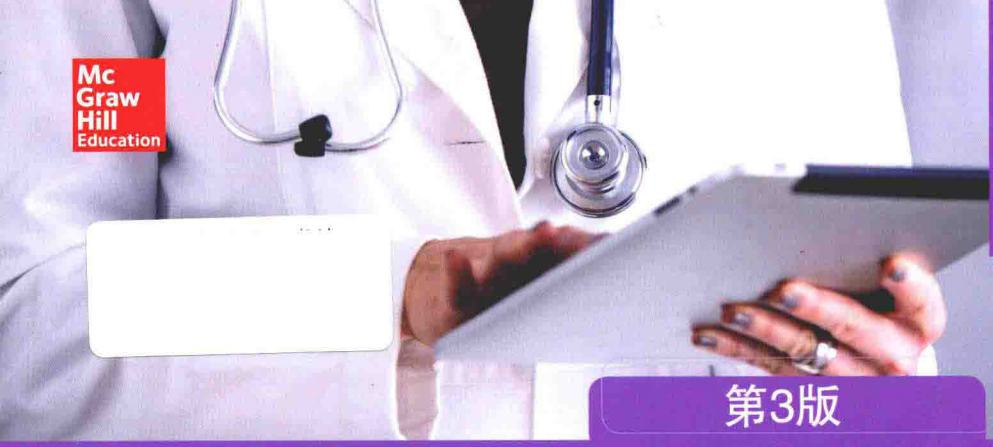

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Case Files 是美国麦格劳 - 希尔教育出版公司医学图书中的著名品牌系列图书，被世界多所著名医学院校选定为教学用书。北京大学医学出版社与麦格劳 - 希尔教育出版公司合作，全套影印出版了该丛书。包括：

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DEDICATION

To my parents, Darrell and Ruth, for their ongoing support;
to my loving husband, Wes, and children Emily, Elliot, and Evan.

—CD

To my patient wife, Betty, and children, Brian, Pamela, and David.

—JK

To my wife and kids who offer me love, support, and perspective.
To my parents who inspired aspirations and then
gave me work ethic to achieve them.
To my boss, colleagues, and residents who help me to grow
on a daily basis.

—AP

To my dear wife Yi for all her love and kindness and my children
Jennifer and Miles for continuing to amaze.
To my parents who have given me more than I can
ever thank them for.

—CM

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We appreciate all the kind remarks and suggestions from the many medical students over the past 5 years. Your positive reception has been an incredible encouragement, especially in light of the short life of the *Case Files* series. In this third edition of *Case Files: Microbiology*, the basic format of the book has been retained. Improvements were made in updating many of the chapters. New cases include rickettsial diseases, brucellosis, West Nile Virus, and *Giardia*. We reviewed the clinical scenarios with the intent of improving them; however, their "real-life" presentations patterned after actual clinical experience were accurate and instructive. The multiple-choice questions have been carefully reviewed and rewritten to ensure that they comply with the National Board and USMLE format. Through this third edition, we hope that the reader will continue to enjoy learn diagnosis and management through the simulated clinical cases. It certainly is a privilege to be teachers for so many students, and it is with humility that we present this edition.

The Authors

ACKNOWLEDGMENTS

The inspiration for this basic science series occurred at an educational retreat led by Dr. Maximilian Buja, who, at the time, was the Dean of the University of Texas Medical School at Houston. It has been such a joy to work together with Drs. DeBord, Wanger, and Mackenzie, all of whom are accomplished scientists and teachers, as well as the other excellent authors and contributors. It has been rewarding to collaborate with Dr. Anush Pillai, a brilliant faculty member. I would like to thank McGraw-Hill for believing in the concept of teaching by clinical cases. I owe a great debt to Catherine Johnson, who has been a fantastically encouraging and enthusiastic editor. It has been amazing to work together with my daughter Allison, who is a senior nursing student at the Scott and White School of Nursing; she is an astute manuscript reviewer and already in her early career she has a good clinical acumen and a clear writing style. At the University of Texas Medical School at Houston, I would like to recognize Dr. Samuel Kaplan, Professor and former Chair of the Department of Microbiology and Molecular Genetics, for his support. At Methodist Hospital, I appreciate Drs. Mark Boom, Alan Kaplan, and Judy Paukert. At St. Joseph Medical Center, I would like to recognize our outstanding administrators: Pat Mathews and Paula Efird. I appreciate Linda Bergstrom's advice and assistance. Without the help from my colleagues, this book could not have been written. Most important, I am humbled by the love, affection, and encouragement from my lovely wife Terri and our four children, Andy and his wife Anna, Michael, Allison, and Christina.

Eugene C. Toy

Often, the medical student will cringe at the "drudgery" of the basic science courses and see little connection between a field such as microbiology and clinical problems. However, clinicians, often wish they knew more about the basic sciences, because it is through the science that we can begin to understand the complexities of the human body and, thus, have rational methods of diagnosis and treatment.

Mastering the knowledge in a discipline such as microbiology is a formidable task. It is even more difficult to retain this information and to recall it when the clinical setting is encountered. To accomplish this synthesis, microbiology is optimally taught in the context of medical situations, and this is reinforced later during the clinical rotations. The gulf between the basic sciences and the patient arena is wide. Perhaps one way to bridge this gulf is with carefully constructed clinical cases that ask basic science-oriented questions. In an attempt to achieve this goal, we have designed a collection of patient cases to teach microbiological related points. More important, the explanations for these cases emphasize the underlying mechanisms and relate the clinical setting to the basic science data. We explore the principles rather than emphasize rote memorization.

This book is organized for versatility: to allow the student "in a rush" to go quickly through the scenarios and check the corresponding answers and to provide more detailed information for the student who wants thought-provoking explanations. The answers are arranged from simple to complex: a summary of the pertinent points, the bare answers, a clinical correlation, an approach to the microbiology topic, a comprehension test at the end for reinforcement or emphasis, and a list of references for further reading. The clinical cases are arranged by system to better reflect the organization within the basic science. Finally, to encourage thinking about mechanisms and relationships, we intentionally used open-ended questions with the clinical cases. Nevertheless, several multiple-choice questions are included at the end of each scenario to reinforce concepts or introduce related topics.

HOW TO GET THE MOST OUT OF THIS BOOK

Each case is designed to introduce a clinically related issue and includes open-ended questions usually asking a basic science question, but at times, to break up the monotony, there will be a clinical question. The answers are organized into 4 different parts:

PART I

1. **Summary**
2. A **straightforward answer** is given for each open-ended question.
3. **Clinical Correlation**—A discussion of the relevant points relating the basic science to the clinical manifestations, perhaps introducing the student to issues such as diagnosis and treatment.

PART II

An **approach to the basic science concept** consisting of 3 parts:

1. **Objectives**—A listing of the 2 to 4 main principles critical for understanding the underlying microbiology to answer the question and relate to the clinical situation
2. **Definitions of basic terminology**
3. **Discussion of topic**

PART III

Comprehension Questions—Each case includes several multiple-choice questions that reinforce the material or introduces new and related concepts. Questions about the material not found in the text are explained in the answers.

PART IV

Microbiology Pearls—A listing of several important points, many clinically relevant reiterated as a summation of the text and to allow for easy review, such as before an examination.

CONTENTS

SECTION I

Applying the Basic Sciences to Clinical Medicine

Part 1. Approach to Learning Microbiology

The student of microbiology should be aware of the scientific characteristics of each microbe, with a particular interest in the relevance to clinical manifestations. The following is a systematic 3-pronged approach:

1. *How does one know that a person is infected?*
2. *Where and how is a person infected?*
3. *What can be done if a person is infected?*

1. **How does one know that a person is infected?** The clinician may have a suspicion of a certain etiologic agent based on clinical clues, but this educated guess must be corroborated by laboratory confirmation. This necessitates an understanding of the basis for presumptive and definitive diagnosis. Possible laboratory tests include culture, polymerase chain reaction of DNA or RNA, antigen tests, or antibody tests.

2. **Where and how is a person infected?** This question translates to understanding about the mechanisms of disease transmission. For example, if a patient is infected with the hepatitis B virus, then the student should be aware that the most common methods of disease acquisition are intravenous drug use, sexual transmission, and vertical transmission. Blood transfusion at one time was a common modality, but now with screening of banked blood, the incidence is very low.

3. **What can be done if a person is infected?** This translates to knowing the best treatment and method of prevention of infection. In other words, once a patient is known to be infected with a certain microbe, what is the best treatment? The student is best served by learning more than 1 antimicrobial therapy and some of the advantages and disadvantages of each therapeutic choice. For example, urinary tract infection caused by *Escherichia coli* may be treated empirically with a variety of antibiotics; however, a quinolone antibiotic, such as ciprofloxacin, is contraindicated in pediatric patients, and gentamicin is relatively contraindicated in those with renal insufficiency.

Likewise, the student should have a systematic approach to classifying microorganisms: viruses, bacteria, protozoa, and fungi.

Virus: A noncellular organism having genetic nucleic acid that requires a host to replicate. They are usually 15 to 450 nanometers in diameter. Viruses do not have a cell membrane or cell wall, but they have a rigid protein coat called the "capsid." The inner cavity contains DNA or RNA. Viruses come in various shapes, including spherical, tetrahedral, polygonal, rod shaped, and polyhedral. One end is usually broader (head), and one end narrower (tail). The tail often has antigenic proteins for attachment to the host. Because viruses do not reproduce without a host, they are considered obligate parasites and not living. See Table I-1 for a schematic of viruses.

Table I-1 • SCHEMATIC DIAGRAM OF SELECTED VIRUS FAMILIES PATHOGENIC TO HUMANS (APPROXIMATE SIZE).

		Genome size (kb)	Envelope	Capsid symmetry
Positive-strand RNA Viruses	Picornaviridae	7.2-8.4	No	Icosahedral
	Caliciviridae	8	No	Icosahedral
	Togaviridae	12	Yes	Icosahedral
	Flaviviridae	10	Yes	Icosahedral
	Coronaviridae	16-21	Yes	Helical
Retroviruses	Retroviridae	3-9	Yes	Icosahedral
Negative-strand RNA Viruses	Rhabdoviridae	13-16	Yes	Helical
	Filoviridae	13	Yes	Helical
	Paramyxoviridae	16-20	Yes	Helical
Segmented Negative-strand RNA Viruses	Orthomyxoviridae	14	Yes	Helical
	Bunyaviridae	13-21	Yes	Helical
	Arenaviridae	10-14	Yes	Helical
Segmented Double-strand RNA Viruses	Reoviridae	16-27	No	Icosahedral
DNA Viruses	Parvoviridae	5	No	Icosahedral
	Papovaviridae	5-9	No	Icosahedral
	Adenoviridae	36-38	No	Icosahedral
	Herpesviridae	100-250	Yes	Icosahedral
	Poxviridae	240	Yes	Complex

Bacteria: These single-celled organisms belong in the kingdom Prokaryotae, and they usually have a cell wall as an outer covering consisting of a complex of sugar and amino acids, and often a cell membrane surrounding the cytoplasm. Being prokaryotes, bacteria do not have a membrane around their nuclei. Some bacteria have flagella, which are cytoplasmic fibrous structures for locomotion. Bacteria may be classified according to shape (cocci, bacilli, or vibrio [comma-shaped], or spirilla

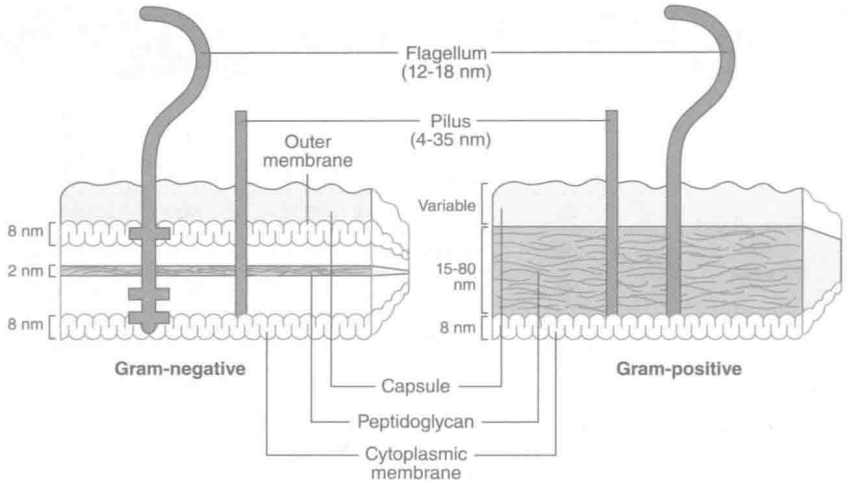

Figure I-1. Schematic diagram of cell walls of gram-negative compared with gram-positive bacteria.

[corkscrew]). Bacteria may also be classified by Gram stain characteristics, metabolism requirements (anaerobic versus aerobic), and presence or absence of cell wall (*Mycoplasma* do not have a cell wall). See Figure I-1 for cell wall characteristics of gram-negative versus gram-positive bacteria.

Parasites: Usually consisting of the protozoa and helminths. Helminths are parasitic worms usually subdivided into flatworms or platyhelminths and roundworms or nemathelminths.

Protozoa: Parasites in humans belonging to the kingdom Protozoa are classified into 3 phyla: Sarcomastigophora (flagellates and amebas), Ciliophora (ciliates), and Apicomplexa (sporozoans).

Fungi: Eukaryotic organisms growing in two basic forms: yeasts and molds. The mold form usually consists of multicellular filamentous colonies. Branching cylinder-like tubules form, called hyphae. The yeast forms are single cells, usually spherical or ellipsoid in shape. Most yeast will reproduce by budding. When the yeast cells bud but fail to break off, they can form elongated yeast cells, called pseudohyphae. Fungi can be classified according to their ability to produce superficial versus deep invasive infection, or by their appearance or sexual reproduction characteristics.

Part 2. Approach to Disease

Physicians usually approach clinical situations by taking a history (asking questions), performing a physical examination, obtaining selective laboratory and imaging tests, and then formulating a diagnosis. The conglomeration of the history, physician examination, and laboratory tests is called the **clinical database.** After reaching a diagnosis, a treatment plan is usually initiated, and the patient is followed

for a clinical response. Rational understanding of disease and plans for treatment are best acquired by learning about the normal human processes on a basic science level, and, likewise, being aware of how disease alters the normal physiologic processes is understood on a basic science level.

Clinicians should be aware of the laboratory methods of diagnosis, including the advantages and disadvantages, cost, time requirements, and potential morbidity to the patient. Various laboratory techniques include detecting DNA or RNA sequences, identifying certain protein components of the microorganism (antigen), or unique enzyme or toxin; microscopic examination such as Gram stain (most bacteria), acid-fast stain (*Mycobacterium*), and immunofluorescence techniques (used to detect difficult-to-culture organisms such as *Legionella*). Cultures are the traditional method of diagnosis, and they must be taken in such a way as to minimize contamination and placed on the appropriate media (or mammalian cell for viruses), with temperature and atmospheric conditions for optimal amplification. Thereafter, the correct identification process should be used to assess characteristics such as colony morphology (both grossly and under the microscope), hemolytic pattern on agar, fermentation profile, Gram stain appearance, and the like.

Once the organism has been identified, susceptibility testing is generally performed to assess the likelihood that certain antimicrobial agents will be effective against the particular strain of pathogen. For example, isolates of *Staphylococcus aureus* should be tested against β-lactam antibiotics such as methicillin to aid the clinician in treating with methicillin versus vancomycin. Susceptibility is generally performed in a qualitative manner (susceptible, intermediate, resistant), or quantitative with minimum inhibitory concentrations or minimum bactericidal concentrations as determined by successive dilutions of the isolate bathed in antimicrobial mixtures.

Part 3. Approach to Reading

There are 7 key questions that help to stimulate the application of basic science information to the clinical setting.

1. *Given a particular microorganism, what is the most likely clinical manifestation?*
2. *Given a particular microorganism, what is the mechanism whereby clinical or subclinical findings arise?*
3. *Given clinical symptoms of infection, what is the most likely causative microorganism?*
4. *Given clinical findings, what are the most likely associated features of the microorganism (such as cell wall characteristics or viral genome)?*
5. *Given the clinical findings, what is the most likely vector of transmission?*
6. *Given the clinical findings, what is the most likely laboratory culture findings?*
7. *Given a particular microorganism, what is the most likely mechanism of resistance acquisition?*

1. **Given a particular microorganism, what is the most likely clinical manifestation?** This is the fundamental knowledge that the student must learn in the broad scope of microbiology, that is, the most likely presentation of clinical disease. Each organism has certain typical patterns of clinical manifestations, based on its characteristics. The interaction between microbe and host, including replication cycle, enzymes released, and host immune response all play roles in the overt symptoms and signs. The student should have an understanding of the common presentations of disease. Likewise, the student should be aware of the mechanisms of the clinical manifestations.

2. **Given a particular microorganism, what is the mechanism whereby clinical or subclinical findings arise?** The student of microbiology is often tempted to memorize the extensive list of microorganisms and clinical disease. Unfortunately, this haphazard approach leads to quick forgetfulness and lack of understanding of the basic science underlying this discipline. Instead, the student should approach the field of microbiology by linking the microorganism, and its particular characteristics, to the mechanisms of disease, such as the interaction with host physiological state, cellular abnormalities that develop, and even cell death. It is the ability of the student to understand the mechanisms that allows for rational approaches to diagnosis and treatment.

3. **Given clinical symptoms of infection, what is the most likely causative microorganism?** The student of microbiology first learns antegrade from microbe toward disease, but patients present instead with disease symptoms and signs. Thus, the student must be able to work backward from clinical presentation to a differential diagnosis (a list of the most likely etiologies) to the probable causative organism. Again, rather than memorization, the student should incorporate mechanisms in the learning process. Thus, the student would best be served to give a reason why the suspected microorganism causes a certain clinical presentation.

   Microorganism → Host defenses/response to invading organism
   → Clinical signs
   Clinical signs → Most likely microbe(s)

4. **Given clinical findings, what are the most likely associated features of the microorganism (such as cell wall characteristics or viral genome)?** This is similar to question 3, but it goes back to the underlying basic science peculiarities of the microbe. First, the student must use the clinical information to discern the likely microorganism, and then the student must relate the characteristics of the microbe. Because a common and effective method of classifying viruses includes the viral genome, this is an important differentiating point. Likewise, bacteria are often subdivided by their cell wall characteristics, which lead to their Gram stain findings. For example, the clinical information may be: "A 66-year-old man complains of blisters erupting on the right chest wall region associated with pain and tingling." The student should remember that a vesicular rash that is unilaterally associated with pain and tingling is characteristic for herpes zoster virus. The etiologic agent is varicella-zoster virus, which causes chickenpox. The virus can lay dormant in the dorsal root ganglia