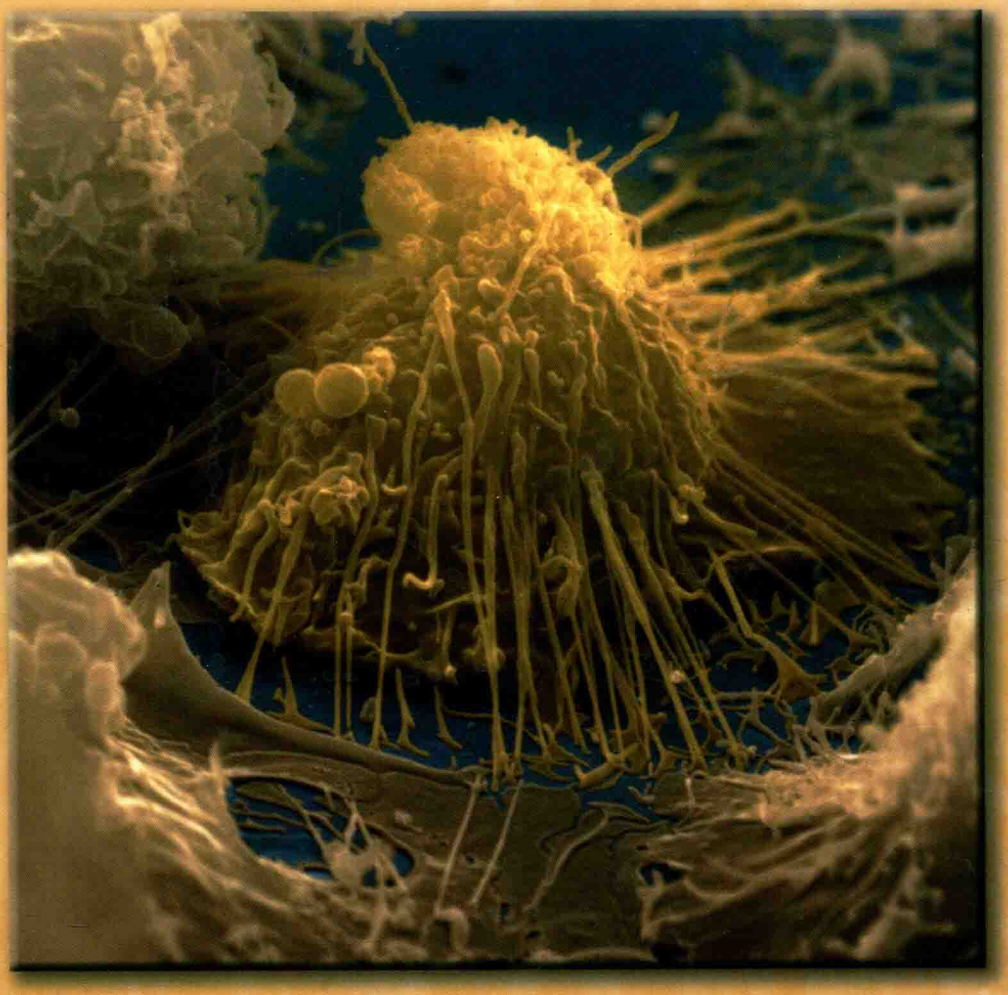
Immunology

FIFTH EDITION



Richard A. Goldsby • Thomas J. Kindt
Barbara A. Osborne • Janis Kuby

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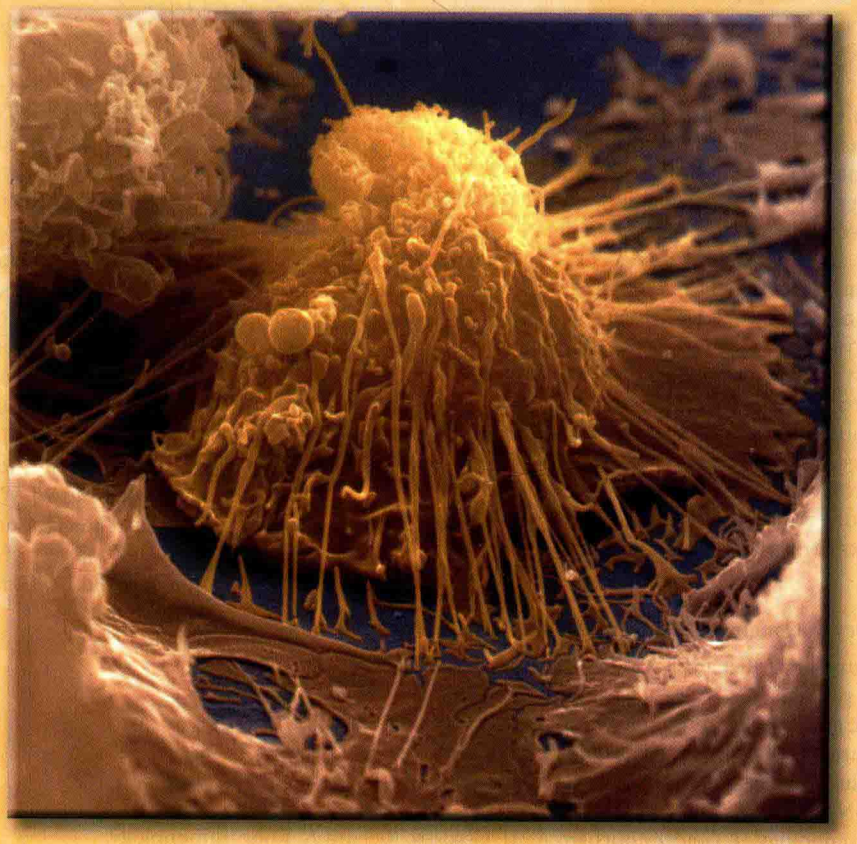

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- **Thomas J. Kindt** National Institutes of Health
- **Barbara A. Osborne** University of Massachusetts at Amherst
- **Janis Kuby** San Francisco State University and University of California at Berkeley

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About the cover

Cellular interactions such as that depicted in this scanning electron micrograph are critical in the initiation and propagation of immune responses. Contact between cell surface receptors and their ligands alert the cell to perform a specific role in the defense of the host against a detected invader. The contact events induce transduction of signals to intracellular molecules, which, upon receipt, may then perform a specific function or, alternatively, may participate as a link in a cascade of events leading to outcomes as diverse as cell activation or cell death. (Meckes/Ottawa/Eye of Science/Photo Researchers, Inc. Also used on pp. iii, vii, ix.)

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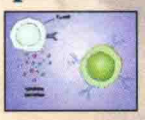
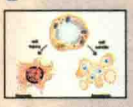
Immunology

Chapter 11 ■ *B-Cell Generation, Activation, and Differentiation*



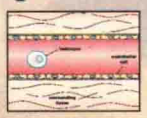
Signal Transduction ANIMATION

Chapter 14 ■ *Cell-Mediated Effector Responses*



Cell Death ANIMATION

Chapter 15 ■ *Leukocyte Activation and Migration*



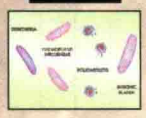
Leukocyte Extravasation ANIMATION

Chapter 16 ■ *Hypersensitive Reactions*

Bee Sting in an Eight-Year-Old Boy CLINICAL CASE STUDY

Chapter 17 ■ *Infection and Immunity*

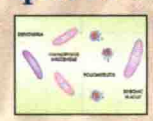
Viral Antigens: Influenza Hemagglutinin and HIV gp120
See Introduction and Flu Virus Hemagglutinin sections. MOLECULAR VISUALIZATION



Vaccine Strategies *See pathogenesis sections.* ANIMATION

Influenza Outbreak in an Elementary School CLINICAL CASE STUDY

Chapter 18 ■ *Vaccines*



Vaccine Strategies ANIMATION

Chicken Pox Vaccine for an Immunosuppressed Fourth-Grade Girl
CLINICAL CASE STUDY

Chapter 19 ■ *AIDS and Other Immunodeficiencies*

Retrovirus ANIMATION

Viral Antigens: Influenza Hemagglutinin and HIV gp120
See Introduction and HIV gp120 sections. MOLECULAR VISUALIZATION

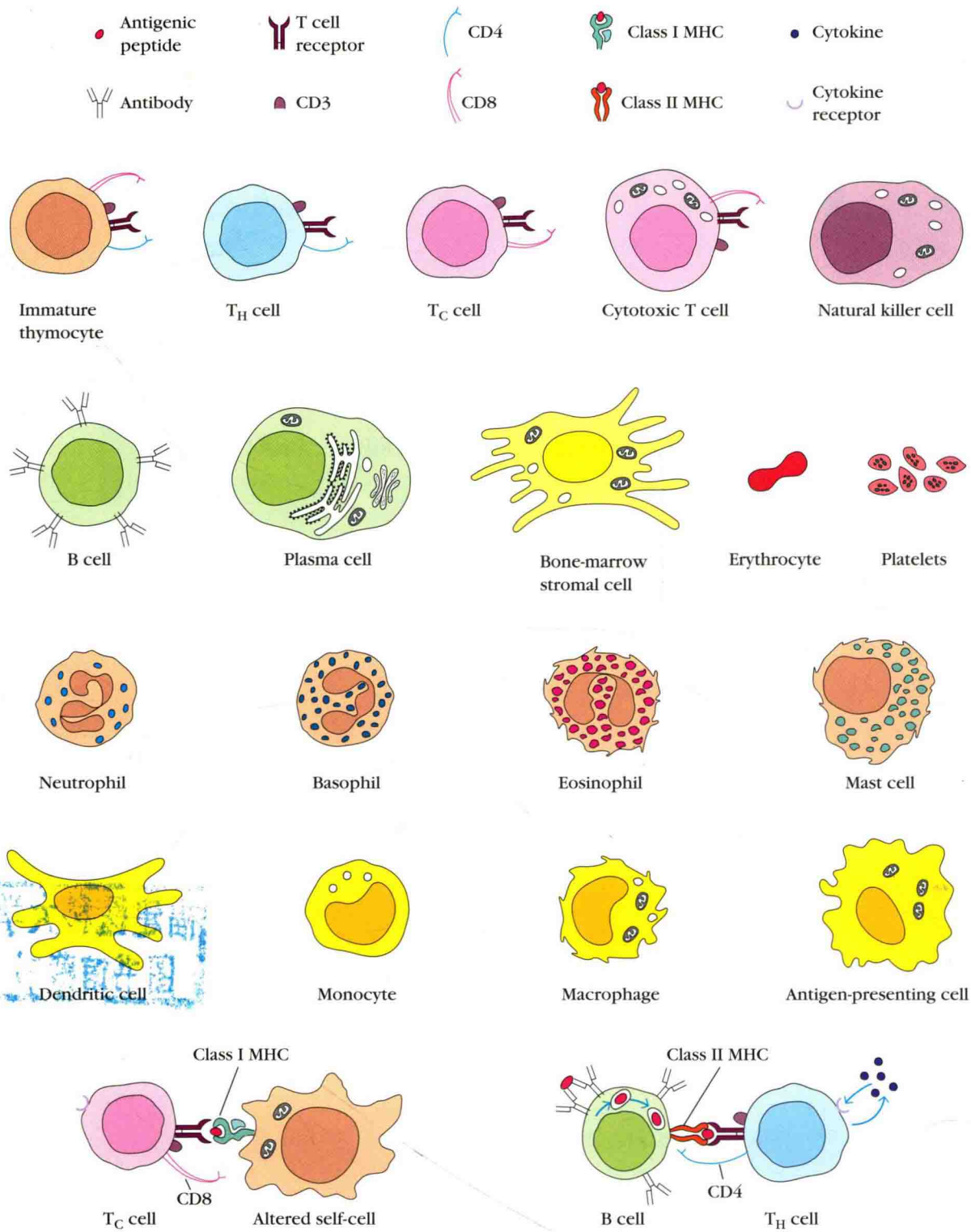
HIV-1 Reverse Transcriptase MOLECULAR VISUALIZATION

AIDS in a Twenty-Nine-Year-Old Man CLINICAL CASE STUDY

Chapter 20 ■ *Autoimmunity*

Glomerulonephritis in a Thirty-Five-Year-Old Woman CLINICAL CASE STUDY

ICONS USED IN THIS BOOK



To all those who provided support and mentorship to us throughout our careers, our special thanks for help, friendship, and encouragement at critical points.

Theodore L. Cross

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Michael J. Potter

Stuart Rudikoff

ABOUT THE AUTHORS

Left to right: Richard A. Goldsby, Barbara A. Osborne, and Thomas J. Kindt

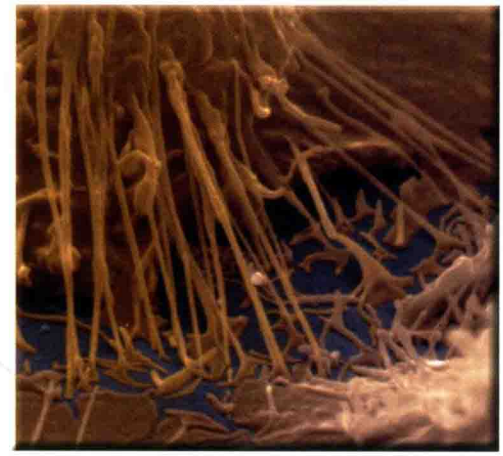
Richard A. Goldsby is a member of the Department of Biology at Amherst College. His research interests include the somatic mutation of antibody genes in the generation of antibody diversity. Since the 1980s, he has served as a course director in the National Science Foundation—Chatauqua Short Course Program for the education of college teachers, where every year presents a course on current advances in immunology.

Thomas J. Kindt, National Institutes of Health, is the Director, Division of Intramural Research at the National Institute of Allergy and Infectious Diseases, which places him in daily contact with the cutting edge of experimental and clinical immunology. As head of the Immunogenetics Research Section, Tom's research interests include the study of retroviral infections in animal models.

Barbara A. Osborne, University of Massachusetts at Amherst, is a recognized contributor to the fast-moving area of apoptosis, or programmed cell death. A highly active researcher, Barbara also teaches immunology to undergraduate and graduate students.

Janis Kuby, who died in 1997, taught at San Francisco State University and the University of California at Berkeley. Professor Kuby was the originator of this textbook and author of the first three editions. Her expert teaching and writing skills made *Immunology* the best-selling text for the course, and her vision for the text as a way to combine cutting-edge content in an accessible, pedagogically rich format lives on in the new edition.

CONTENTS IN BRIEF



PREFACE

". . . the continued growth of immunology is inevitable and challenges both the medical and academic community to stay current."

Janis Kuby's words, introducing the second edition of *Immunology,* capture the relentless expansion of immunological knowledge that makes regular revisions of the text both necessary and exciting. The growth of both experimental and clinical immunology has only continued to accelerate as immunology has become one of the most inclusive and integrative of the sciences, dependent on insights and information from many other fields of biology. Transmitting and interpreting the major currents of this dynamic field is a major objective of this fifth edition.

The swift pace of immunological research generates new findings that expand knowledge and force the periodic revision and sometimes the replacement of established concepts. Consequently, this edition includes a significant amount of new information, and it has been necessary to make changes in some established ideas. Many of the changes are small but essential adjustments to what remain, for now, rather settled areas of immunology. But there are areas where new information, better techniques or even new realizations have forced the inclusion of concepts and findings that are more than incremental additions to the last edition.

Comprehensive Updating and Streamlined Coverage

To make room for the most current information, we have distilled the discussion of some topics down to key points, and presented much of the historical information more economically. This more concise approach has led to a text that is ten percent shorter, and as a result is a more effective teaching tool, while still covering the leading edge of the science. We have improved the organization of each chapter by adding one-sentence summary headings throughout, and added new pedagogy, such as critical thinking questions to accompany each Clinical Focus essay, to help students to better understand the material.

We have continued to focus on the experimental foundations of immunology, keeping pace with the leading edge of research in cell biology, antigen presentation, cell death, signal transduction, and cytokine biology. For example, as structural biology continues to inform immunology, the coverage of the T-cell receptor includes new findings that provide significant insight into the nature of ligand recognition by the long mysterious γδ T-cell receptor.

The rapid growth of basic immunological knowledge and understanding has been accompanied by equally impressive developments in clinical immunology. From its beginnings, immunology has been an eager servant to medicine, and this role continues to play out in the design of vaccination strategies, the creation of new therapeutics for inflammation and allergy, and in new weapons for the fight against cancer. Immunology is a major tool in attempts to understand the devastating diseases of autoimmunity and to halt the ravages of HIV and other difficult and intractable infectious diseases.

Because the frontiers of immunology are advancing so rapidly in both the basic and clinical science, putting all of immunology into a textbook can seem like trying to bottle a geyser. A few of the areas where we have added coverage of the most ground-breaking areas of the science follow.

New Coverage of T-Cell Receptors

Rapid advances in structural biology have continually provided arresting and illuminating images of the nature and interactions of the molecules of immunology. About twenty years ago, X-ray crystallography revealed the first portraits of antigen-antibody complexes. Now, structural biologists have advanced our understanding of αβ T-cells by giving us definitive images of ligand bound to αβ T-cell receptors. Exciting new material on αβ and γδ T-cell receptors can be found in Chapter 9.

Revealing new structural data is presented on the interaction of MHC II/CD4 interactions and on the interaction of MHC-like CD1 family molecules with nonpeptide antigens in Chapters 7 and 8. The coverage of signal transduction from B- and T-cell receptors has been updated and reorganized to emphasize principles and rather than details. Significant advancements in our understanding of the generation of T_H1 and T_H2 subsets are discussed and new insights into the roles of perforin, granzyme B, and the mannose 6-phosphate receptor in CTL killing are presented in Chapters 12 and 14.

New Coverage of Innate Immunity

Until quite recently, the work and thought of immunologists has been dominated by adaptive immunity, the immunity presided over by antigen-specific lymphocytes. Although adaptive immunity continues to dominate much of the work and thought of immunologists, awareness of the extensive and essential interdependence of innate and adaptive immunity is increasing. Hence, we have expanded our coverage of the innate immune system, and its interdependence with adaptive immunity is recognized and highlighted in several places in the new edition.

New Coverage of Clinical and Technical Advances

For many years, the derivation of vaccines for cancer has been a major goal of tumor immunology; recently, there has been significant progress toward this goal. The Clinical Focus box in Chapter 22 provides a discussion of the different approaches being explored in the laboratory and in clinical trials. Some other examples of new coverage of clinical and technical advances in this edition are

- A section on the agents of bioterrorism and the role of immunology in combating this threat. (Chapter 17)
- Expanded coverage of specific monoclonal antibodies and cytokines in clinical use. (Chapters 4, 5 and 12)
- Expanded coverage of stem cell biology and the clinical implications of stem cell research. (Chapter 2)
- Revised and updated information on nonsteriodal anti-inflammatory agents. (Chapter 15)
- Thoroughly updated coverage of the continuing global AIDS emergency. (Chapter 19)
- New discussion of the progress and obstacles to the use of xenotransplantation. (Chapter 21)
- Added coverage of powerful new techniques such as microarray analysis and MHC tetramer labeling. (Chapter 23)

This is a time of great excitement in immunology and writing a text that surveys the entire field provides a wide window through which to view its broad and dynamic landscape. Once again, we hope that *Immunology* will invite a new generation of students to acquire a familiarity with the immune system that will make them better doctors, researchers, and teachers.

For complete chapter-by-chapter details of the many other additions of new material and updated material in the fifth edition of *Immunology*, please visit

Web-Site URL: www.whfreeman.com/immunology5e

Pedagogic Tools

Clinical Focus Essays

Examples encountered in a clinical setting provide incentive to learn the underlying principles and demonstrate the immediate practical value of immunology. New to this edition is a Clinical Focus essay in *every* chapter. Some Clinical Focus essays have been revised, and some have been replaced; many new topics are covered in the new essays, such as bioterrorism, tumor vaccines, and xenotransplantation. Additionally, each essay is linked to a new Clinical Focus Question that appears at the beginning of the Study Questions section of each chapter.

Visualizing Concepts

A number of concepts are especially crucial for students to grasp in developing a firm understanding of immunology. These concepts are illustrated in key diagrams called Visualizing Concepts. These figures summarize important ideas and processes in a way that written text alone cannot convey. Figures from the previous edition have been carefully reviewed, and in a number of cases the most important summary figures have been converted to "walk-through" illustrations—a new style of figure with more extensive and systematic labels that help the student absorb concepts and provide an anchor for students studying for exams. A good example appears in Chapter 8, illustrating the differences and implications of dual pathways for processing exogenous and endogenous antigen.

Full-Color Illustrations

Well-chosen and carefully colored figures enhance the understanding of the text. Recurring elements—such as various immune system cells and important membrane molecules—are depicted consistently by icons, facilitating recognition of the elements in different contexts. A table of these iconic elements appears as the frontispiece of the book, providing an easily accessible guide.

Study Questions

The study questions of earlier editions have proven extremely popular with both instructors and students—they are a useful teaching tool that provides a challenging and thoughtful review for students. New questions have been added, some have been retired, and in every chapter, a new question relating to that chapter's Clinical Focus essay leads off the list.

Study Aids

Key terms appear in boldface type within the text. Definitions of these terms appear in the revised and updated Glossary at the end of the book.

Chapter Summaries, which appear as bulleted lists in this edition, provide a concise review of the material in the chapter.

Updated References at the end of each chapter enable students to sample the primary literature relating to topics of interest. Useful Web Sites are also listed under References. In addition, Web icons at the bottom of some pages guide students to relevant animations and additional information located at the *Immunology* Web site. Web address updates may be found at

Web-Site URL: www.whfreeman.com/immunology5e

Complete annotated tables of CD markers and cytokines are included in two appendixes.

Supplements

Instructor's Resource CD-ROM

Available to adopters, this electronic resource now includes *all* text images in both JPEG and Power Point formats. (All text images are also available from the **Instructor's Resource Center** on the book's companion Web site.) In addition, the CD-ROM contains all animations from the Web site.

Web-Site URL: www.whfreeman.com/immunology

The Web site provides students with a chapter-by-chapter online study guide that includes a variety of exercises and resources. Students can apply their knowledge of immunology in a medical context by analyzing **Clinical Case Studies. Animations** of key concepts facilitate understanding of complex immunological processes by adding a dimension beyond the printed page. In **Molecular Visualizations** by David Marcey of California Lutheran University, dynamic guided tours of three-dimensional molecular models make the relationship between molecular structure and function easier to grasp. **Flashcards** allow students to review and then quiz and grade themselves on definitions of key terms from the text. Students can also access the **Useful Web Sites** mentioned in the textbook for further research.

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CONTENTS