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Connect Insight® is a powerful data analytics tool that allows instructors to leverage aggregated information about their courses and students to provide a more personalized teaching and learning experience.




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Through Innovative Digital Solutions

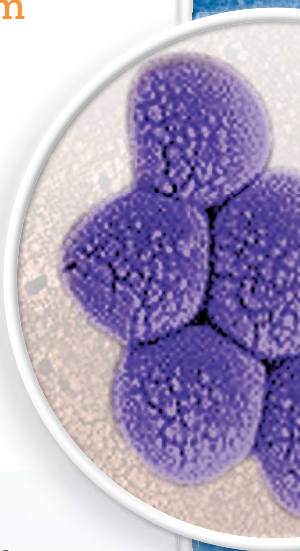
Unique Interactive Question Types in Connect, Tagged to ASM's Curriculum Guidelines for Undergraduate Microbiology

- 1 Case Study:** Case studies come to life in a learning activity that is interactive, self-grading, and assessable. The integration of the cases with videos and animations adds depth to the content, and the use of integrated questions forces students to stop, think, and evaluate their understanding. Pre- and post-testing allow instructors and students to assess their overall comprehension of the activity.
- 2 Concept Maps:** Concept maps allow students to manipulate terms in a hands-on manner in order to assess their understanding of chapter-wide topics. Students become actively engaged and are given immediate feedback, enhancing their understanding of important concepts within each chapter.
- 3 What's the Diagnosis:** Specifically designed for the disease chapters of the text, this is an integrated learning experience designed to assess the student's ability to utilize information learned in the preceding chapters to successfully culture, identify, and treat a disease-causing microbe in a simulated patient scenario. This question type is true experiential learning and allows the students to think critically through a real-life clinical situation.
- 4 Animations:** Animation quizzes pair our high-quality animations with questions designed to probe student understanding of the illustrated concepts.
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- 6 Labeling:** Using the high-quality art from the textbook, check your students' visual understanding as they practice interpreting figures and learning structures and relationships.
- 7 Classification:** Ask students to organize concepts or structures into categories by placing them in the correct "bucket."
- 8 Sequencing:** Challenge students to place the steps of a complex process in the correct order.
- 9 Composition:** Fill in the blanks to practice vocabulary, and then reorder the sentences to form a logical paragraph (these exercises may qualify as "writing across the curriculum" activities!).

All McGraw-Hill Connect content is tagged to Learning Outcomes for each chapter as well as topic, section, Bloom's Level, ASM topic, and ASM Curriculum Guidelines to assist you in customizing assignments and in reporting on your students' performance against these points. This will enhance your ability to assess student learning in your courses by allowing you to align your learning activities to peer-reviewed standards from an international organization.

NCLEX®

NCLEX® Prep Questions: Sample questions are available in Connect to assign to students, and there are questions throughout the book as well.



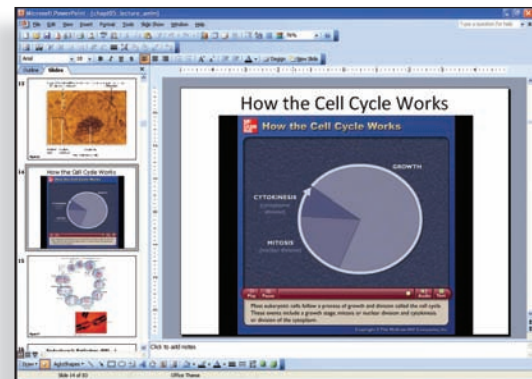
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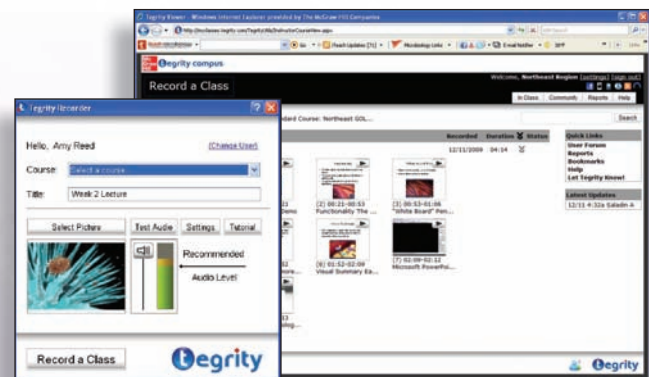


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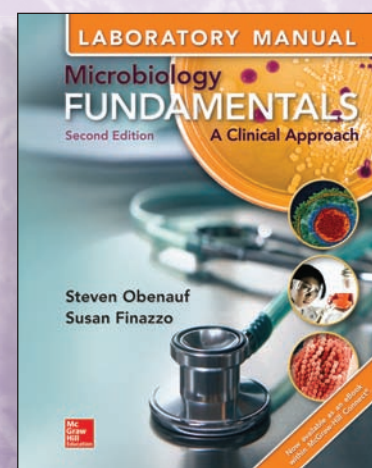
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Microbiology Fundamentals Laboratory Manual, Second Edition

Steven Obenauf, Broward College
Susan Finazzo, Georgia Perimeter College

Written specifically for pre-nursing and allied health microbiology students, this manual features brief, visual exercises with a clinical emphasis.



Clinical applications help students see the relevance of microbiology.

Case File Each chapter begins with a case written from the perspective of a former microbiology student.

These high-interest introductions provide a specific example of how the chapter content is relevant to real life and future health care careers.

Clinical Contributor

This textbook features a clinical advisor, Jennifer Bunn, RN, who authored the following features, described on these pages:

- ▶ Added clinical relevance throughout the chapter
- ▶ Relevant case files
- ▶ Medical Moment boxes
- ▶ NCLEX® prep questions

"Jen added things that were fascinating to ME! And will enrich my own teaching. Pre-allied health students are so eager to start 'being' nurses, etc., they love these clinical details."

—Kelly Cowan

NCLEX® PREP

1. The physician has ordered that a urine culture be taken on a client. What priority information should the nurse know in order to complete the collection of this specimen?
 - a. Date and time of collection
 - b. Method of collection
 - c. Whether the client is NPO (to have nothing by mouth)
 - d. Age of client

NCLEX® Prep Questions Found throughout the chapter, these multiple-choice questions are application-oriented and designed to help students learn the microbiology information they will eventually need to pass the NCLEX examination. Students will begin learning to think critically, apply information, and over time, prep themselves for the examination.

Additional questions are available in Connect for homework and assessment.

Inside the Clinic Each chapter ends with a reading that emphasizes the nursing aspect of microbiology.

Fever: To Treat or Not to Treat?


Our immune system helps to protect us from invading microorganisms. One manner in which our body protects itself is by mounting a fever in response to microbes present in the body (body temperature can also rise in response to inflammation or injury).

The hypothalamus, located in the brain, serves as the temperature-control center of the body. Fever occurs when the hypothalamus actually resets itself at a higher temperature. The hypothalamus raises body temperature by shunting blood away from the skin and into the body's core. It also raises temperature by inducing shivering, which is a result of muscle contraction and serves to increase temperature. This is why people experience chills and shivering when they have a fever. Once the new, higher temperature is reached (warmer blood reaches the hypothalamus), the hypothalamus works to maintain this temperature. When the "thermostat" is reset once again to a lower level, the body reverses the process, shunting blood to the skin. This is why people become diaphoretic (sweaty) when a fever breaks.

When microorganisms gain entrance to the body and begin to proliferate, the body responds with an onslaught of macrophages and monocytes, whose pur-

Inside the Clinic

Clinical Examples Throughout Clinical insights and examples are woven throughout the chapter—not just in boxed elements.



CASE FILE

Puzzle in the Valley

Working as a newly graduated radiology technologist in a rural hospital in California, I encountered a case that would prove to be a challenge for everyone involved. The patient was a male migrant farm worker in his mid-30s who presented to the ER with common flulike symptoms: fever, chills, weakness, cough, muscular aches and pains, and headache. He also had a painful red rash on his lower legs.

It was summertime, so influenza was unlikely. The emergency room physician believed that the patient likely had pneumonia, but she found the rash puzzling. She asked me to obtain a chest X ray. I performed anterior-

Medical Moment

Outsmarting Encapsulated Bacteria

Catheter-associated infections in critically ill patients requiring central venous access are unfortunately all too common. It has been estimated that bloodstream infection, a condition called **sepsis**, affects 3% to 8% of patients requiring an indwelling catheter for a prolonged period of time. Sepsis increases morbidity and mortality and can increase the cost of a patient's care by approximately \$30,000.

In order to colonize a catheter, microorganisms must first adhere to the surface of the tip on this medical device. Fimbriae and glycoalyces are bacterial structures most often used for this purpose.

Medical Moment

These boxes give students a more detailed clinical application of a nearby concept in the chapter.

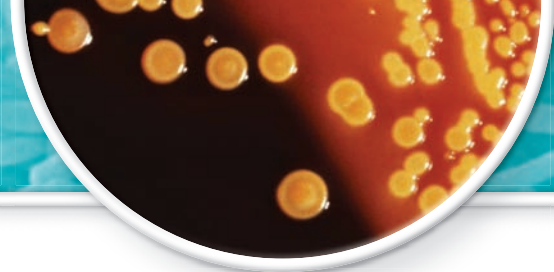
...excess spasms in the respiratory smooth muscle. In anaphylactic attacks are urged to carry at all times injectable epinephrine (adrenaline) and an identification tag indicating their sensitivity. Epinephrine reverses constriction of the airways and slows the release of allergic mediators. Although epinephrine works quickly and well, it has a very short half-life. It is very common to require more than one dose in anaphylactic reactions. Injectable epinephrine buys the individual time to get to a hospital for continuing treatment.

ergy "Vaccines"

...70% of allergic patients benefit from controlled in-
...skin tests. This techni-

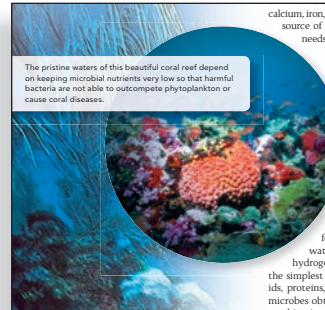


VISUAL



Visually appealing layouts and vivid art closely linked to narrative complement the way 21st-century students learn.

Engaging, Accurate, and Educational Art Visually appealing art and page layouts engage students in the content, while carefully constructed figures help them work through difficult concepts.



calcium, iron, sodium, chlorine, magnesium, and certain other elements. But the source of a particular element, its chemical form, and how much of it there are all points of variation between different types of organisms. Any substance that must be provided to an organism is an **essential nutrient**. Two categories of essential nutrients are **macronutrients** and **micronutrients**. Macronutrients are required in relatively large quantities and play principal roles in cell structure and metabolism. Examples of macronutrients are carbon, hydrogen, and oxygen. Micronutrients, or **trace elements**, such as iron, zinc, and nickel, are present in much smaller amounts and are involved in enzyme function and maintenance of cellular structure. Another way to categorize nutrients is according to their chemical form. An inorganic nutrient is an atom or simple molecule that contains a combination of atoms other than carbon. The natural reservoirs of inorganic nutrients are in the crust of the earth, bodies of water, and the atmosphere. Examples include metals and their salts (magnesium sulfate, sodium phosphate), gases (oxygen, carbon dioxide), and water. In contrast, the molecules of organic nutrients contain carbon and hydrogen atoms and are usually the products of living things. They range from the simplest organic molecule, methane (CH₄), to large polymers (carbohydrates, proteins, and nucleic acids). The source of nutrients is extremely varied; microbes obtain their nutrients entirely from inorganic sources, and other organisms obtain theirs from a combination of organic and inorganic sources.

Chemical Analysis of Microbial Cytoplasm

Table 6.1 lists the major contents of the bacterium *Escherichia coli*. Some components are absorbed in a ready-to-use form, and others must be synthesized from simple nutrients. The important features of cell composition are summarized as follows:

3.1 Form and Function of Bacteria and Archaea

In chapter 1, we described bacteria and archaea as being cells with no true nucleus. Let's look at how bacteria and archaea are different from eukaryotes.

- The main their DNA is packaged. Bacteria and archaea have nucleoid material that is free inside the cytoplasm (i.e., they do not have a nucleus). Eukaryotes have a membrane around their DNA (making up a nucleus). Bacteria don't bind their DNA around histones; eukaryotes do.
- The majority of their cell walls. Bacteria and archaea generally have a wall structure that is unique compared to eukaryotes. Bacteria have sturdy walls made of a chemical called peptidoglycan. Archaeal walls are also tough and made of other chemicals, distinct from bacteria and distinct from eukaryotic walls.
- Their internal structures. Bacteria and archaea don't have complex, membrane-bound organelles in their cytoplasm (eukaryotes do). A few bacteria and archaea have internal membranes, but they don't surround organelles.

Both non-eukaryotic and eukaryotic microbes are ubiquitous in the world today. Although both can cause infectious diseases, treating them with drugs requires different types of approaches. In this chapter and coming chapters, you'll discover why that is. The evolutionary history of non-eukaryotic cells extends back at least 2.0 billion years. The fact that these organisms have endured for so long in such a variety of habitats can be attributed to a cellular structure and function that are amazingly versatile and adaptable.

The Structure of the Bacterial Cell

In this chapter, the descriptions, except where otherwise noted, refer to bacterial cells. Although bacteria and archaea share many of the same basic structural elements, we will focus on the features of bacteria because you will encounter them more often in a clinical environment. We will analyze the significant ways in which archaea are unique later in the chapter.

The general cellular organization of a bacterial cell can be represented with this flowchart:

External	<ul style="list-style-type: none"> Appendages (flagella, pili, fimbriae) Spore Slime layer Cell wall Outer membrane Cell membrane
Cell envelope	<ul style="list-style-type: none"> Cell wall Outer membrane Cell membrane
Internal	<ul style="list-style-type: none"> Cytoplasm Inclusion bodies Cytoplasmic membrane Cytoplasm Plasmid Chromosomes

All bacterial cells inevitably have a cytoplasmic membrane (cytoplasm, cytoskeleton, and one (or a few) chromosome(s)). The majority have a cell wall and a surface coating called glycocalyx. Specific structures that are found in some but not all bacteria are flagella, an outer membrane, pili, fimbriae, plasmids, inclusion bodies, endospores, and microtubules. None of these structures are observed in archaea as well.

Figure 3.1 presents a three-dimensional anatomical view of a generalized, rod-shaped bacterial cell. As we survey the principal anatomical features of this cell, we

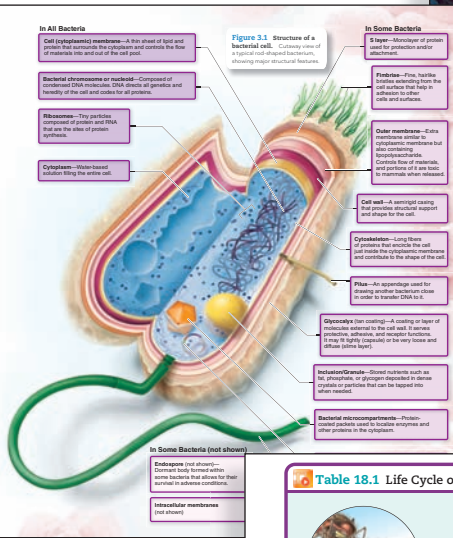
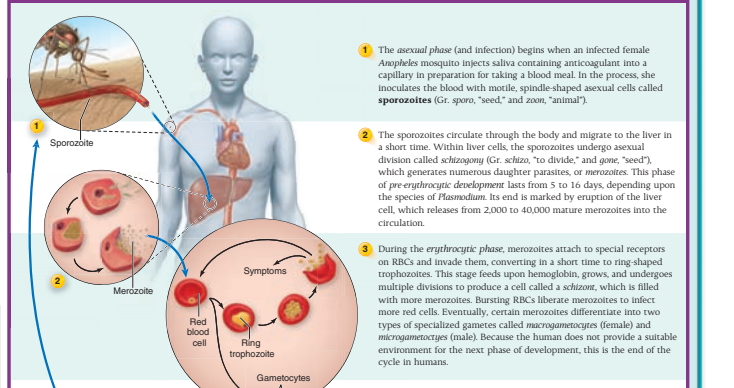
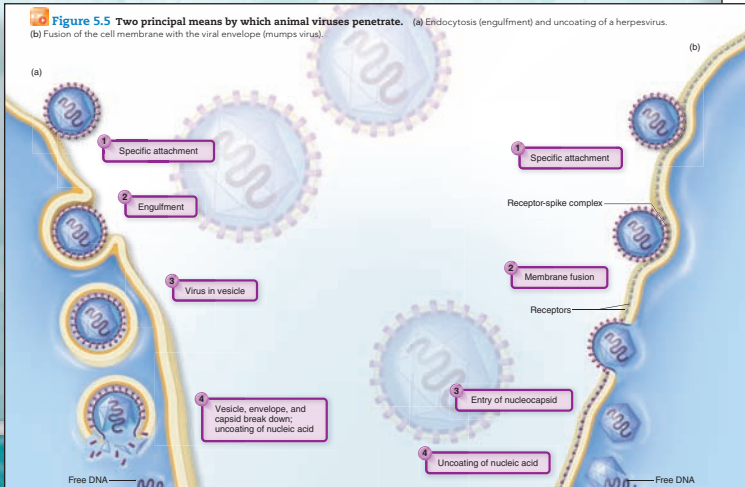


Table 18.1 Life Cycle of the Malarial Parasite



Visual Tables The most important points explaining a concept are distilled into table format and paired with explanatory art.



Process Figures Complex processes are broken into easy-to-follow steps. Numbered steps in the art coordinate with numbered text boxes to walk students through the figure.

Streamlined coverage of core concepts help students retain the information they will need for advanced courses.

Chemistry topics required for understanding microbiology are combined with the foundation content found in chapter 1.

Genetics content is synthesized into one chapter covering the concepts that are key to microbiology students.

A chapter in microbiology textbooks that is often not used in health-related classes becomes relevant because it presents the 21st-century idea of "One Health"—that the environment and animals influence human health and infections.

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Contributed by Ronald M. Atlas	



"The textbook is unique in that it was written with the health science student in mind. Unlike most texts, which just claim to be appropriate for nursing students, this textbook actually incorporates real world health care using the features such as Inside the Clinic and Case Files. The textbook also incorporates critical thinking and visual connections to illustrate how a student would 'function' in the field."

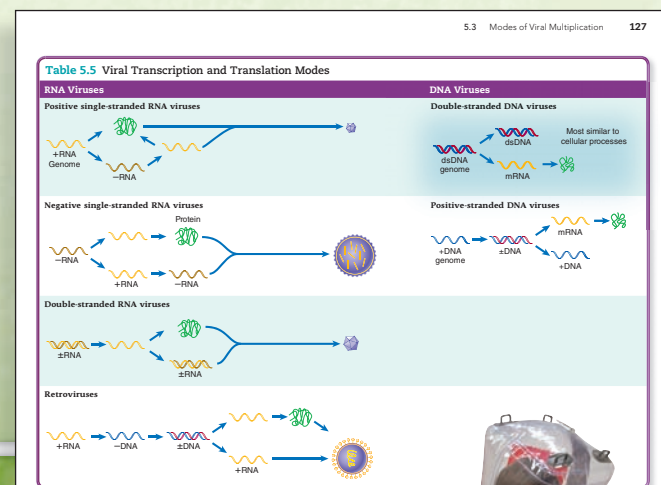
—Jill Roberts, University of South Florida

Duplication Eliminated Detail is incorporated into figures so students can learn in context with the art. This allows a more concise narrative flow while still retaining core information.

Tables Tables are used to further streamline content and help students understand relationships between concepts.

Step	Microscopic Appearance of Cell		Chemical Reaction in Cell Wall (very magnified view)	
	Gram (+)	Gram (-)	Gram (+)	Gram (-)
1. Crystal violet First, crystal violet is added to the cells in a smear. It stains them all the same purple color.				
2. Gram's iodine Then, the mordant, Gram's iodine, is added. This is a stabilizer that causes the dye to form large complexes in the peptidoglycan meshwork of the cell wall. The thicker gram-positive cell walls are able to more firmly trap the large complexes than those of the gram-negative cells.				
3. Alcohol Application of alcohol dissolves lipids in the outer membrane and removes the dye from the peptidoglycan layer—only in the gram-negative cells.				
4. Safranin (red dye) Because gram-negative bacteria are colorless after decolorization, their presence is demonstrated by applying the counterstain safranin in the final step.				

Figure 3.17 The steps in a Gram stain.



Changes to the Second Edition

Significant Changes

Epidemiological data (who, where, how common) are added for every organism in every disease table!

Twenty new chapter-opener case files include: a measles case, *C. diff*, Valley fever, Norwalk virus, gas gangrene, rheumatoid arthritis, UTI, and a bloodstream infection.

Throughout the Book

This edition has improved Learning Outcomes, new Critical Thinking questions, many new Medical Moments scattered throughout, and new Inside the Clinic scenarios at the ends of the chapters. Also, antibiotic-resistant bacteria are uniformly identified throughout the book according to CDC threat status, and neglected parasitic infections (NPIs) are highlighted.

Chapter Highlights

The Human Microbiome Project results have altered nearly every chapter. Other noteworthy changes are described here.

Chapters 1 and 4 Updates about origin of cells.

Chapter 2 New emphasis on nonculture methods.

Chapter 3 Much more information on biofilms; new material on S layers and microcompartments.

Chapter 6 Improved diffusion and osmosis discussion and exponential growth figures.

Chapter 9 Added concept of critical, semicritical disinfection.

Chapter 10 Significant changes and enhancements to the antibiotic-resistance section, incorporating information about resistance not ONLY being created in response to antibiotic presence; introduction of CDC threat report (used throughout disease chapters).

Chapter 11 Extensive revisions to normal biota sections based on Human Microbiome Project and information about

normal biota in lungs, and so on; new information about polymicrobial infections, quorum sensing; added the built environment as a reservoir and the impact on epidemiology of Internet and social media.

Chapter 12 Updated to include gamma-delta T cells/NKT/NK cells as functioning in both specific and nonspecific immunity; added inflammasomes; updated discussion of interferon; complement section much clearer.

Chapter 13 Added detail on gamma-delta T cells and their important role; Medical Moment addresses Facebook group about pox parties.

Chapter 14 Updates on allergies and the microbiome.

Chapter 15 Many redrawn figures; new section titled "Breakthrough Methodologies" to discuss use of deep sequencing, mass spectrometry, and imaging as diagnostic techniques.

Chapter 16 Added *MRSA skin and soft-tissue infection* as first Highlight Disease; great emphasis on measles and recent outbreaks.

Chapter 18 Up-to-the-moment Inside the Clinic about the 2014 Ebola epidemic, including its presence in the United States.

Chapter 19 Extensive updates on influenza, TB, MDR-TB, and XDR-TB.

Chapter 20 Emphasis on neglected parasitic infections; addition of cysticercosis as a separate condition; addition of norovirus as a significant cause of diarrhea.

Chapter 21 UTI section completely rewritten to emphasize hospital and long-term-care infections.

Chapter 22 Completely new, revolutionary chapter by Ronald M. Atlas (One Health) which ties together the environment, animals and human health.

Acknowledgments

I am always most grateful to my students in my classes. They teach me every darned day how to do a better job helping them understand these concepts that are familiar to me but new to them. All the instructors who reviewed the manuscript for me were also great allies. I thank them for lending me some of their microbiological excellence. I had several contributors to the book and digital offerings—Hank Stevens, Andrea Rediske, Kimberly Harding, Kathleen Sandman and Heidi Smith chief among them. Jennifer Bunn, my coauthor, teaches me many things about many things. I would especially like to thank Ronald

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—Kelly Cowan

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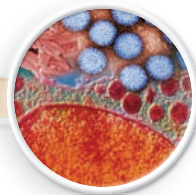
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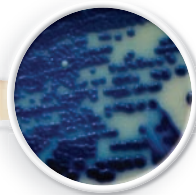
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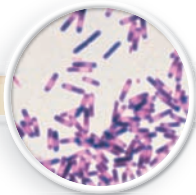
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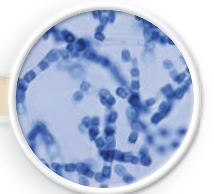
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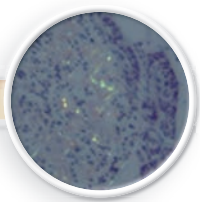
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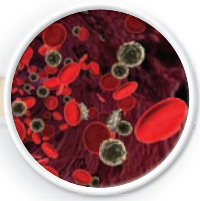
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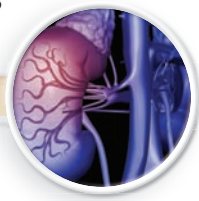
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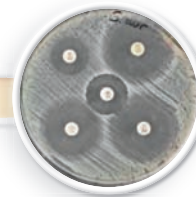
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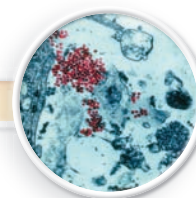
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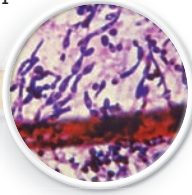
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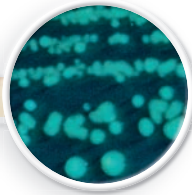
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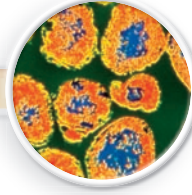
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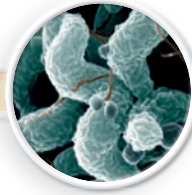
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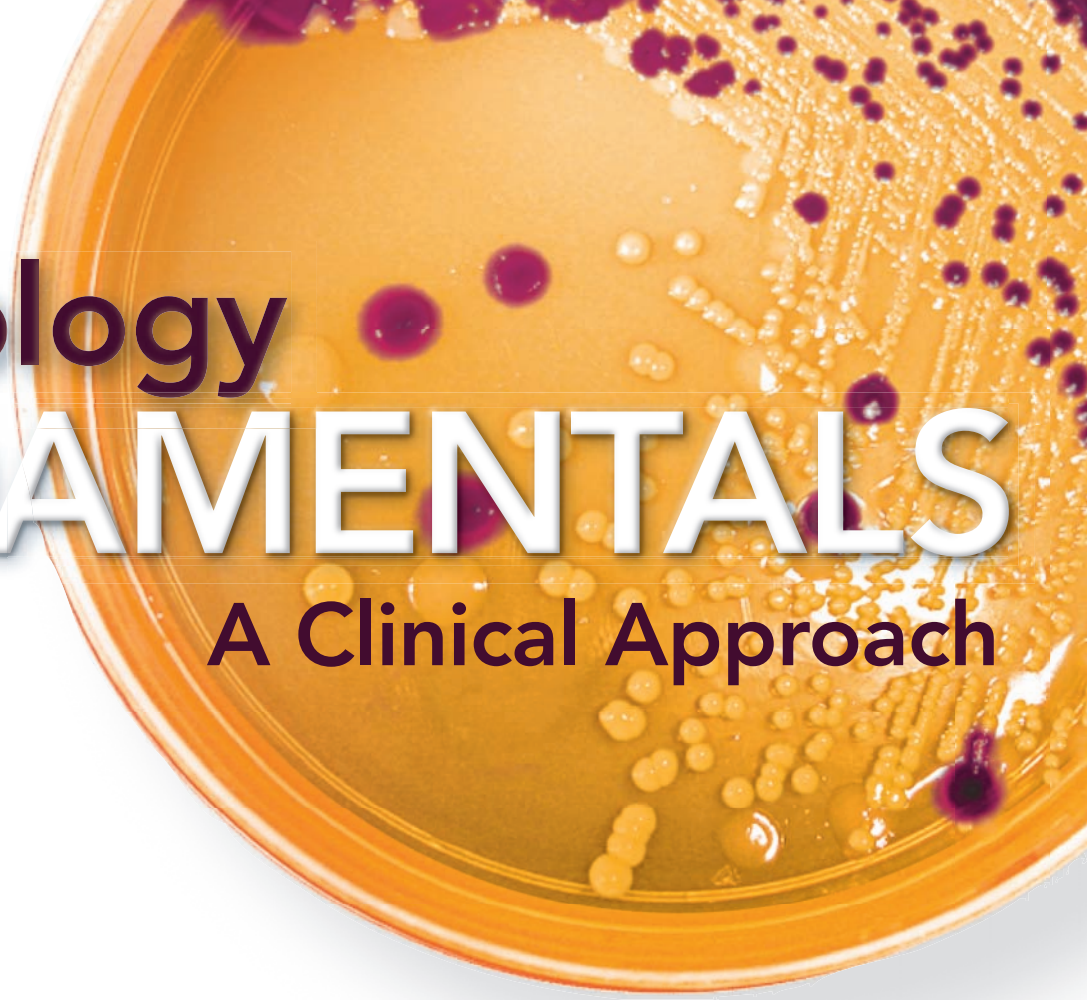
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Microbiology

FUNDAMENTALS

A Clinical Approach





CASE FILE

The Subject Is You!

At the beginning of every chapter in this book a different health care worker will tell you a story about something “microbiological” that happened to him or her in the line of duty. For this first chapter, though, I am claiming “dibs” as author and am going to introduce myself to you by telling you about the first day of class in my course.

Long ago I noticed that students have a lot of anxiety about their microbiology course. I know that starts you out with one strike against you, as attitudes are such powerful determinants of our success. So on the first day of class I often spend some time talking with students about how much they already know about microbiology.

Sometimes I start with “How many of you have taken your kids for vaccinations?” since in the classes I teach very many students are parents. Right away students will tell me why they or friends they know have not vaccinated their children and I can tell them there’s a sophisticated microbiological concept they are referencing, even if they aren’t naming it: *herd immunity*, discussed in chapter 11 of this book.

My favorite question (now that we’re all warmed up) is “Who knows someone—whom you don’t have to identify—who has had a really unusual or scary infection?” A surprising number of people have known someone who has had malaria, or leptospirosis, or endocarditis, or encephalitis. Then the conversation gets interesting as students begin to understand how much they already know about microbiology, and the class is not going to be as intimidating as they thought.

- Think about how many times you have taken antibiotics in the past few years. What is special about antibiotics that they are only given to treat infections?
- What is the most unusual infection you have ever encountered among family or friends or patients you have cared for?

Case File Wrap-Up appears on page 30.

Introduction to Microbes and Their Building Blocks

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1.1 Microbes: Tiny but Mighty

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8. Compare and contrast the relative sizes of the different microbes.

1.2 Microbes in History

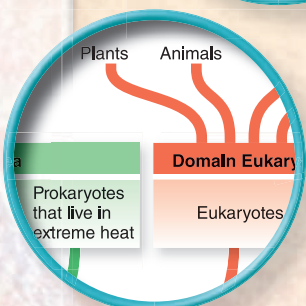
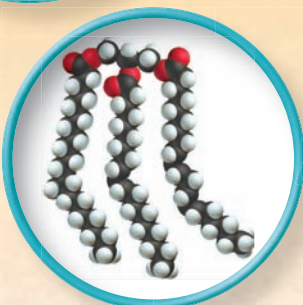
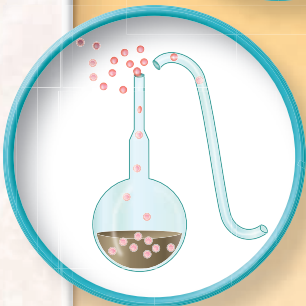
9. Make a time line of the development of microbiology from the 1600s to today.
10. List some recent microbiology discoveries of great impact.

1.3 Macromolecules: Superstructures of Life

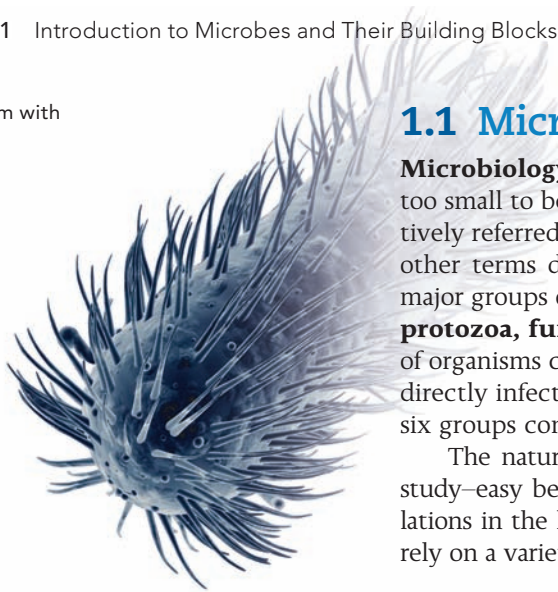
11. Name the four main families of biochemicals.
12. Provide examples of cell components made from each of the families of biochemicals.
13. Differentiate among primary, secondary, tertiary, and quaternary levels of protein structure.
14. List the three components of a nucleotide.
15. Name the nitrogen bases of DNA and RNA.
16. List the three components of ATP.
17. Recall three characteristics common to all cells.

1.4 Naming, Classifying, and Identifying Microorganisms

18. Differentiate among the terms *nomenclature*, *taxonomy*, and *classification*.
19. Create a mnemonic device for remembering the taxonomic categories.
20. Correctly write the binomial name for a microorganism.
21. Draw a diagram of the three major domains.
22. Explain the difference between traditional and molecular approaches to taxonomy.



A rod-shaped bacterium with numerous flagella.



1.1 Microbes: Tiny but Mighty

Microbiology is a specialized area of biology that deals with living things ordinarily too small to be seen without magnification. Such **microscopic** organisms are collectively referred to as **microorganisms** (my''-kroh-or'-gun-izms), **microbes**, or several other terms depending on the kind of microbe or the purpose. There are several major groups of microorganisms that we'll be studying. They are **bacteria**, **archaea**, **protozoa**, **fungi**, **helminths**, and **viruses**. There is another very important group of organisms called **algae**. They are critical to the health of the biosphere but do not directly infect humans, so we will not consider them in this book. Each of the other six groups contains members that colonize humans, so we will focus on them.

The nature of microorganisms makes them both very easy and very difficult to study—easy because they reproduce so rapidly and we can quickly grow large populations in the laboratory, and difficult because we usually can't see them directly. We rely on a variety of indirect means of analyzing them in addition to using microscopes.

Microbes and the Planet

For billions of years, microbes have extensively shaped the development of the earth's habitats and the evolution of other life forms. It is understandable that scientists searching for life on other planets first look for signs of microorganisms.

Single-celled organisms that preceded our current cell types arose on this planet about 3.5 billion years ago, according to the fossil record. At that time, three types of cells arose from the original (now extinct) cell type: bacteria, archaea, and a specific cell type called a **eukaryote** (yoo-kar'-ee-ote). *Eu-kary* means "true nucleus," and these were the only cells containing a nucleus. Bacteria and archaea have no true nucleus. For that reason, they have traditionally been called **prokaryotes** (pro-kar'-ee-otes), meaning "prenucleus." But researchers are suggesting we no longer use the term *prokaryote* to lump them together because archaea and bacteria are so distinct genetically.

Bacteria and archaea are predominantly single-celled organisms. Many, many, eukaryotic organisms are also single-celled; but the eukaryotic cell type also developed into highly complex multicellular organisms, such as worms and humans. In terms of numbers, eukaryotic cells are a small minority compared to the bacteria and archaea; but their larger size (and our own status as eukaryotes!) makes us perceive them as dominant to—and more important than—bacteria and archaea.

For a long time, it was believed that eukaryotes evolved long after bacteria and archaea and actually derived *from* them. Most evidence today points to the near simultaneous rise of bacteria, archaea, and eukaryotes from an earlier cell type.

Figure 1.1 illustrates the history of life on earth. On the scale pictured in the figure, humans seem to have just appeared. Bacteria and archaea preceded even the earliest animals by more than 2 billion years. This is a good indication that humans are not likely to—nor should we try to—eliminate bacteria from our environment. We have survived and adapted to many catastrophic changes over the course of our geologic history.

Another indication of the huge influence bacteria exert is how **ubiquitous** they are. Microbes can be found nearly everywhere, from deep in the earth's crust, to the polar ice caps and oceans, to inside the bodies of plants and animals. Being mostly invisible, the actions of microorganisms are usually not as obvious or familiar as those of larger plants and animals. They make up for their small size by occurring in large numbers and living in places that many other organisms cannot survive. Above all, they play central roles in the earth's landscape that are essential to life.

When we point out that single-celled organisms have adapted to a wide range of conditions over the 3.5 billion years of their presence on this planet, we are talking about evolution. The presence of life in its present form would not be possible if the earliest life forms had not changed constantly, adapting to their environment and circumstances. Getting from the far left in figure 1.1 to the far right, where humans appeared, involved billions and billions of tiny changes, starting with the first cell that appeared about a billion years after the planet itself was formed.

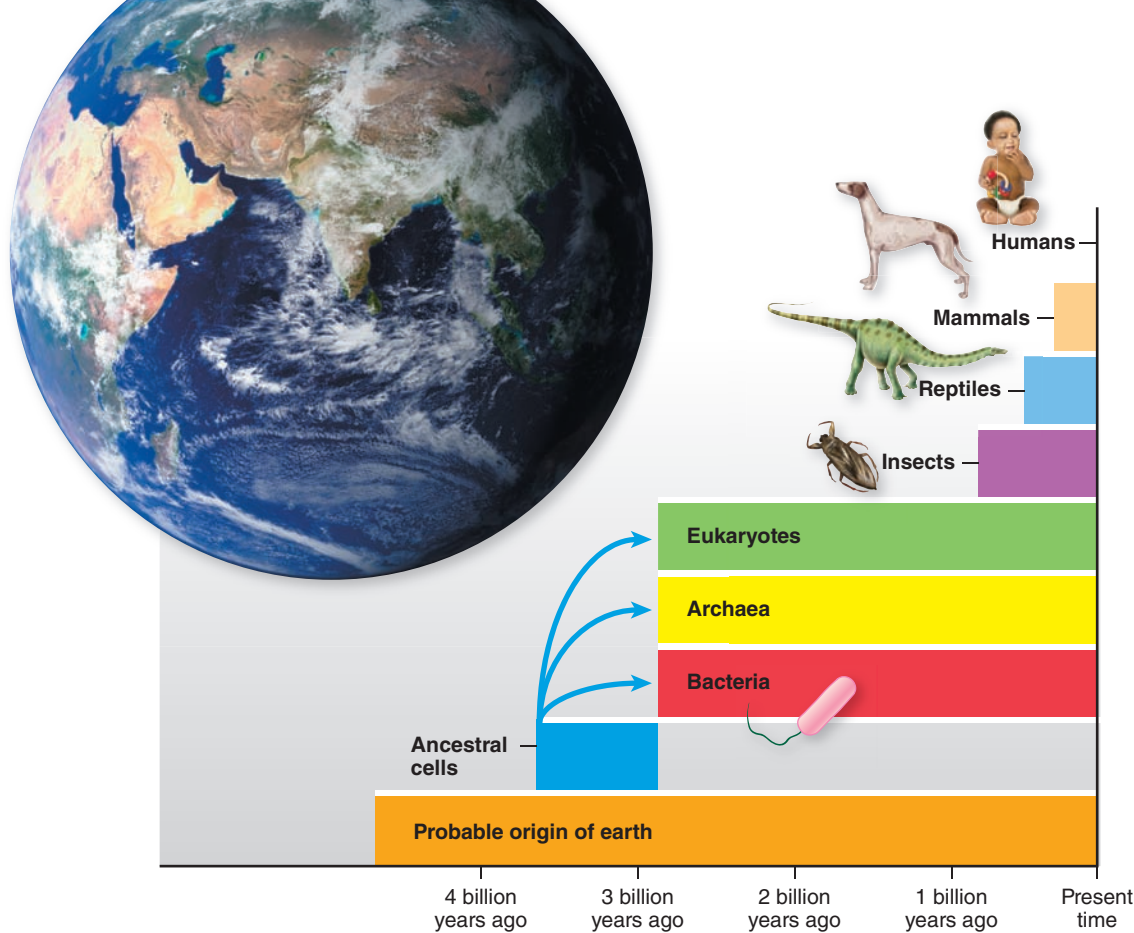


Figure 1.1 Evolutionary time line.

You have no doubt heard this concept described as the **theory of evolution**. Let's clarify some terms. **Evolution** is the accumulation of changes that occur in organisms as they adapt to their environments. It is documented every day in all corners of the planet, an observable phenomenon testable by science. Scientists use the term *theory* in a different way than the general public does, which often leads to great confusion. In science, a theory begins as a hypothesis, or an educated guess to explain an observation. By the time a hypothesis has been labeled a *theory* in science, it has undergone years and years of testing and not been disproved. It is taken as fact. This is much different from the common usage, as in "My theory is that he overslept and that's why he was late." The theory of evolution, like the germ theory and many other scientific theories, refers to a well-studied and well-established natural phenomenon, not just a random guess.

How Microbes Shape Our Planet

Microbes are deeply involved in the flow of energy and food through the earth's ecosystems. Most people are aware that plants carry out **photosynthesis**, which is the light-fueled conversion of carbon dioxide to organic material, accompanied by the formation of oxygen (called oxygenic photosynthesis). However, bacteria invented photosynthesis long before the first plants appeared, first as a process that did not produce oxygen (*anoxygenic photosynthesis*). This anoxygenic photosynthesis later evolved into oxygenic photosynthesis, which not only produced oxygen but also was much more efficient in extracting energy from sunlight. Hence, these ancient, single-celled microbes were responsible for changing the atmosphere of the earth from one without oxygen to one with oxygen. The production of oxygen also led to the use of oxygen for aerobic respiration and the formation of ozone, both of which set off an explosion in species diversification. Today, photosynthetic microorganisms (mainly bacteria and algae) account for more than 70% of the earth's photosynthesis, contributing the majority of the oxygen to the atmosphere (**figure 1.2**).

Figure 1.2 A rich photosynthetic community.

Summer pond with a thick mat of algae.





Medical Moment

Medications from Microbes

Penicillin is a worthy example of how microorganisms can be used to improve human life. Alexander Fleming, a Scottish bacteriologist, discovered penicillin quite by accident in 1928. While growing several bacterial cultures in Petri dishes, he accidentally forgot to cover them. They remained uncovered for several days; when Fleming checked the Petri dishes, he found them covered with mold. Just before Fleming went to discard the Petri dishes, he happened to notice that there were no bacteria to be seen around the mold—in other words, the mold was killing all of the bacteria in its vicinity.

Recognizing the importance of this discovery, Fleming experimented with the mold (of the genus *Penicillium*) and discovered that it effectively stopped or slowed the growth of several bacteria. The chemical that was eventually isolated from the mold—penicillin—became widely used during the Second World War and saved many soldiers' lives, in addition to cementing Fleming's reputation.

In the long-term scheme of things, microorganisms are the main forces that drive the structure and content of the soil, water, and atmosphere. For example:

- The temperature of the earth is regulated by gases, such as carbon dioxide, nitrous oxide, and methane, which create an insulation layer in the atmosphere and help retain heat. Many of these gases are produced by microbes living in the environment and the digestive tracts of animals.
- The most abundant cellular organisms in the oceans are not fish but bacteria. Think of a 2-liter bottle that soda comes in. Two liters of surface ocean water contains approximately 1,000,000,000,000,000 (1 quintillion) bacteria. Each of these bacteria likely harbors thousands of viruses inside of it, making viruses the most abundant inhabitants of the oceans. The bacteria and their viruses are major contributors to photosynthesis and other important processes that create our environment.
- Bacteria and fungi live in complex associations with plants that assist the plants in obtaining nutrients and water and may protect them against disease. Microbes form similar interrelationships with animals, notably, in the stomach of cattle, where a rich assortment of bacteria digests the complex carbohydrates of the animals' diets and causes the release of large amounts of methane into the atmosphere.

Microbes and Humans

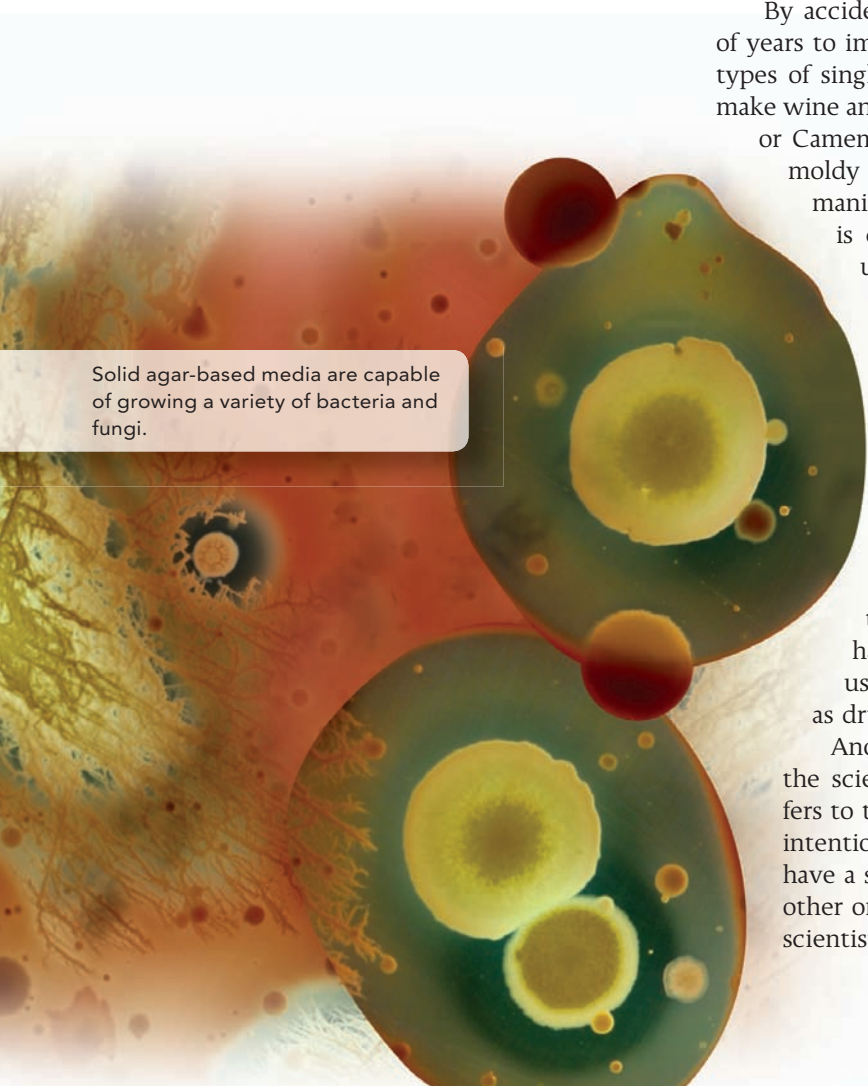
Microorganisms clearly have monumental importance to the earth's operation. Their diversity and versatility make them excellent candidates for being used by humans for our own needs, and for them to "use" humans for their needs, sometimes causing disease along the way. We'll look at both of these kinds of microbial interactions with humans in this section.

By accident or choice, humans have been using microorganisms for thousands of years to improve life and even to shape civilizations. Baker's and brewer's yeasts, types of single-celled fungi, cause bread to rise and ferment sugar into alcohol to make wine and beers. Other fungi are used to make special cheeses such as Roquefort or Camembert. Historical records show that households in ancient Egypt kept moldy loaves of bread to apply directly to wounds and lesions. When humans manipulate microorganisms to make products in an industrial setting, it is called **biotechnology**. For example, some specialized bacteria have unique capacities to mine precious metals or to clean up human-created contamination.

Genetic engineering is an area of biotechnology that manipulates the genetics of microbes, plants, and animals for the purpose of creating new products and genetically modified organisms (GMOs). One powerful technique for designing GMOs is termed **recombinant DNA technology**. This technology makes it possible to transfer genetic material from one organism to another and to deliberately alter DNA. Bacteria and fungi were some of the first organisms to be genetically engineered. This was possible because they are single-celled organisms and they are so adaptable to changes in their genetic makeup. Recombinant DNA technology has unlimited potential in terms of medical, industrial, and agricultural uses. Microbes can be engineered to synthesize desirable products such as drugs, hormones, and enzymes.

Another way of tapping into the unlimited potential of microorganisms is the science of **bioremediation** (by'-oh-ree-mee-dee-ay'-shun). This term refers to the ability of microorganisms—ones already present or those introduced intentionally—to restore stability or to clean up toxic pollutants. Microbes have a surprising capacity to break down chemicals that would be harmful to other organisms (**figure 1.3**). This includes even human-made chemicals that scientists have developed and for which there are no natural counterparts.

Solid agar-based media are capable of growing a variety of bacteria and fungi.



Microbes Harming Humans

One of the most fascinating aspects of the microorganisms with which we share the earth is that, despite all of the benefits they provide, they also contribute significantly to human misery as **pathogens** (path'-oh-jenz). The vast majority of microorganisms that associate with humans cause no harm. In fact, they provide many benefits to their human hosts. Note that a diverse microbial biota living in and on humans is an important part of human well-being. However, humankind is also plagued by nearly 2,000 different microbes that can cause various types of disease. Infectious diseases still devastate human populations worldwide, despite significant strides in understanding and treating them. The World Health Organization (WHO) estimates there are a total of 10 billion new infections across the world every year. Infectious diseases are also among the most common causes of death in much of humankind, and they still kill a significant percentage of the U.S. population. **Table 1.1** depicts the 10 top causes of death per year (by all causes, infectious and noninfectious) in the United States and worldwide.

Adding to the overload of infectious diseases, we are also witnessing an increase in the number of new (emerging) and older (reemerging) diseases. AIDS, hepatitis C, West Nile virus, and tuberculosis are examples. It is becoming clear that human actions in the form of reforestation, industrial farming techniques, and chemical and antibiotic usage can foster the emergence or reemergence of particular infectious diseases. These patterns will be discussed in chapter 22.

One of the most eye-opening discoveries in recent years is that many diseases that used to be considered noninfectious probably do involve microbial infection. One well-known example is that of gastric ulcers, now known to be caused by a bacterium called *Helicobacter*. But there are more. Associations have been established between certain cancers and bacteria and viruses, between diabetes and the Cocksackie virus, and between schizophrenia and a virus called the Borna agent. Diseases as different as multiple sclerosis, obsessive compulsive disorder, coronary artery disease, and even obesity have been linked to chronic infections with microbes. It seems that the golden age of microbiological discovery, during which all of the "obvious" diseases were characterized and cures or preventions were devised for them, should more accurately be referred to as the *first* golden age. We're now discovering the subtler side of microorganisms.

Another important development in infectious disease trends is the increasing number of patients with weakened defenses, who, because of welcome medical advances, are living active lives instead of enduring long-term disability or death from their conditions. They are subject to infections by common microbes that are not



Figure 1.3 The 2011 Gulf oil spill. There is evidence that ocean bacteria metabolized ("chewed up") some of the spilled oil.

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1. For which of the following disease processes has microbial infection been implicated? Select all that apply.

- a. gastric ulcers
- b. diabetes type 1
- c. renal artery stenosis
- d. schizophrenia
- e. obesity
- f. deep vein thrombosis

Table 1.1 Top Causes of Death—All Diseases

United States	No. of Deaths	Worldwide	No. of Deaths
1. Heart disease	617,000	1. Heart disease	7 million
2. Cancer	565,000	2. Stroke	6.2 million
3. Chronic lower-respiratory disease	141,000	3. Lower-respiratory infections (influenza and pneumonia)	3.2 million
4. Cerebrovascular disease	134,000	4. Chronic obstructive pulmonary disease	3 million
5. Accidents (unintentional injuries)	122,000	5. Diarrheal diseases	1.9 million
6. Alzheimer's disease	82,000	6. HIV/AIDS	1.5 million
7. Diabetes	71,000	7. Trachea, bronchus, lung cancers	1.5 million
8. Influenza and pneumonia	56,000	8. Diabetes mellitus	1.4 million
9. Kidney disease	48,000	9. Road injury	1.3 million
10. Suicide	36,000	10. Prematurity	1.2 million

*Diseases in red are those most clearly caused by microorganisms.

Source: Data from the World Health Organization and the Centers for Disease Control and Prevention. Data published in 2014 representing final figures for the year 2011.

pathogenic to healthy people. There is also an increase in microbes that are resistant to drugs. It appears that even with the most modern technology available to us, microbes still have the “last word,” as the great French scientist Louis Pasteur observed.

What Are They Exactly?

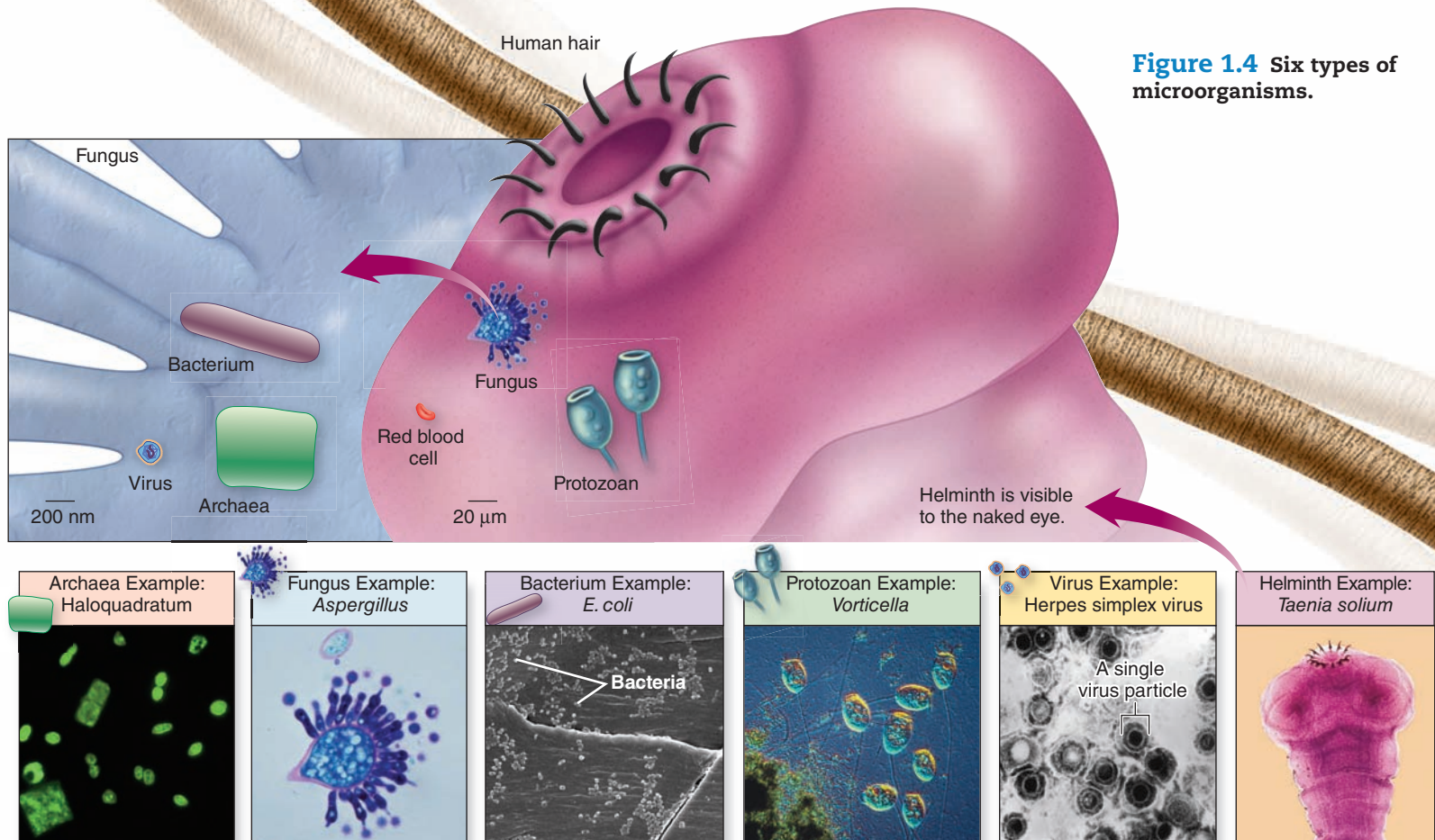
Cellular Organization

As discussed earlier, two basic cell types appeared during evolutionary history. The bacteria and archaea, along with **eukaryotic cells**, differ not only in the complexity of their cell structure but also in contents and function.

In general, bacterial and archaeal cells are about 10 times smaller than eukaryotic cells, and they lack many of the eukaryotic cell structures such as **organelles**. Organelles are small, double-membrane-bound structures in the eukaryotic cell that perform specific functions and include the nucleus, mitochondria, and chloroplasts. Examples of bacteria, archaea, and eukaryotic microorganisms are covered in more detail in chapters 3 and 4.

All bacteria and archaea are microorganisms, but only some eukaryotes are microorganisms (**figure 1.4**). Also, of course, humans are eukaryotes. Certain small eukaryotes—such as helminths (worms), many of which can be seen with the naked eye—are also included in the study of infectious diseases because of the way they are transmitted and the way the body responds to them, though they are not microorganisms.

Viruses are subject to intense study by microbiologists. They are not independently living cellular organisms. Instead, they are small particles that exist at the level of complexity somewhere between large molecules and cells. Viruses are much simpler than cells; outside their host, they are composed essentially of a small amount of hereditary material (either DNA or RNA but never both) wrapped up in a protein covering that is sometimes enveloped by a protein-containing lipid membrane. When inside their host



organism, in the intracellular state, viruses usually exist only in the form of genetic material that confers a partial genetic program on the host organisms.

1.1 LEARNING OUTCOMES—Assess Your Progress

1. List the various types of microorganisms that can colonize humans.
2. Describe the role and impact of microbes on the earth.
3. Explain the theory of evolution and why it is called a theory.
4. Explain the ways that humans manipulate organisms for their own uses.
5. Summarize the relative burden of human disease caused by microbes.
6. Differentiate among bacteria, archaea, and eukaryotic microorganisms.
7. Identify a fourth type of microorganism.
8. Compare and contrast the relative sizes of the different microbes.

1.2 Microbes in History

If not for the extensive interest, curiosity, and devotion of thousands of microbiologists over the last 300 years, we would know little about the microscopic realm that surrounds us. Many of the discoveries in this science have resulted from the prior work of men and women who toiled long hours in dimly lit laboratories with the crudest of tools. Each additional insight, whether large or small, has added to our current knowledge of living things and processes. This section summarizes the prominent discoveries made in the past 300 years.

Spontaneous Generation

From very earliest history, humans noticed that when certain foods spoiled, they became inedible or caused illness, and yet other “spoiled” foods did no harm and even had enhanced flavor. Indeed, several centuries ago, there was already a sense that diseases such as the Black Plague and smallpox were caused by some sort of transmissible matter. But the causes of such phenomena were vague and obscure because, frankly, we couldn’t *see* anything amiss. Consequently, they remained cloaked in mystery and regarded with superstition—a trend that led even well-educated scientists to believe in a concept called **spontaneous generation**. This was the belief that invisible vital forces present in matter led to the creation of life. The belief was continually reinforced as people observed that meat left out in the open soon “produced” maggots, that mushrooms appeared on rotting wood, that rats and mice emerged from piles of litter, and other similar phenomena. Though some of these early ideas seem quaint and ridiculous in light of modern knowledge, we must remember that, at the time, mysteries in life were accepted and the scientific method was not widely practiced.

Even after single-celled organisms were discovered during the mid-1600s, the idea of spontaneous generation continued to exist. Some scientists assumed that microscopic beings were an early stage in the development of more complex ones.

Over the subsequent 200 years, scientists waged an experimental battle over the two hypotheses that could explain the origin of simple life forms. Some tenaciously clung to the idea of **abiogenesis** (*a* = “without”; *bio* = “life”; *genesis* = “beginning”—“beginning in absence of life”), which embraced spontaneous generation. On the other side were



Medical Moment

Diabetes and the Viral Connection

Scientists have long believed that type 1 diabetes is triggered by an infection. Enteroviruses, such as Coxsackie virus B, have been the focus of intensive research. Several studies support this hypothesis. For example, a study published in 2010 showed that enteroviruses can play a role in the early development of type 1 diabetes through the infection of beta cells in the pancreas, which results in inflammation as a result of innate immunity. This study and others like it seem to suggest that many type 1 diabetic patients have persistent enterovirus infection, which is associated with inflammation in the gut mucosa.

Studies like these that are attempting to determine how diabetes develops are the first step in discovering a cure. If researchers definitively determine that type 1 diabetes is caused by a virus, perhaps one day there will be a vaccine to prevent the disease. Before this can be accomplished, however, researchers will need to determine why it is that not all individuals who become infected with the virus develop diabetes.

Source: 2010. *Nature Reviews Endocrinology* 6(5): 279–89.

Wine, cheese, and bread are each made using bacteria and fungi.

