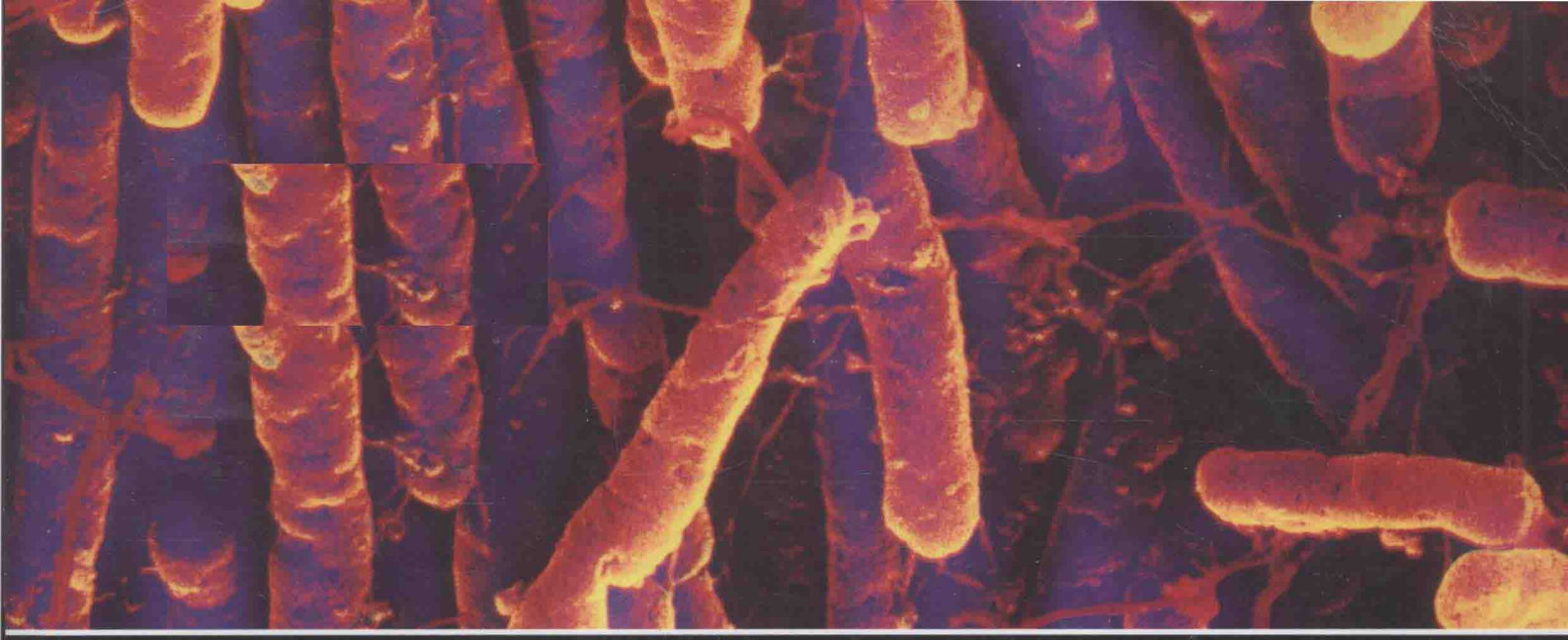

REVIEW OF
Medical Microbiology and Immunology

WARREN LEVINSON

Thirteenth Edition

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Review of Medical Microbiology and Immunology

Thirteenth Edition

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New York Chicago San Francisco Athens London Madrid
Mexico City Milan New Delhi Singapore Sydney Toronto

Review of Medical Microbiology & Immunology, Thirteenth Edition

2 3 4 5 6 7 8 9 0 DOW/DOW 19 18 17 16 15

ISBN 978-0-07-181811-7
MHID 0-07-181811-1
ISSN 1042-8070

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The editors were Michael Weitz and Kim J. Davis.
The production supervisor was Richard Ruzycka.
Project management was provided by Anupriya Tyagi, Cenveo Publisher Services.
The designer was Elise Lansdon.
Cover photo: colorized electron micrograph of *Clostridium difficile;* credit: David M. Phillips / Science Source.
RR Donnelley was the printer and binder.

This book is printed on acid-free paper.

International Edition ISBN 978-1-25-925517-5; MHID 1-25-925517-4.

Preface

This book is a concise review of the medically important aspects of microbiology and immunology. It covers both the basic and clinical aspects of bacteriology, virology, mycology, parasitology, and immunology. It also discusses important infectious diseases using an organ system approach.

Its two major aims are (1) to assist those who are preparing for the USMLE (National Boards) and (2) to provide students who are currently taking medical microbiology courses with a brief and up-to-date source of information. The goal is to provide the reader with an accurate source of clinically relevant information at a level appropriate for those beginning their medical education.

This new edition presents current, medically important information in the rapidly changing fields of microbiology and immunology. It contains many color micrographs of stained microorganisms as well as images of important laboratory tests. It also includes many images of clinical lesions and highlights current information on antimicrobial drugs and vaccines.

These aims are achieved by using several different formats, which should make the book useful to students with varying study objectives and learning styles:

1. A narrative text for complete information.
2. A separate section containing summaries of important microorganisms for rapid review of the high-yield essentials.
3. Sample questions in the USMLE (National Board) style, with answers provided after each group of questions.
4. A USMLE (National Board) practice examination consisting of 80 microbiology and immunology questions. The questions are written in a clinical case format and simulate the computer-based examination. Answers are provided at the end of each block of 40 questions.
5. Self-assessment questions at the end of the chapters so you can evaluate whether the important information has been mastered. Answers are provided.
6. Clinical case vignettes to provide both clinical information and practice for the USMLE.
7. A section titled "Pearls for the USMLE" describing important epidemiologic information helpful in answering questions on the USMLE.
8. Many images of clinically important lesions seen in patients with infectious diseases described in this book are available on the McGraw-Hill Online Learning Center's Web site (www.langetextbooks.com).

The following features are included to promote a successful learning experience for students using this book:

1. The information is presented succinctly, with stress on making it clear, interesting, and up to date.
2. There is strong emphasis in the text on the clinical application of microbiology and immunology to infectious diseases.
3. In the clinical bacteriology and virology sections, the organisms are separated into major and minor pathogens. This allows the student to focus on the most important clinically relevant microorganisms.
4. Key information is summarized in useful review tables. Important concepts are illustrated by figures using color.
5. Important facts called "Pearls" are listed at the end of each basic science chapter.
6. Self-assessment questions with answers are included at the end of the chapters.
7. The 654 USMLE (National Board) practice questions cover the important aspects of each of the subdisciplines on the USMLE: Bacteriology, Virology, Mycology, Parasitology, and Immunology. A separate section containing *extended* matching questions is included. In view of the emphasis placed on clinical relevance in the USMLE, another section provides questions set in a clinical case context.
8. Brief summaries of medically important microorganisms are presented together in a separate section to facilitate rapid access to the information and to encourage comparison of one organism with another.
9. Fifty clinical cases are presented as unknowns for the reader to analyze in a brief, problem-solving format. These cases illustrate the importance of basic science information in clinical diagnosis.
10. Color images depicting clinically important findings, such as infectious disease lesions, Gram stains of bacteria, electron micrographs of viruses, and microscopic images of fungi, protozoa, and worms, are included in the text.
11. New in the thirteenth edition are nine chapters on infectious diseases from an organ system perspective. They are written concisely and are appropriate for a medical student's introduction to this subject. These chapters include Bone and Joint Infections, Cardiac Infections, Central Nervous System Infections, Gastrointestinal Tract Infections, Pelvic Infections, Upper Respiratory Tract Infections,

Lower Respiratory Tract Infections, Skin and Soft Tissue Infections, and Urinary Tract Infections.

After teaching both medical microbiology and clinical infectious disease for many years, I believe that students appreciate a book that presents the essential information in a readable, interesting, and varied format. I hope you find that this book meets those criteria.

Warren Levinson, MD, PhD
San Francisco, California
January 2014

Acknowledgments

The author welcomes Brian S. Schwartz, MD, as a contributor to the thirteenth edition of this book. Brian is an Assistant Professor of Clinical Medicine in the School of Medicine, University of California, San Francisco, specializing in infectious diseases. He contributed three excellent chapters in the new infectious diseases part of this book.

The author also welcomes Peter Chin-Hong, MD, as a contributor to the thirteenth edition of this book. Peter is an Associate Professor of Clinical Medicine in the School of Medicine, University of California, San Francisco, specializing in infectious diseases. He contributed four outstanding chapters in the new infectious diseases part of this book.

I am indebted to the editor of the first five editions, Yvonne Strong; to the editor of the sixth edition, Cara Lyn Coffey; to the editor of the seventh and ninth editions, Jennifer Bernstein; to the editor of the eighth edition, Linda Conheady; to the editor of the tenth and eleventh editions, Sunita Dogra; to the editor of the twelfth edition, Rebecca Kerins; and to the editor of the thirteenth edition, Caroline Define; all of whom ensured that the highest standards of grammar, spelling, and style were met.

The invaluable assistance of my wife, Barbara, in making this book a reality is also gratefully acknowledged.

I dedicate this book to my father and mother, who instilled a love of scholarship, the joy of teaching, and the value of being organized.

How to Use This Book

1. **CHAPTER CONTENTS:** The main headings in each chapter are listed so the reader can determine, at a glance, the topics discussed in the chapter.
2. **TEXT:** A concise, complete description of medically important information for the professional student. Includes basic and clinical bacteriology (pages 1–218), basic and clinical virology (pages 219–382), mycology (fungi) (pages 383–408), parasitology (pages 409–474), immunology (pages 475–568), and ectoparasites (pages 569–576).

   The text also includes nine chapters on infectious diseases. These chapters include Bone and Joint Infections (pages 577–581), Cardiac Infections (pages 582–588), Central Nervous System Infections (pages 589–596), Gastrointestinal Tract Infections (pages 597–603), Pelvic Infections (pages 604–610), Upper Respiratory Tract Infections (pages 611–616), Lower Respiratory Tract Infections (pages 617–621), Skin and Soft Tissue Infections (pages 622–628), and Urinary Tract Infections (pages 629–632).
3. **SUMMARIES OF ORGANISMS:** A quick review for examinations describing the important characteristics of the organisms (pages 633–670).
4. **SELF-ASSESSMENT QUESTIONS**: USMLE-style questions with answers are included at the end of the chapters.
5. **PEARLS FOR THE USMLE:** 11 tables containing important clinical and epidemiologic information that will be useful for answering questions on the USMLE (pages 681–688).
6. **USMLE-TYPE QUESTIONS:** 654 practice questions that can be used to review for the USMLE and class examinations (pages 689–730).
7. **USMLE PRACTICE EXAM:** Two 40-question practice examinations in USMLE format (pages 731–740).
8. **PEARLS:** Summary points at the end of each basic science chapter.
9. **CLINICAL CASES:** 50 cases describing important infectious diseases with emphasis on diagnostic information (pages 671–680).
10. **CLINICAL IMAGES:** More than 50 images of clinically important lesions illustrate the text. Additional clinical lesions can be seen on the McGraw-Hill Online Learning Center's Web site (www.langetextbooks.com/levinson/gallery/).

Contents

PART I BASIC BACTERIOLOGY

CHAPTER 1

Bacteria Compared with Other Microorganisms

CHAPTER CONTENTS

MICROBES THAT CAUSE INFECTIOUS DISEASES

The agents of human infectious diseases belong to five major groups of organisms: bacteria, fungi, protozoa, helminths, and viruses. Bacteria belong to the prokaryote kingdom, fungi (yeasts and molds) belong to the kingdom of fungi, and protozoa are members of the kingdom of protists. Helminths (worms) are classified in the animal kingdom (Table 1–1). Protists and fungi are distinguished from animals and plants by being either unicellular or relatively simple multicellular organisms. In contrast, helminths are complex multicellular organisms. Taken together, the helminths and the protozoa are commonly called parasites. Viruses are quite distinct from other organisms—they are not cells but can replicate only within cells.

IMPORTANT FEATURES OF MICROBES

Many of the essential characteristics of these organisms are described in Table 1–2. One salient feature is that bacteria, fungi, protozoa, and helminths are cellular, whereas viruses are not. This distinction is based primarily on three criteria:

(1) **Structure.** Cells have a nucleus or nucleoid (see below), which contains DNA; this is surrounded by cytoplasm, within which proteins are synthesized and energy is generated. Viruses have an inner core of genetic material (either DNA or RNA) but no cytoplasm, and so they depend on host cells to provide the machinery for protein synthesis and energy generation.

TABLE 1–1 Biologic Relationships of Pathogenic Microorganisms

Kingdom	Pathogenic Microorganisms	Type of Cells
Animal	Helminths (worms)	Eukaryotic
Protists	Protozoa	Eukaryotic
Fungi	Fungi (yeasts and molds)	Eukaryotic
Prokaryote	Bacteria	Prokaryotic
	Viruses	Noncellular

TABLE 1-2 Comparison of Medically Important Organisms

Characteristic	Viruses	Bacteria	Fungi	Protozoa and Helminths
Cells	No	Yes	Yes	Yes
Approximate diameter (μm)[1]	0.02–0.2	1–5	3–10 (yeasts)	15–25 (trophozoites)
Nucleic acid	Either DNA or RNA	Both DNA and RNA	Both DNA and RNA	Both DNA and RNA
Type of nucleus	None	Prokaryotic	Eukaryotic	Eukaryotic
Ribosomes	Absent	70S	80S	80S
Mitochondria	Absent	Absent	Present	Present
Nature of outer surface	Protein capsid and lipoprotein envelope	Rigid wall containing peptidoglycan	Rigid wall containing chitin	Flexible membrane
Motility	None	Some	None	Most
Method of replication	Not binary fission	Binary fission	Budding or mitosis[2]	Mitosis[3]

[1]For comparison, a human red blood cell has a diameter of 7 μm.

[2]Yeasts divide by budding, whereas molds divide by mitosis.

[3]Helminth cells divide by mitosis, but the organism reproduces itself by complex, sexual life cycles.

(2) **Method of replication.** Cells replicate either by binary fission or by mitosis, during which one parent cell divides to make two progeny cells while retaining its cellular structure. Prokaryotic cells (e.g., bacteria) replicate by binary fission, whereas eukaryotic cells replicate by mitosis. In contrast, viruses disassemble, produce many copies of their nucleic acid and protein, and then reassemble into multiple progeny viruses. Furthermore, viruses must replicate within host cells because, as mentioned previously, they lack protein-synthesizing and energy-generating systems. With the exception of rickettsiae and chlamydiae, which also require living host cells for growth, bacteria can replicate extracellularly.

(3) **Nature of the nucleic acid.** Cells contain both DNA and RNA, whereas viruses contain either DNA or RNA but not both.

EUKARYOTES & PROKARYOTES

Cells have evolved into two fundamentally different types, **eukaryotic** and **prokaryotic**, which can be distinguished on the basis of their structure and the complexity of their organization. Fungi and protozoa are eukaryotic, whereas bacteria are prokaryotic.

(1) The eukaryotic cell has a true **nucleus** with multiple chromosomes surrounded by a nuclear membrane and uses a mitotic apparatus to ensure equal allocation of the chromosomes to progeny cells.

(2) The **nucleoid** of a prokaryotic cell consists of a single circular molecule of loosely organized DNA, lacking a nuclear membrane and mitotic apparatus (Table 1–3).

In addition to the different types of nuclei, the two classes of cells are distinguished by several other characteristics:

(1) Eukaryotic cells contain **organelles**, such as mitochondria and lysosomes, and larger (80S) ribosomes, whereas prokaryotes contain no organelles and smaller (70S) ribosomes.

(2) Most prokaryotes have a rigid external cell wall that contains **peptidoglycan**, a polymer of amino acids and sugars, as its unique structural component. Eukaryotes, on

TABLE 1–3 Characteristics of Prokaryotic and Eukaryotic Cells

Characteristic	Prokaryotic Bacterial Cells	Eukaryotic Human Cells
DNA within a nuclear membrane	No	Yes
Mitotic division	No	Yes
DNA associated with histones	No	Yes
Chromosome number	One	More than one
Membrane-bound organelles, such as mitochondria and lysosomes	No	Yes
Size of ribosome	70S	80S
Cell wall containing peptidoglycan	Yes	No

PEARLS

- The agents of human infectious diseases are ***bacteria, fungi (yeasts and molds), protozoa, helminths (worms),*** and ***viruses.***
- Bacterial cells have a ***prokaryotic*** nucleus, whereas human, fungal, protozoan, and helminth cells have a ***eukaryotic*** nucleus. Viruses are not cells and do not have a nucleus.
- All cells contain both DNA and RNA, whereas viruses contain either DNA or RNA, but not both.
- Bacterial and fungal cells are surrounded by a rigid cell wall, whereas human, protozoan, and helminth cells have a flexible cell membrane.
- The bacterial cell wall contains ***peptidoglycan***, whereas the fungal cell wall contains chitin.

the other hand, do not contain peptidoglycan. Either they are bound by a flexible cell membrane, or, in the case of fungi, they have a rigid cell wall with chitin, a homopolymer of *N*-acetylglucosamine, typically forming the framework.

(3) The eukaryotic cell membrane contains **sterols**, whereas no prokaryote, except the wall-less *Mycoplasma*, has sterols in its membranes.

Motility is another characteristic by which these organisms can be distinguished. Most protozoa and some bacteria are motile, whereas fungi and viruses are nonmotile. The protozoa are a heterogeneous group that possess three different organs of locomotion: flagella, cilia, and pseudopods. The motile bacteria move only by means of flagella.

TERMINOLOGY

Bacteria, fungi, protozoa, and helminths are named according to the binomial Linnean system, which uses genus and species, but viruses are not so named. For example, regarding the name of the well-known bacteria *Escherichia coli*, *Escherichia* is the genus and *coli* is the species name. Similarly, the name of the yeast *Candida albicans* consists of *Candida* as the genus and *albicans* as the species. But viruses typically have a single name, such as poliovirus, measles virus, or rabies virus. Some viruses have names with two words, such as herpes simplex virus, but those do not represent genus and species.

SELF-ASSESSMENT QUESTIONS

1. You're watching a television program that is discussing viruses called bacteriophages that can kill bacteria. Your roommate says, "Wow, maybe viruses can be used to kill the bacteria that infect people! You're taking the Microbiology course now; what's the difference between viruses and bacteria?" Which one of the following would be the most accurate statement to make?
   (A) Viruses do not have mitochondria, whereas bacteria do.
   (B) Viruses do not have a nucleolus, whereas bacteria do.
   (C) Viruses do not have ribosomes, whereas bacteria do.
   (D) Viruses replicate by binary fission, whereas bacteria replicate by mitosis.
   (E) Viruses are prokaryotic, whereas bacteria are eukaryotic.
2. Bacteria, fungi (yeasts and molds), viruses, and protozoa are important causes of human disease. Which one of the following microbes contains either DNA or RNA but not both?
   (A) Bacteria
   (B) Molds
   (C) Protozoa
   (D) Viruses
   (E) Yeasts
3. Which one of the following contains DNA that is not surrounded by a nuclear membrane?
   (A) Bacteria
   (B) Molds
   (C) Protozoa
   (D) Yeasts

ANSWERS

1. (C)
2. (D)
3. (A)

PRACTICE QUESTIONS: USMLE & COURSE EXAMINATIONS

Questions on the topics discussed in this chapter can be found in the Basic Bacteriology section of Part XIII: USMLE (National Board) Practice Questions starting on page 689. Also see Part XIV: USMLE (National Board) Practice Examination starting on page 731.

CHAPTER 2

Structure of Bacterial Cells

CHAPTER CONTENTS

SHAPE & SIZE OF BACTERIA

Bacteria are classified by shape into three basic groups: **cocci, bacilli,** and **spirochetes** (Figure 2–1). The cocci are round, the bacilli are rods, and the spirochetes are spiral-shaped. Some bacteria are variable in shape and are said to be **pleomorphic** (many-shaped). The shape of a bacterium is determined by its rigid cell wall. The microscopic appearance of a bacterium is one of the most important criteria used in its identification.

In addition to their characteristic shapes, the arrangement of bacteria is important. For example, certain cocci occur in pairs (**diplococci**), some in chains (**streptococci**), and others in grapelike clusters (**staphylococci**). These arrangements are determined by the orientation and degree of attachment of the bacteria at the time of cell division. The arrangement of rods and spirochetes is medically less important and is not described in this introductory chapter.

Bacteria range in size from about 0.2 to 5 μm (Figure 2–2). The smallest bacteria (*Mycoplasma*) are about the same size as the largest viruses (poxviruses) and are the smallest organisms capable of existing outside a host. The longest bacteria rods are the size of some yeasts and human red blood cells (7 μm).

STRUCTURE OF BACTERIA

The structure of a typical bacterium is illustrated in Figure 2–3, and the important features of each component are presented in Table 2–1.

Cell Wall

The cell wall is the outermost component common to all bacteria (except *Mycoplasma* species, which are bounded by a cell membrane, not a cell wall). Some bacteria have surface features external to the cell wall, such as a capsule,

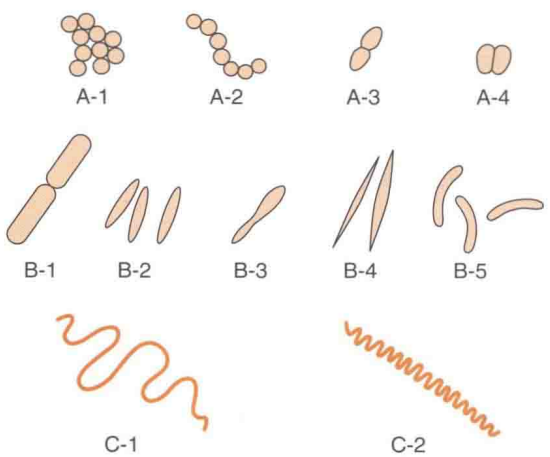

FIGURE 2–1 Bacterial morphology. **A:** Cocci in clusters (e.g., *Staphylococcus;* A-1); chains (e.g., *Streptococcus;* A-2); in pairs with pointed ends (e.g., *Streptococcus pneumoniae;* A-3); in pairs with kidney bean shape (e.g., *Neisseria;* A-4). **B:** Rods (bacilli): with square ends (e.g., *Bacillus;* B-1); with rounded ends (e.g., *Salmonella;* B-2); club-shaped (e.g., *Corynebacterium;* B-3); fusiform (e.g., *Fusobacterium;* B-4); comma-shaped (e.g., *Vibrio;* B-5). **C:** Spirochetes: relaxed coil (e.g., *Borrelia;* C-1); tightly coiled (e.g., *Treponema;* C-2). (Modified and reproduced with permission from Joklik WK et al. *Zinsser Microbiology*. 20th ed. Originally published by Appleton & Lange. Copyright 1992 by McGraw-Hill.)

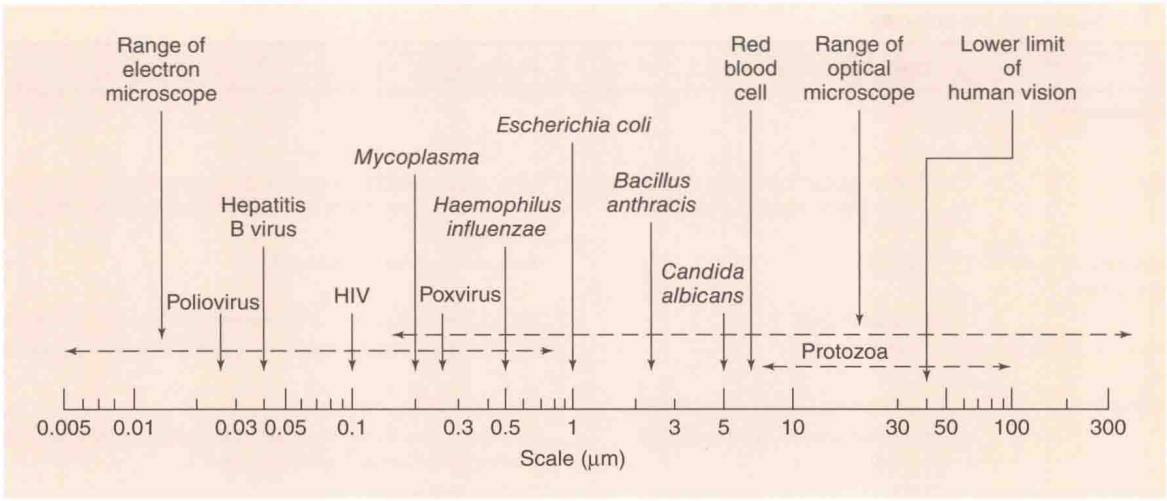

FIGURE 2–2 Sizes of representative bacteria, viruses, yeasts, protozoa, and human red cells. The bacteria range in size from *Mycoplasma,* the smallest, to *Bacillus anthracis,* one of the largest. The viruses range from poliovirus, one of the smallest, to poxviruses, the largest. Yeasts, such as *Candida albicans,* are generally larger than bacteria. Protozoa have many different forms and a broad size range. HIV, human immunodeficiency virus. (Modified and reproduced with permission from Joklik WK et al. *Zinsser Microbiology*. 20th ed. Originally published by Appleton & Lange. Copyright 1992 McGraw-Hill.)

flagella, and pili, which are less common components and are discussed next.

The cell wall is located external to the cytoplasmic membrane and is composed of **peptidoglycan** (see page 6). The peptidoglycan provides structural support and maintains the characteristic shape of the cell.

Cell Walls of Gram-Positive and Gram-Negative Bacteria

The structure, chemical composition, and thickness of the cell wall differ in gram-positive and gram-negative bacteria (Table 2–2, Figure 2–4, and "Gram Stain" box).

(1) The peptidoglycan layer is much thicker in gram-positive than in gram-negative bacteria. Many gram-positive bacteria also have fibers of teichoic acid, which protrude outside the peptidoglycan, whereas gram-negative bacteria do not have teichoic acids.

(2) In contrast, the gram-negative bacteria have a complex outer layer consisting of lipopolysaccharide, lipoprotein, and phospholipid. Lying between the outer-membrane layer and the cytoplasmic membrane in gram-negative bacteria is the **periplasmic space,** which is the site, in some species, of enzymes called β-lactamases that degrade penicillins and other β-lactam drugs.

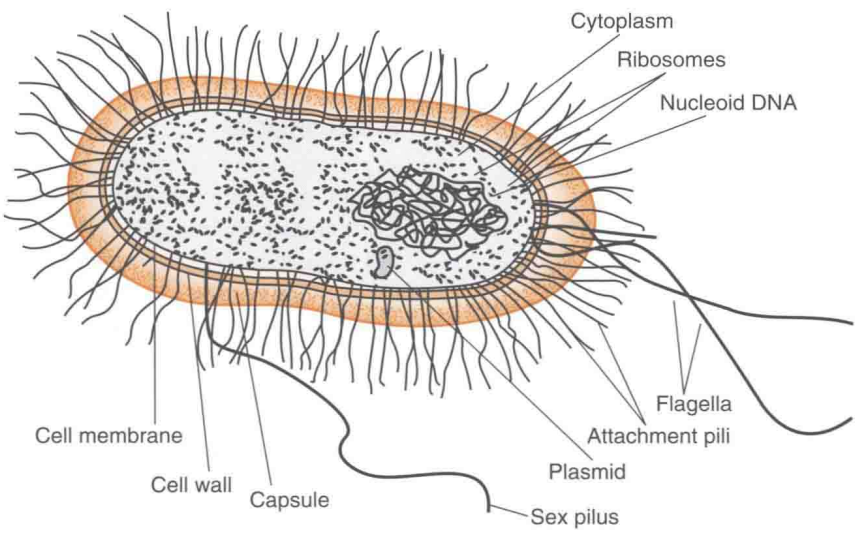

FIGURE 2–3 Bacterial structure. (Modified with permission from Ryan K et al. *Sherris Medical Microbiology*. 4th ed. Copyright 2004 McGraw-Hill.)

TABLE 2–1 Bacterial Structures

Structure	Chemical Composition	Function
Essential components		
Cell wall		
Peptidoglycan	Glycan (sugar) backbone with peptide side chains that are cross-linked	Gives rigid support, protects against osmotic pressure, is the site of action of penicillins and cephalosporins, and is degraded by lysozyme
Outer membrane of gram-negative bacteria	Lipid A	Toxic component of endotoxin
	Polysaccharide	Major surface antigen used frequently in laboratory diagnosis
Surface fibers of gram-positive bacteria	Teichoic acid	Major surface antigen but rarely used in laboratory diagnosis
Plasma membrane	Lipoprotein bilayer without sterols	Site of oxidative and transport enzymes
Ribosome	RNA and protein in 50S and 30S subunits	Protein synthesis; site of action of aminoglycosides, erythromycin, tetracyclines, and chloramphenicol
Nucleoid	DNA	Genetic material
Mesosome	Invagination of plasma membrane	Participates in cell division and secretion
Periplasm	Space between plasma membrane and outer membrane	Contains many hydrolytic enzymes, including β-lactamases
Nonessential components		
Capsule	Polysaccharide[1]	Protects against phagocytosis
Pilus or fimbria	Glycoprotein	Two types: (1) mediates attachment to cell surfaces; (2) sex pilus mediates attachment of two bacteria during conjugation
Flagellum	Protein	Motility
Spore	Keratinlike coat, dipicolinic acid	Provides resistance to dehydration, heat, and chemicals
Plasmid	DNA	Contains a variety of genes for antibiotic resistance and toxins
Granule	Glycogen, lipids, polyphosphates	Site of nutrients in cytoplasm
Glycocalyx	Polysaccharide	Mediates adherence to surfaces

[1]Except in *Bacillus anthracis,* in which it is a polypeptide of D-glutamic acid.

The cell wall has several other important properties:

(1) In gram-negative bacteria, it contains **endotoxin,** a lipopolysaccharide (see pages 8 and 44).

(2) Its polysaccharides and proteins are antigens that are useful in laboratory identification.

(3) Its **porin** proteins play a role in facilitating the passage of small, hydrophilic molecules into the cell. Porin proteins in the outer membrane of gram-negative bacteria act as a channel to allow the entry of essential substances such as sugars, amino acids, vitamins, and metals as well as many antimicrobial drugs such as penicillins.

Cell Walls of Acid-Fast Bacteria

Mycobacteria (e.g., *Mycobacterium tuberculosis*) have an unusual cell wall, resulting in their inability to be Gram-stained.

TABLE 2–2 Comparison of Cell Walls of Gram-Positive and Gram-Negative Bacteria

Component	Gram-Positive Cells	Gram-Negative Cells
Peptidoglycan	Thicker; multilayer	Thinner; single layer
Teichoic acids	Yes	No
Lipopolysaccharide (endotoxin)	No	Yes

These bacteria are said to be **acid-fast** because they resist decolorization with acid–alcohol after being stained with carbolfuchsin. This property is related to the high concentration of lipids, called **mycolic acids,** in the cell wall of mycobacteria.

In view of their importance, three components of the cell wall (i.e., peptidoglycan, lipopolysaccharide, and teichoic acid) are discussed in detail here.

Peptidoglycan

Peptidoglycan is a complex, interwoven network that surrounds the entire cell and is composed of a single covalently linked macromolecule. It is found *only* in bacterial cell walls. It provides rigid support for the cell, is important in maintaining the characteristic shape of the cell, and allows the cell to withstand media of low osmotic pressure, such as water. A representative segment of the peptidoglycan layer is shown in Figure 2–5. The term **peptidoglycan** is derived from the peptides and the sugars (glycan) that make up the molecule. Synonyms for peptidoglycan are **murein** and **mucopeptide**.

Figure 2–5 illustrates the carbohydrate backbone, which is composed of alternating *N*-acetylmuramic acid and *N*-acetylglucosamine molecules. Attached to each of the muramic acid molecules is a tetrapeptide consisting of both