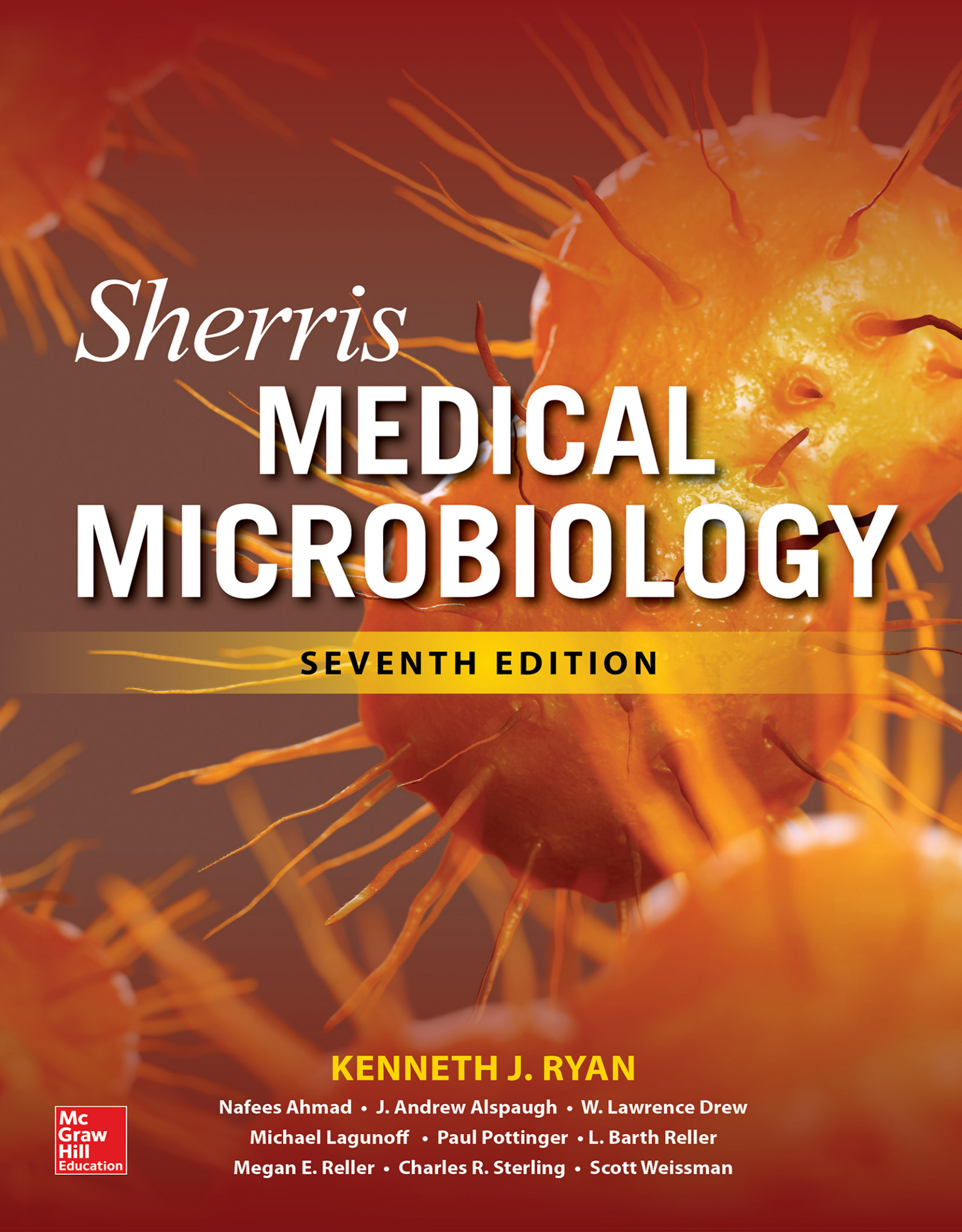

# *Sherris* MEDICAL MICROBIOLOGY

SEVENTH EDITION

KENNETH J. RYAN

Nafees Ahmad • J. Andrew Alspaugh • W. Lawrence Drew
Michael Lagunoff • Paul Pottinger • L. Barth Reller
Megan E. Reller • Charles R. Sterling • Scott Weissman

Mc Graw Hill Education

Seventh Edition

# SHERRIS MEDICAL MICROBIOLOGY


**EDITOR**

KENNETH J. RYAN, MD



Mc Graw Hill Education

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## DEDICATION

# Founders of *Sherris Medical Microbiology*

C. George Ray, MD
James J. Plorde, MD
Elizabeth Sherris
Frederick C. Neidhardt, PhD

Between the sixth and this seventh edition we have lost four scholars who significantly aided founding editor **John Sherris** in the formation and character of this book now known as *Sherris Medical Microbiology*.

**George Ray** was a founding author, writing on viral diseases, infectious disease syndromes, and laboratory diagnosis. For the fourth through the sixth editions, he was also coeditor of the book. Gorge, a national leader in rapid viral diagnosis, was also a decorated teacher of medical students at three medical schools, the University of Washington, the University of Arizona, and St. Louis University. At SLU, he finished his career as Chairman of Pediatrics.

**Jim Plorde,** also a founding author, wrote on antibiotics, bacterial diseases, parasitic diseases and infectious disease syndromes in the first through the fifth editions. Jim's Peace Corps and international experience was reflected in his writing, particularly on parasitic diseases. In his faculty career at Washington he served as Chief of Infectious Diseases and Microbiology at the Seattle Veterans Administration Medical Center.

**Elizabeth Sherris** not only contributed to the organization of the book, she typed the first draft at a time before computers, copiers, and the Internet. Elizabeth had a keen sense of language particularly concerning the clear use of medical language which earned her the respect of the authors and the publisher. She followed later editions closely, remarking especially on the introduction of full color artwork in the fifth edition.

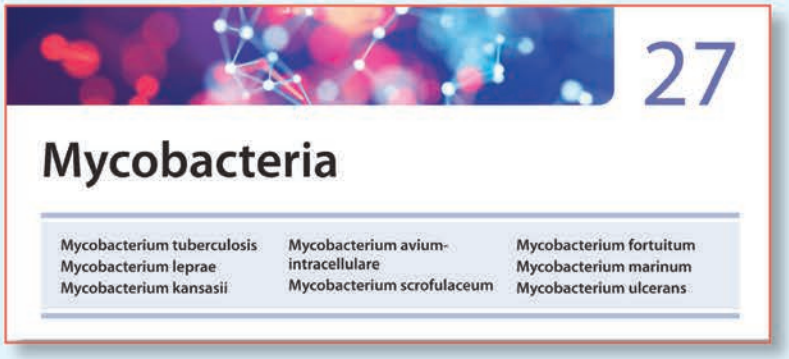
**Fred Neidhardt** was recruited as an author for the second edition during a sabbatical at Washington and continued through the fourth edition. Fred set the standard and style for the presentation of basic bacteriology to medical students, which continues today. A towering figure in bacterial physiology highlighted by his two-volume book on *Escherichia coli,* Fred held faculty positions at Harvard, Purdue, and Michigan, where he was Chair of Microbiology.

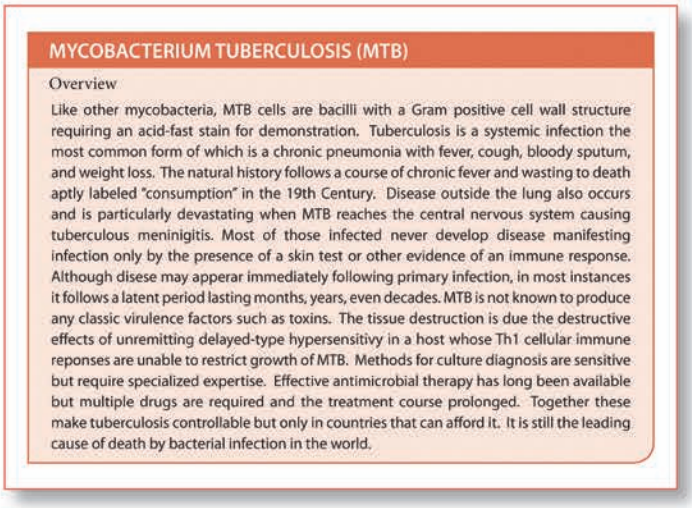
# Key Features

Based on recommendations from our Student Advisory Group a number of changes in chapter presentation have been implemented in the 7th edition of *Sherris Medical Microbiology*. These changes are particularly evident in the 40 chapters which describe the microbiology, disease (epidemiology, pathogenesis, immunity) and clinical aspects (manifestations, diagnosis, treatment, prevention) of the viral, bacterial, fungal, and parasitic human pathogens. These features are designed to highlight the most important elements for both course study and preparation for USMLE examinations. Examples of each are demonstrated below.

## PATHOGEN LIST

Immediately below the title the pathogens for which at least a paragraph of discussion is included in the chapter are listed.



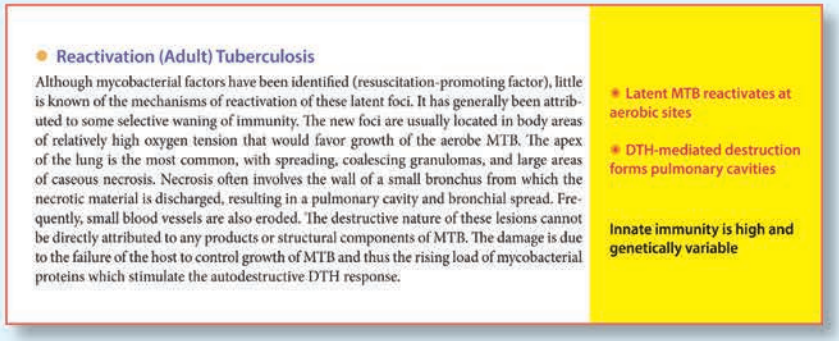




## OVERVIEW

The chapter opens with a boxed narrative paragraph explaining the big picture of the organism and disease features. If the chapter contains more than one major pathogen, an OVERVIEW is given for each.

## MARGINAL NOTES

Marginal notes, a feature of *Sherris Medical Microbiology* since the first edition, give a brief statement of the text material in the immediately opposite paragraph. For the 7th edition this has been enhanced by highlighting those items likely to be the subject of USMLE Step 1 questions.



### Reactivation Tuberculosis

The times of life when persons infected with MTB are most likely to develop clinical disease are infancy (primary), young adult (primary or reactivation), or old age (reactivation). In Western countries, reactivation of previous quiescent lesions occurs most often after age 50.

**How can it take this long for disease to develop?**

and is more common in men. Reactivation is associated with a period of immunosuppression precipitated by malnutrition, alcoholism, diabetes, old age, or a dramatic change in the individual's life, such as loss of a spouse. In areas in which tuberculosis is more prevalent , reactivation is more frequently seen in young adults experiencing the immunosuppression that accompanies puberty and pregnancy. Recently, reactivation and progressive primary tuberculosis among younger adults have increased as a complication of AIDS.

## DIAGNOSIS

### Tuberculin Test

The tuberculin skin test (**Figure 27–6**) measures DTH to an international reference tuberculoprotein preparation called PPD. The test involves an intradermal injection that is read 48 to 72 hours later. An area of induration of 15 mm or more accompanied by erythema constitutes a positive reaction, and no induration indicates a negative reaction. A positive PPD test indicates that the individual has developed DTH through infection at some time with MTB, but carries no implication as to whether the disease is active. Persons who have been infected with another mycobacterial species or immunized with the bacillus Calmette-Guérin (BCG) vaccine may also be reactive, but the induration is usually in the 5 to 10 mm. range. Patients with severe disseminated disease, those on immunosuppressive drugs, or those with immunosuppressive diseases such as AIDS may fail to react or produce

Think ⇨ Apply 27-1. This is due to latency. The MTB have been inert but "alive". Alive all this time.

## THINK → APPLY

At random points the author interrupts the text to pose a question. These are designed to challenge the student to think about what they have read earlier in the chapter and apply it to the question much as might be done during a lecture. The answer is given at the bottom of the page.

## KEY CONCLUSIONS

At the end of each chapter or major section of a chapter a bulleted list of sentences giving the major conclusions the student should be able to draw from that section is displayed. This includes microbiologic, disease, and clinical features of the pathogen and is particularly intended for review during preparation for exams.

### KEY CONCLUSIONS

- High lipid mycobacterial cell wall contains mycolic acids and lipoarabinomannan (LAM) which are responsible for the difficult staining property called acid-fastness.
- Infection is by inhalation of respiratory droplets coughed up by human cases.
- Primary pulmonary infection leads to systemic spread of MTB.
- MTB interferes with killing mechanisms of alveolar macrophages.
- MTB-specific macrophage activation by IFNg leads to resolution in most infected persons.
- Incomplete macrophage activation leads to progressive disease (tuberculosis).
- DTH is the sole known cause of injury.
- Entry of MTB into inactive latent state creates risk of reactivation disease in the lung or other sites (much less often) years to decades later.
- DTH response to tuberculin (PPD) indicates previous infection but not active disease.
- Definitive diagnosis is by AFB smear, culture, or NAA procedures on sputum or other tissues.
- BCG vaccine offers childhood protection but does not prevent reactivation. It also causes a DTH reponse to PPD.
- Antimicrobiol chemotherapy of tuberculosis is effective but few agents are able to penetrate the MTB cell wall. Cost and compliance limit worldwide effectiveness.
- Up to four drugs are used simultaneously to prevent expression of resistant mutants.

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# Preface

With this seventh edition, *Sherris Medical Microbiology* will complete its fourth decade. We are pleased to welcome new authors, Andy Alspaugh (mycology) and Megan Reller (epidemiology) from Duke and Scott Weissman (bacteriology) from the University of Washington. Sadly, George Ray a founding author and coeditor of the last three editions is no longer with us (see Dedication). John Sherris, the founding editor, continues to act as an inspiration to all of us.

## BOOK STRUCTURE

The goal of *Sherris Medical Microbiology* remains unchanged from that of the first edition (1984). This book is intended to be the primary text for students of medicine and medical science who are encountering microbiology and infectious diseases for the first time. **Part I** opens with a chapter that explains the nature of infection and the infectious agents at the level of a general reader. The following four chapters give more detail on the immunologic, diagnostic, and epidemiologic nature of infection with minimal detail about the agents themselves. **Parts II** through **V** form the core of the text with chapters on the major viral, bacterial, fungal, and parasitic diseases, and each begins with its own chapters on basic biology, pathogenesis, and antimicrobial agents.

## CHAPTER STRUCTURE

In the specific organism/disease chapters, the same presentation sequence is maintained throughout the book. First, features of the **Organism** (structure, metabolism, genetics, etc.) are described; then mechanisms of the **Disease** (epidemiology, pathogenesis, immunity) the organism causes are explained; the sequence concludes with the **Clinical Aspects** (manifestations, diagnosis, treatment, prevention) of these diseases. A clinical **Case Study** followed by questions in USMLE format concludes each of these chapters. In *Sherris Medical Microbiology,* the emphasis is on the text narrative, which is designed to be read comprehensively, not as a reference work. Considerable effort has been made to supplement this text with other learning aids such as the above-mentioned cases and questions as well as tables, photographs, and illustrations.

## STUDENT-DRIVEN STUDY AIDS

This edition includes a number of new study aids which are the product of a **Student Advisory** Group (see Authors page) conceived and lead by Laura Bricklin, then a second-year medical student. They include a boxed narrative **OVERVIEW** opening each disease-oriented chapter or major section, highlighted **MARGINAL NOTES** judged to be "high yield" for Step 1 preparation, and bulleted lists of **KEY CONCLUSIONS** at the end of major sections. A **THINK ➔ APPLY** feature randomly inserts thought-provoking questions into the body of the text, which are answered at the bottom of the page. These new features are explained in detail and illustrated on pages iv and v.

The back of the book includes two more review tools. **Infectious Diseases: Syndromes and Etiologies** is a set of tables that brings together the infectious agents (viruses, bacteria, fungi, parasites) discussed separately in Parts II through V as probable causes of the major infection syndromes (pneumonia, arthritis, diarrhea, etc.). It is hoped these will be of value when the student prepares for case discussion exercises or sees patients. The **100 Practice Questions** are in USMLE format and in addition to the ones at the end of earlier chapters.

For any textbook, dealing with the onslaught of new information is a major challenge. In this edition, much new material has been included, but to keep the student from being overwhelmed, older or less important information has been deleted to keep the size of this book no larger than of the sixth edition. As a rule of thumb, material on classic microbial structures, toxins, and the like in the Organism section has been trimmed unless its role is clearly explained in the Disease section. At the same time, we have tried not to eliminate detail to the point of becoming synoptic and uninteresting. Genetics is one of the greatest challenges in this regard. Without doubt this is where major progress is being made in understanding infectious diseases, but a coherent discussion may require using the names and abbreviations of genes, their products, and multiple regulators to tell a complete story. Whenever possible we have tried to tell the story without all the code language. We have also tried to fully describe the major genetic mechanisms in general chapters and then refer to them again when that mechanism is deployed by a pathogen. For example, *Neisseria gonorrhoeae* is used to explain the genetic mechanisms for antigenic variation in a general chapter on bacterial pathogenesis (Chapter 22), but how it influences its disease, gonorrhea, is taken up with its genus *Neisseria* (Chapter 30).

A saving grace is that our topic is important, dynamic, and fascinating—not just to us but to the public at large. Newspaper headlines now carry not only the new names of emerging threats like Zika virus but also the antigenic formulas of more familiar pathogens like *E coli* and influenza virus. Resistance to antimicrobial agents and the havoc created by antivaccine movements are regular topics on the evening news. I1t is not all bad news. We sense a new optimism that deeper scientific understanding of worldwide scourges like HIV/AIDS, tuberculosis, and malaria will lead to their control. We are hopeful that the basis for understanding these changes is clearly laid out in the pages of this book.

**Kenneth J. Ryan**
Editor

# PART I
# Infection

L. Barth Reller • Megan E. Reller • Kenneth J. Ryan

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1

# Infection—Basic Concepts

Humanity has but three great enemies: fever, famine and war; of these by far the greatest, by far the most terrible, is fever.

— Sir William Osler, 1896*

When Sir William Osler, the great physician/humanist, wrote these words, fever (infection) was indeed the scourge of the world. Tuberculosis and other forms of pulmonary infection were the leading causes of premature death among the well to do and the less fortunate. The terror was due to the fact that, although some of the causes of infection were being discovered, little could be done to prevent or alter the course of disease. In the 20th century, advances in public sanitation and the development of vaccines and antimicrobial agents changed this (**Figure 1–1**), but only for the nations that could afford these interventions. As we move through the second decade of the 21st century, the world is divided into countries in which heart attacks, cancer, and stroke have surpassed infection as causes of premature death and those in which infection is still the leader.

A new uneasiness that is part evolutionary, part discovery, and part diabolic has taken hold. Infectious agents once conquered have shown resistance to established therapy, such as multiresistant *Mycobacterium tuberculosis*, and diseases, such as acquired immunodeficiency syndrome (AIDS), have emerged. The spectrum of infection has widened, with discoveries that organisms earlier thought to be harmless can cause disease under certain circumstances. Who could have guessed that *Helicobacter pylori,* not even mentioned in the first edition of this book (1984), would be the major cause of gastric and duodenal ulcers and an officially declared carcinogen? Finally, bioterrorist forces have unearthed two previously controlled infectious diseases—anthrax and smallpox—and threatened their distribution as agents of biological warfare. For students of medicine, understanding the fundamental basis of infectious diseases has more relevance than ever.

## BACKGROUND

The science of medical microbiology dates back to the pioneering studies of Pasteur and Koch, who isolated specific agents and proved that they could cause disease by introducing the experimental method. The methods they developed lead to the first golden age of microbiology (1875-1910), when many bacterial diseases and the organisms responsible for them were defined. These efforts, combined with work begun by Semmelweis and Lister, which showed how these diseases spread, led to the great advances in public health that initiated the decline in disease and death. In the first half of the 20th century, scientists studied the structure, physiology, and genetics of microbes in detail and began to answer

*Osler W. *JAMA*. 1896;26:999.

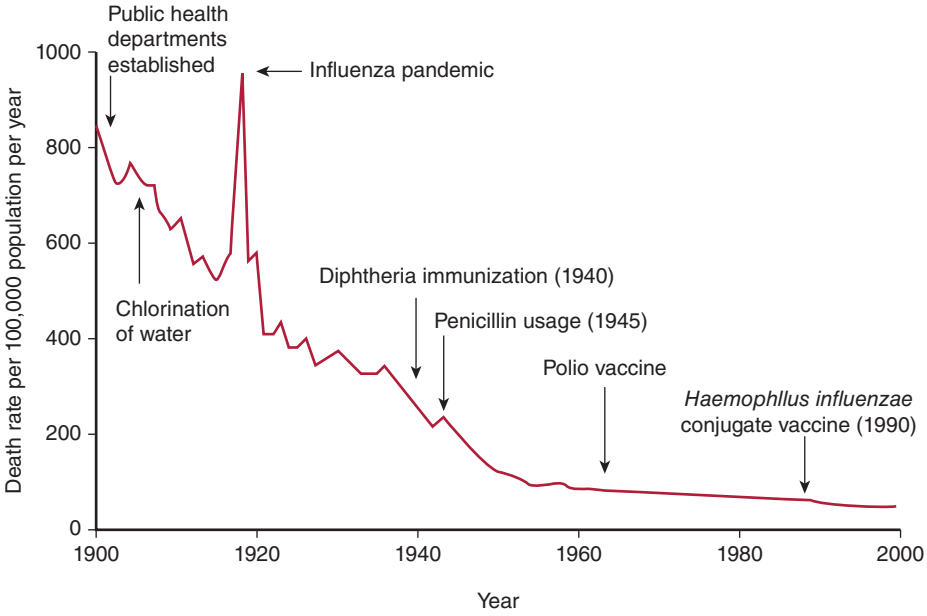


**FIGURE 1–1.** Death rates for infectious disease in the United States in the 20th century. Note the steady decline in death rates related to the introduction of public health, immunization, and antimicrobial interventions.

questions relating to the links between specific microbial properties and disease. By the end of the 20th century, the sciences of molecular biology, genetics, genomics, and proteomics extended these insights to the molecular level. Genetic advances have reached the point at which it is possible to know not only the genes involved but also to understand how they are regulated. The discoveries of penicillin by Fleming in 1929 and of sulfonamides by Domagk in 1935 opened the way to great developments in chemotherapy. These gradually extended from bacterial diseases to fungal, parasitic, and finally viral infections. Almost as quickly, virtually all categories of infectious agents developed resistance to all categories of antimicrobial agents to counter these chemotherapeutic agents.

## INFECTIOUS AGENTS: THE MICROBIAL WORLD

**Microbes are small**

Microbiology is a science defined by smallness. Its creation was made possible by the invention of the microscope (Gr. *micro,* small + *skop,* to look, see), which allowed visualization of structures too small to see with the naked eye. This definition of microbiology as the study of microscopic living forms still holds if one can accept that some organisms can live only in other cells (eg, all viruses and some bacteria) and that others include macroscopic forms in their life cycle (eg, fungal molds, parasitic worms). The relative sizes of some microorganisms are shown in **Figure 1–2.**

**Most play benign roles in the environment**

Microorganisms are responsible for much of the breakdown and natural recycling of organic material in the environment. Some synthesize nitrogen-containing compounds that contribute to the nutrition of living things that lack this ability; others (oceanic algae) contribute to the atmosphere by producing oxygen through photosynthesis. Because microorganisms have an astounding range of metabolic and energy-yielding abilities, some can exist under conditions that are lethal to other life forms. For example, some bacteria can oxidize inorganic compounds such as sulfur and ammonium ions to generate energy. Others can survive and multiply in hot springs at temperatures higher than 75°C.

**Products of microbes contribute to the atmosphere**

Some microbial species have adapted to a symbiotic relationship with higher forms of life. For example, bacteria that can fix atmospheric nitrogen colonize root systems of legumes and of a few trees, such as alders, and provide the plants with their nitrogen requirements. When these plants die or are plowed under, the fertility of the soil is enhanced by nitrogenous compounds originally derived from the metabolism of the bacteria. Ruminants can use grasses as their prime source of nutrition, because the abundant flora of anaerobic bacteria in the rumen break down cellulose and other plant compounds to usable carbohydrates and amino acids and synthesize essential nutrients including some amino acids and vitamins. These few examples illustrate the protean nature of microbial life and their essential place in our ecosystem.

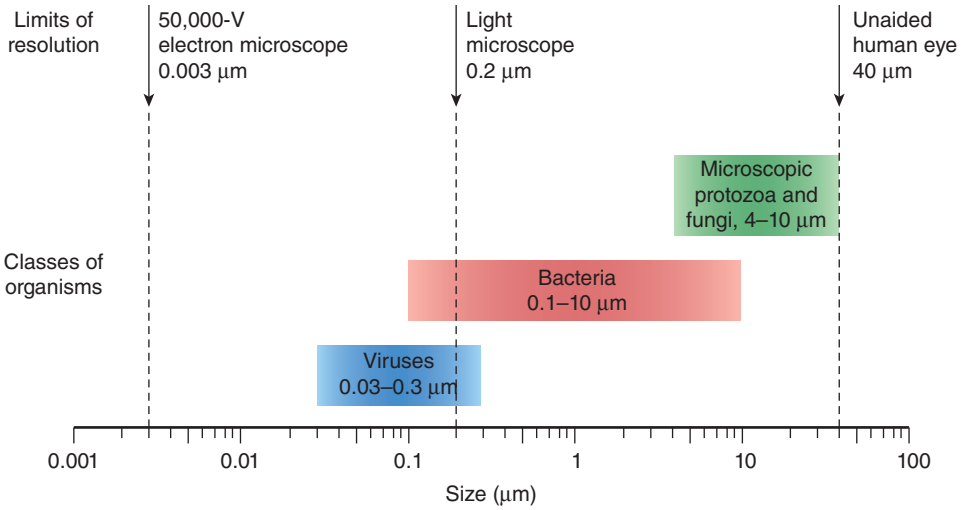


**FIGURE 1–2.** Relative size of microorganisms.

The major classes of microorganisms in terms of ascending size and complexity are viruses, bacteria, fungi, and parasites. Parasites exist as single or multicellular structures with the same compartmentalized eukaryotic cell plan of our own cells including a nucleus and cytoplasmic organelles like mitochondria. Fungi are also eukaryotic, but have a rigid external wall that makes them seem more like plants than animals. Bacteria also have a cell wall, but with a cell plan called "prokaryotic" that lacks the organelles of eukaryotic cells. Viruses are not cells at all. They have a genome and some structural elements, but must take over the machinery of another living cell (eukaryotic or prokaryotic) to replicate. The four classes of infectious agents are summarized in **Table 1–1,** and generic examples of each are shown in **Figure 1–3.**

**Increasing complexity: viruses → bacteria → fungi → parasites**

## VIRUSES

Viruses are strict intracellular parasites of other living cells, not only of mammalian and plant cells, but also of simple unicellular organisms, including bacteria (the bacteriophages). Viruses are simple forms of replicating, biologically active particles that carry genetic information in either DNA or RNA molecules. Most mature viruses have a protein coat over their nucleic acid and, sometimes, a lipid surface membrane derived from the cell they infect. Because viruses lack the protein-synthesizing enzymes and structural apparatus necessary for their own replication, they bear essentially no resemblance to a true eukaryotic or prokaryotic cell.

**Viruses contain little more than DNA or RNA**

Viruses replicate by using their own genes to direct the metabolic activities of the cell they infect to bring about the synthesis and reassembly of their component parts. A cell infected with a single viral particle may, thus, yield thousands of viral particles, which can

**TABLE 1–1** Features of Infectious Agents

| | VIRUSES | BACTERIA | FUNGI | PARASITES |
|---|---|---|---|---|
| Size (µm) | <1 | 2-8 | 4+ | 2+ |
| Cell wall | No | Yes | Yes | No/yes[a] |
| Cell plan | None | Prokaryotic | Eukaryotic | Eukaryotic |
| Free living | No | Yes[b] | Yes | Yes |
| Intracellular | Yes | No/yes | No | No/yes[c] |

[a]Parasitic cysts have cell walls.
[b]A few bacteria grow only within cells.
[c]The life cycle of some parasites includes intracellular multiplication.

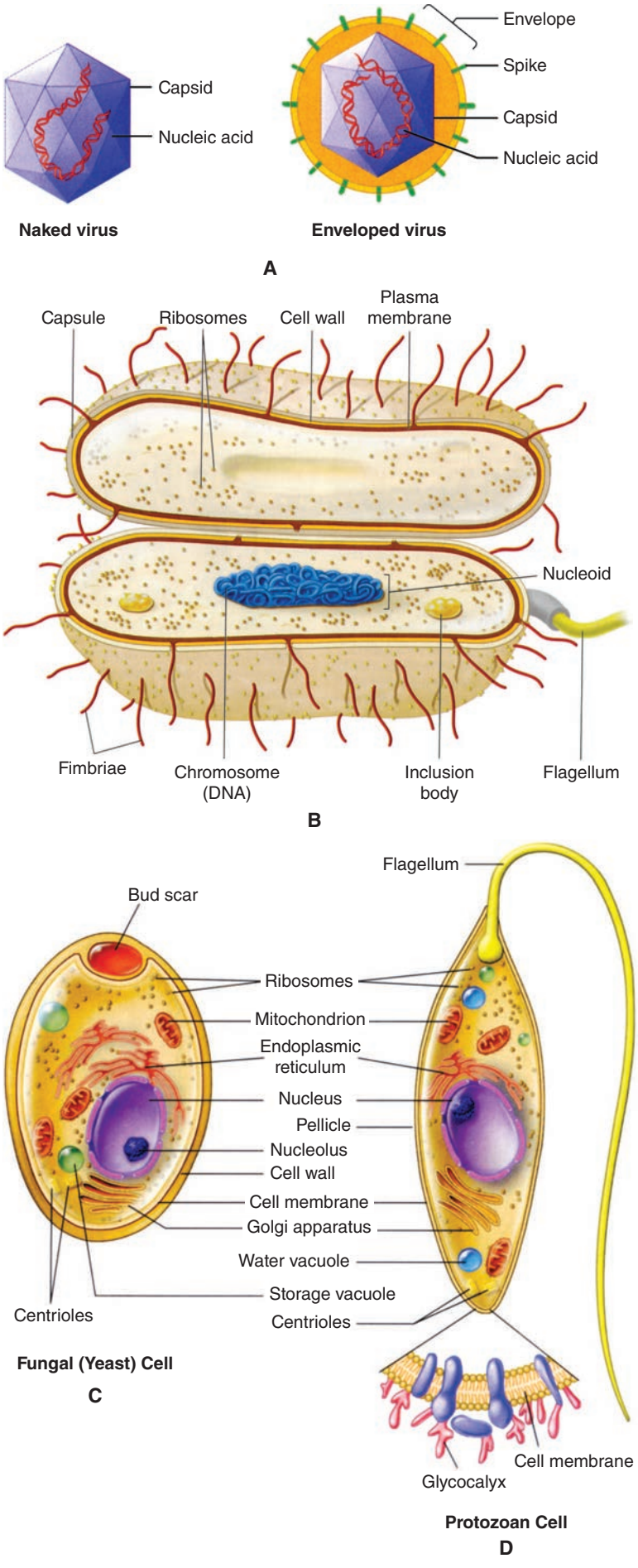


**FIGURE 1–3. Infectious agents.** **A.** Virus. **B.** Bacterium. **C.** Fungus. **D.** Parasite. (Reproduced with permission from Willey JM: *Prescott, Harley, & Klein's Microbiology,* 7th edition. McGraw-Hill, 2008.)

be assembled almost simultaneously under the direction of the viral nucleic acid. Infection of other cells by the newly formed viruses occurs either by seeding from or lysis of the infected cells. Sometimes, viral and cell reproduction proceed simultaneously without cell death, although cell physiology may be affected. The close association of the virus with the cell sometimes results in the integration of viral nucleic acid into the functional nucleic acid of the cell, producing a latent infection that can be transmitted intact to the progeny of the cell.

**Replication is by control of the host cell metabolic machinery**

**Some integrate into the genome**

## BACTERIA

Bacteria are the smallest (0.1-10 μm) independently living cells. They have a cytoplasmic membrane surrounded by a cell wall; a unique interwoven polymer called peptidoglycan makes the wall rigid. The simple prokaryotic cell plan includes no mitochondria, lysosomes, endoplasmic reticulum, or other organelles (**Table 1–2**). In fact, most bacteria are approximately the size of mitochondria. Their cytoplasm contains only ribosomes and a single, double-stranded DNA chromosome. Bacteria have no nucleus, but all the chemical elements of nucleic acid and protein synthesis are present. Although their nutritional requirements vary greatly, most bacteria are free living if given an appropriate energy source. Tiny metabolic factories, they divide by binary fission and can be grown in artificial culture, often in less than 1 day. The Archaea are similar to bacteria but evolutionarily distinct. They are prokaryotic, but differ in the chemical structure of their cell walls and other features. The Archaea (archebacteria) can live in environments humans consider hostile (eg, hot springs, high salt areas) but are not associated with disease.

**Smallest living cells**

**Prokaryotic cell plan lacks nucleus and organelles**

## FUNGI

Fungi exist in either yeast or mold forms. The smallest of yeasts are similar in size to bacteria, but most are larger (2-12 μm) and multiply by budding. Molds form tubular extensions called hyphae, which, when linked together in a branched network, form the fuzzy structure seen on neglected bread slices. Fungi are eukaryotic, and both yeasts and molds have a rigid external cell wall composed of their own unique polymers, called glucan, mannan, and chitin. Their genome may exist in a diploid or haploid state and replicate by meiosis or simple mitosis. Most fungi are free living and widely distributed in nature. Generally, fungi grow more slowly than bacteria, although their growth rates sometimes overlap.

**Yeasts and molds are surrounded by cell wall**

**TABLE 1–2** Distinctive Features of Prokaryotic and Eukaryotic Cells

| CELL COMPONENT | PROKARYOTES | EUKARYOTES |
|---|---|---|
| Nucleus | No membrane, single circular chromosome | Membrane bounded, a number of individual chromosomes |
| Extrachromosomal DNA | Often present in form of plasmid(s) | In organelles |
| Organelles in cytoplasm | None | Mitochondria (and chloroplasts in photosynthetic organisms) |
| Cytoplasmic membrane | Contains enzymes of respiration; active secretion of enzymes; site of phospholipid and DNA synthesis | Semipermeable layer not possessing functions of prokaryotic membrane |
| Cell wall | Rigid layer of peptidoglycan (absent in Mycoplasma) | No peptidoglycan (in some cases cellulose present) |
| Sterols | Absent (except in Mycoplasma) | Usually present |
| Ribosomes | 70 S in cytoplasm | 80 S in cytoplasmic reticulum |

## PARASITES

Range from tiny amoebas to meter-long worms

Parasites are the most diverse of all microorganisms. They range from unicellular amoebas of 10 to 12 μm to multicellular tapeworms 1 m long. The individual cell plan is eukaryotic, but organisms such as worms are highly differentiated and have their own organ systems. Most worms have a microscopic egg or larval stage, and part of their life cycle may involve multiple vertebrate and invertebrate hosts. Most parasites are free living, but some depend on combinations of animal, arthropod, or crustacean hosts for their survival.

## THE HUMAN MICROBIOTA

Before moving on to discuss how, when, and where the previously mentioned agents cause human disease, we should note that the presence of microbes on or in humans is not, by itself, abnormal. In fact, from shortly after birth on, it is universal; we harbor 10 times the number of microbial cells than human cells. This population formerly called the normal flora is now referred to as our **microbiota** or microbiome. These microorganisms, which are overwhelmingly bacteria, are frequently found colonizing various body sites in healthy individuals. The constituents and numbers of the microbiota vary in different areas of the body and, sometimes, at different ages and physiologic states. Their names are mostly unfamiliar because they have not (yet) been associated with disease. They comprise microorganisms whose morphologic, physiologic, and genetic properties allow them to colonize and multiply under the conditions that exist in particular sites, to coexist with other colonizing organisms, and to inhibit competing intruders. Thus, each accessible area of the body presents a particular ecologic niche, colonization of which requires a particular set of properties of the colonizing microbe.

Flora may stay for short or extended periods

If pathogens are involved, the relationship is called the carrier state

Organisms of the microbiota may have a symbiotic relationship that benefits the host or may simply live as commensals with a neutral relationship to the host. A parasitic relationship that injures the host would not be considered "normal," but, in most instances, not enough is known about the organism–host interactions to make such distinctions. Like houseguests, the members of the normal flora may stay for highly variable periods. **Residents** are strains that have an established niche at one of the many body sites, which they occupy indefinitely. **Transients** are acquired from the environment and establish themselves briefly, but they tend to be excluded by competition from residents or by the host's innate or immune defense mechanisms. The term **carrier state** is used when organisms known to be potentially pathogenic are involved, although its implication of risk is not always justified. For example, *Streptococcus pneumoniae,* a cause of pneumonia, and *Neisseria meningitidis,* a cause of meningitis, may be isolated from the throat of 5% to 40% of healthy people. Whether these bacteria represent transient flora, resident flora, or carrier state is largely semantic. The possibility that their presence could be the prelude to disease is presently impossible to determine in advance.

It is important for students of medical microbiology and infectious disease to understand the role of the microbiota because of its significance both as a defense mechanism against infection and as a source of potentially pathogenic organisms. In addition, it is important for physicians to know the typical composition of the microbiota at various sites to avoid confusion when interpreting laboratory culture results. The following excerpt indicates that the English poet W.H. Auden understood the need for balance between the microbiota and its host. He was influenced by an article in *Scientific American* about the flora of the skin.

*On this day tradition allots*
*to taking stock of our lives,*
*my greetings to all of you, Yeasts,*
*Bacteria, Viruses,*
*Aerobics and Anaerobics:*
*A Very Happy New Year*
*to all for whom my ectoderm*
*is as Middle Earth to me.*

*For creatures your size I offer*
*a free choice of habitat,*
*so settle yourselves in the zone*
*that suits you best, in the pools*

*of my pores or the tropical*
*forests of arm-pit and crotch,*
*in the deserts of my fore-arms,*
*or the cool woods of my scalp.*

*Build colonies: I will supply*
*adequate warmth and moisture,*
*the sebum and lipids you need,*
*on condition you never*
*do me annoy with your presence,*
*but behave as good guests should,*
*not rioting into acne*
*or athlete's-foot or a boil.*

—W.H. Auden, "A New Year Greeting"

## ORIGIN AND NATURE

The healthy fetus is sterile until the birth membranes rupture. During and after birth, the infant is exposed to the flora of the mother's vagina and to other organisms in the environment. During the infant's first few days of life, the microbiota reflects chance exposure to organisms that can colonize particular sites in the absence of competitors. Subsequently, as the infant is exposed to a broader range of organisms, those best adapted to colonize particular sites become predominant. Thereafter, the flora generally resembles that of other individuals in the same age group and cultural milieu.

**Initial flora is acquired during and immediately after birth**

Local physiologic and ecologic conditions determine the microbial makeup of the flora. These conditions are sometimes highly complex, differing from site to site, and sometimes with age. Conditions include the amounts and types of nutrients available, pH, oxidation–reduction potentials, and resistance to local antibacterial substances such as bile and lysozyme. Many bacteria have adhesin-mediated affinity for receptors on specific types of epithelial cells; this facilitates colonization and multiplication and prevents removal by the flushing effects of surface fluids and peristalsis. Various microbial interactions also determine their relative prevalence in the flora. These interactions include competition for nutrients and inhibition by the metabolic products of other organisms.

**Physiologic conditions such as local pH influence colonization**

**Adherence factors counteract mechanical flushing**

**Ability to compete for nutrients is an advantage**

## MICROBIOTA AT DIFFERENT SITES

At any one time, the microbiota of a single person contains hundreds if not thousands of species of microorganisms, mostly bacteria. The major members known to be important in preventing or causing disease, as well as those that may be confused with etiologic agents of local infections, are summarized in **Table 1–3** and are described in greater detail in subsequent chapters. The **Human Microbiome Project** is an ongoing effort to bring this information together.

### Blood, Body Fluids, and Tissues

In health, the blood, body fluids, and tissues are sterile. Occasional organisms may be displaced across epithelial barriers as a result of trauma or during childbirth; they may be briefly recoverable from the bloodstream before they are filtered out in the pulmonary capillaries or removed by cells of the reticuloendothelial system. Such transient bacteremia may be the source of infection when structures such as damaged heart valves and foreign bodies (prostheses) are in the bloodstream.

**Tissues and body fluids such as blood are sterile in health**

**Transient bacteremia can result from trauma**

### Skin

The skin surface provides a dry, slightly acidic, aerobic environment. It plays host to an abundant flora that varies according to the presence of its appendages (hair, nails) and the activity of sebaceous and sweat glands. The flora is more abundant on moist skin areas (axillae, perineum, and between toes). Staphylococci and members of the *Propionibacterium* genus occur all over the skin, and facultative diphtheroids (corynebacteria) are found in moist areas. Propionibacteria are slim, anaerobic, or microaerophilic gram-positive rods that grow in subsurface sebum and break down skin lipids to fatty acids. Thus, they are most numerous in the ducts of hair follicles and of the sebaceous glands that drain into them. Even with antiseptic scrubbing, it is difficult to eliminate bacteria from skin sites, particularly those bearing pilosebaceous units. Organisms of the skin flora are resistant to

**Propionibacteria and staphylococci are dominant bacteria**

**Skin flora is not easily removed**

**Conjunctiva resembles skin**