Understanding Viruses

THIRD EDITION

Teri Shors, PhD
Professor
Department of Biology
University of Wisconsin – Oshkosh

JONES & BARTLETT
LEARNING

World Headquarters
Jones & Bartlett Learning
5 Wall Street
Burlington, MA 01803
978-443-5000
info@jblearning.com
www.jblearning.com

Jones & Bartlett Learning books and products are available through most bookstores and online booksellers. To contact Jones & Bartlett Learning directly, call 800-832-0034, fax 978-443-8000, or visit our website, www.jblearning.com.

Substantial discounts on bulk quantities of Jones & Bartlett Learning publications are available to corporations, professional associations, and other qualified organizations. For details and specific discount information, contact the special sales department at Jones & Bartlett Learning via the above contact information or send an email to specialsales@jblearning.com.

05789-8

Production Credits

VP, Executive Publisher: David D. Cella
Executive Editor: Matthew Kane
Associate Editor: Audrey Schwinn
Senior Production Editor: Nancy Hitchcock
Marketing Manager: Lindsay White
Production Services Manager: Colleen Lamy
Manufacturing and Inventory Control Supervisor: Amy Bacus
Composition: Cenveo® Publisher Services
Cover Design: Kristin E. Parker
Rights & Media Specialist: Jamey O'Quinn
Media Development Editor: Troy Liston
Cover Image: © National Institute of Allergy and Infectious Diseases (NIAID).
Printing and Binding: RR Donnelley
Cover Printing: RR Donnelley

The cover image is a digitally colorized scanning electron micrograph of Ebola viruses budding from the surface of Vero (African green monkey kidney epithelial) cells in culture. Ebola virus particles are long and filamentous and often described as being shaped like spaghetti noodles.

Library of Congress Cataloging-in-Publication Data
Names: Shors, Teri, author.
Title: Understanding viruses / Teri Shors.
Other titles: Viruses
Description: Third edition. | Burlington, Massachusetts : Jones & Bartlett Learning, [2017] | Includes bibliographical references and index.
Identifiers: LCCN 2016018705 (print) | LCCN 2016020526 (ebook) | ISBN 9781284025927
Subjects: | MESH: Viruses | Virus Physiological Phenomena | Virus Diseases
Classification: LCC RC114.5 (print) | LCC RC114.5 (ebook) | NLM QW 160 | DDC 616.9/1—dc23
LC record available at https://lccn.loc.gov/2016018705

6048

Printed in the United States of America
20 19 18 17 16 10 9 8 7 6 5 4 3 2 1

Dedication

To the late Elaine (Motschke) Gross, my mother. *Ich vermisse dich jeden Tag*.

To John Cronn, my undergraduate microbiology mentor, colleague, and friend
who opened my eyes to the invisible world of microbes and viruses.

To Robert I. Krasner, who shared the same passion for microbiology
education, music, art, and photography.

To Denise M. McGuire (1954–2002), an undergraduate mentor who taught biotechnology.
She always made time for my endless questions. Her unique laugh could conquer gloom.

To Roger and Sylvia Gasser, dedicated teachers and lifelong learners.

To the thousands of students I have taught, past and present.

"We know nothing of what will happen in the future, but by the analogy of experience."
—Abraham Lincoln

Brief Contents

Contents

INDEX OF BOXES

Chapter 4

Chapter 5

Chapter 6

Chapter 7

Chapter 13

Chapter 14

Chapter 15

Chapter 16

Chapter 17

Foreword

Despite progress over the past century, the world continues to face substantial, and even growing, infectious disease challenges, including antibiotic resistance; Ebola; Zika; Middle East respiratory syndrome (MERS); avian influenza, including H5N1 and H7N9; tuberculosis, and even HIV/AIDS. These diseases present challenges that are in need of technological advancements (e.g., development of rapid diagnostics and new drugs and vaccines) and the political commitment to invest in global prevention and control. The subsequent reviews of the public health response to the Ebola outbreak in West Africa by three different groups exposed the major gaps in our public health and medical capability to rapidly and effectively address these ever-increasing infectious disease crises.

A number of factors favor the emergence of infectious diseases in our 21st-century world. International travel and commerce greatly enhance the movement of infected people and animals, including arthropod vectors, throughout the world. Rapid growth in both human and food-production animal populations creates the ideal environment for mixing and the emergence of new infectious disease problems and the reemergence of previous infectious challenges. Today, with a global human population of 7.4 billion people, one out of every eight people who has ever lived is currently on the face of the earth. Population growth is greatest in developing world megacities, where the squalid conditions of slums, with millions of people, greatly enhances the likelihood of the rapid emergence of infectious diseases.

Although it may be impossible to predict which pathogens may emerge or reemerge into a potential global crisis, early detection through comprehensive disease surveillance systems is a key factor in responding to these epidemics. We must also keep focused on the transmission of infectious diseases at the human–animal interface, because so many current diseases are zoonoses, diseases transmitted between humans and animals. This is why a "one health approach" to reducing infectious diseases, where humans and animals are seen as one "contiguous population," is critical.

The threat of new pandemics fosters innovation and opportunities for collaboration and sharing, among countries and across governments. Global health is driving interdisciplinary approaches in education, requiring students to synthesize, evaluate, and apply knowledge relevant to complex real-world challenges, such as emerging viruses that are contributors to the rise of infectious disease outbreaks. Embracing global health through undergraduate liberal arts programs in education makes it possible for students to connect classroom learning to field testing of solutions. Students who are encouraged to think creatively and holistically about global health challenges may foster a culture of reciprocity.

Michael T. Osterholm, PhD, MPH
Regents Professor
McKnight Endowed Presidential Chair in Public Health
Director, Center for Infectious Disease Research and Policy
Distinguished University Teaching Professor
Environmental Health Sciences, School of Public Health
Professor, Technological Leadership Institute College of Science and Engineering
Adjunct Professor, Medical School
http://www.cidrap.umn.edu

Preface

This third edition of *Understanding Viruses* is the product of nearly 20 years of teaching introductory virology to undergraduate students majoring in biology, microbiology, and medical technology and to premed and other preprofessional students. Because many of the students in my courses had not taken a microbiology or cellular and molecular biology course, I found that they lacked knowledge about the fundamental concepts of cell biology and needed some form of "refresher" to aid them through the course material. It was a struggle to find a textbook that combined a holistic approach to understanding viral diseases. Most virology textbooks are focused on the pathogenesis/clinical aspect of viral diseases or the molecular biology of viral replication. Students were more enthusiastic to learn the molecular aspects of viral diseases if the historical and clinical perspectives were presented with it. *Understanding Viruses, Third Edition* uses an interdisciplinary approach by covering the historical perspectives along with the molecular biology of virus structure and replication, pathobiology (the observed nature of disease, its causes, processes, development, and consequences), and epidemiological impact of viral diseases on local and global populations.

Virology is a dynamic discipline. Emerging viral diseases such as the 2014–2015 Ebola epidemic in West Africa; the spread of Zika virus infections to Brazil in 2015, which was associated with microcephaly in newborns; the threat of pandemic avian influenza A viruses; the spread of Chikungunya virus infections to the Americas in 2013; the impact of global climate change on infectious disease (e.g. insect vectors); the need for the development of new vaccines and antivirals to combat viral diseases; and new cancer therapies that utilize viruses to replicate within cancer cells and kill them while inducing the adaptive immunity of the body to attack and destroy tumor cells are popular topics covered by news media. My intent was to create a resource that provides a "big picture" or systematic approach to understanding viruses, including historical perspectives and epidemiological accounts of viral diseases, along with the relationships between the host, virus, and environment (disease triangle model of disease causation) and the molecular biology of viral structure and replication.

New to This Edition

Understanding Viruses, Third Edition contains a Foreword by Dr. Michael T. Osterholm that discusses the fast-paced and interdisciplinary nature of virology. The revision was focused on addressing peer reviews, improving the text's content and overall quality. For this reason, the order of chapters has been rearranged slightly to accommodate reviewers' comments. For example, "Viruses and Cancer" has been moved to Chapter 16, and "The History of Medicine, Clinical Trials, Gene Therapy, and Xenotransplantation" has been moved to Chapter 17, because this information may not be covered in a one-semester course. Although it is impossible to create a textbook that is current with most recent events and discoveries, every effort has been made to include the most up-to-date information before the text was printed. For example, it includes new information about the Ebola epidemic in West Africa and information on the Zika virus epidemic in Brazil that was taking place while the text was in production.

All chapters in this edition now open with a quote, relevant opener figure, case study, and a set of learning objectives. Much effort has been put into restructuring and updating the introductory chapters of the textbook. Chapter 1 includes several new topics, including how scientists can learn from viruses, helpful or collaborative viruses, human and aquatic viromes, and a brief introduction to epidemiology through coverage of the transmission and pathogenesis of viral infections. Chapter 1 summarizes recent epidemics caused by Ebola virus in West Africa, hantavirus in Yosemite National Park, Middle East respiratory syndrome, measles virus in the United States, and Schmallenberg viruses in Europe.

Chapters 2 and 4 have been merged to create Chapter 3. This chapter now presents an overview of eucaryotic molecular biology, along with the basics of virus replication, as a refresher for those students lacking prerequisite knowledge of cell biology. It contains new Virus File boxes about RNA splicing (reviewing early experiments on adenovirus R-loop mapping), real-time virus tracking in live cells, and a reverse pharmacology approach

to antiviral drug discovery. It also explores the molecular hurdles overcome by replicating viruses through inclusion of such topics as host cell receptors and polymerases, actin remodeling, ribosomes and viral mRNA compatibility, and the competition between virus–host cell mRNAs for cellular translational machinery.

A concerted effort has been made to provide examples of worldwide epidemics caused by viruses. The majority of the chapters contain new chapter opener figures and introductory case studies. There are new case studies about Ebola, West Nile, variola, varicella zoster, measles, avian and swine influenza A, Heartland and amoebic viruses; human immunodeficiency virus (HIV, in particular the 2015 epidemic in Indiana); and other topics, such as the use of a modified poliovirus to treat glioblastoma. Case studies include a list of references that were used to create the case study and questions to involve students in problem-solving activities, higher-order thinking, and opportunities to extend their learning.

Along with the global approach to viral diseases, we have incorporated terminology associated with viral diseases used by the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC). New Virus Files are provided throughout the textbook on a variety of engaging topics:

- "Now I take My Pen in Hand . . ." (letters from a Wisconsin soldier chronicling disease during the Civil War)
- Isolated Reminders of Smallpox Epidemics During the 1800s in America
- Wakefield's Syndrome ("Autistic Enterocolitis") and the MMR Vaccination Scare
- The Massie Puzzle Piece Hiding on Chromosome 6
- Virus Cold Cases: Brainerd Diarrhea, Sweating Sickness, and Picardy Sweat
- Development of a Rapid Test to Determine if Respiratory Illnesses Are Caused by a Virus or Bacterium
- Human Viruses Lurking in Porta-Potties and Outhouses
- Voluntary Quarantine and the Village of Eyam
- The Pap-Test Controversy: Papanicolaou vs. Babes
- Brain-Shrinking Zika Virus Bound for the United States?

The book includes a consistent art package of illustrations. For the first time, animations previously not found in other resources are bundled with the textbook. The animations in *Understanding Viruses* are used to explain the mechanisms of the following antivirals:

- Neuraminidase inhibitors of influenza A viruses
- HIV protease inhibitors
- HIV integrase inhibitors
- Herpesvirus acyclovir inhibitor
- Hepatitis C virus protease inhibitors
- ZMapp inhibitor of Ebola virus

To ensure that students become familiar with credible resources beyond the classroom, numerous tables and maps are provided that present epidemiological information. Chapter 6 contains tables that list modes of transmission, incubation periods, and R-nought values for various viral diseases, as well as website addresses for traveler's health information and global partnerships. Additional chapters contain lists of FDA-approved antiviral drugs, vaccination recommendation schedules, and lists of vaccines in use today.

For the first time, this new edition includes appendices containing in-depth information on a number of topics that may be of interest to students:

- Appendix A: Properties of Human Viruses
- Appendix B: Baltimore Virus Classification
- Appendix C: Bonus case study: "Combating the Worst Epidemic of Ebola Virus Disease in Human History"

This text is unlike many others on the market today. The end of every chapter contains additional cases studies with questions and a list of resources that have been updated and separated into primary literature, reviews, popular press books, and video productions (listed in reverse chronological order). These resources allow for flexibility in course design. Primary literature and reviews can be assigned as outside readings to engage and familiarize students during class discussions and to inform debates about discoveries and current topics in the field of virology. Video resources serve as excellent and timely supplements to the text. The glossary was revised extensively. The textbook is not the only tool for instruction, but rather a guide that can be judiciously adapted to a graduate-level virology course.

The Student Experience

The main goals in the development of the third edition of *Undertanding Viruses* have been to arouse student interest and to create a tool for instruction that contains all of the educational "bells and whistles" that books for first-year biology students are expected to include, such as e-book access and other current pedagogy that engages students in the learning process. The textbook has a number of special features to prompt student engagement and interest:

Learning Objectives—NEW to the third edition, these give students a concise overview of the important chapter concepts they will be asked to master.

Chapter Outlines—A detailed outline at the beginning of the chapter offers a quick snapshot of the topics that will be presented.

Case Studies—Real-world cases are presented at the beginning of each chapter and connected with questions placed at the end of the chapter in order to promote student interest and engagement. Additional Case Studies at the end of most chapters provide additional real-world examples and applications of the chapter content.

Virus Files—The Virus Files within each chapter connect chapter topics to current research or virology techniques.

VIRUS FILE 7-2 **Development of a Rapid Test to Determine Whether Respiratory Illnesses Are Caused by a Virus or Bacterium**

All too often a person shows up at a clinic or hospital emergency room suffering from symptoms of a respiratory tract infection and the doctor prescribes antibiotics just in case the patient is suffering from a bacterial infection. *Antibiotics will not work if a virus is the cause of the illness.* Symptoms alone are not enough to diagnose a respiratory infection. Today, if it is influenza season a rapid test may be done to determine whether the patient is suffering from influenza A or B or strep throat caused by the bacterium *Streptococcus pyogenes*.

A group of researchers at Duke University are developing a rapid blood test that can distinguish whether a respiratory illness is caused by a *viral or bacterial pathogen*. In order to develop the test, small studies were done using healthy volunteers who agreed to be infected with different strains of influenza A virus. Their blood was drawn during the course of infection and genetically analyzed (**FIGURE 1**). The Duke researchers discovered that the expression of 30 cellular genes involved in the immune response were turned on in different ways during the viral infection. The cellular immune response was referred to as a specific **viral** or **genetic signature**. *When infected by a virus, a person's immune system responds differently than it would when fighting a bacterial infection.* The researchers developed an RT-PCR test to detect the viral signature of influenza A viruses in patient blood samples.

The viral signatures of the volunteers infected with influenza A viruses were compared to blood samples collected from people who went to hospital emergency rooms complaining of fever and respiratory illness. Their rapid blood test identified positive viral signatures or infections in 89% of the cases and correctly ruled out negative cases 94% of the time. *Early differentiation between viral and bacterial respiratory infections can direct treatment appropriately (e.g., Tamiflu for influenza A patients who are at high risk for complications of influenza A infection). It can curb the misuse of antibiotics or improve triage in settings of a potential pandemic.* The development of this rapid diagnostic assay and its testing in a "real-world" patient setting are paving the way for establishing this new type of diagnostic testing in the clinic.

Courtesy of Amanda Mills/CDC.

FIGURE 1 Test tube rack containing purple-capped blood collection tubes. In the future, blood may be analyzed for protein profiles of immune system genes expressed during infection for diagnostic purposes.

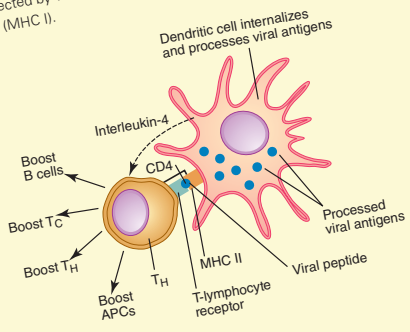
References

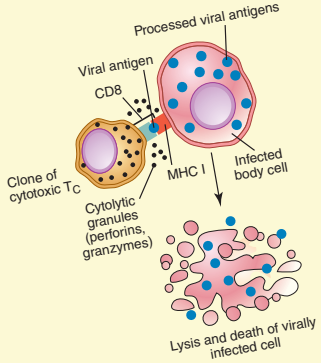
Ramilo, O., et al. 2007. "Gene expression patterns in blood leukocytes discriminate patterns with acute infections." *Blood* 109:2066–2077.
Zaas, A. K., et al. 2013. "A host-based RT-PCR gene expression signature to identify acute respiratory viral infection." *Sci Transl Med* 5:203ra126.

Refreshers—Reviews are presented to provide students the opportunity to brush up on important biological concepts.

Refresher **Immunology**

The primary function of **major histocompatibility complex (MHC)** is to present a sampling of all peptides that were produced in a nucleated cell of the body (for MHC I) or that were engulfed by an antigen-presenting cell (for MHC II). (See **FIGURE 1**.) B cells present MHC II to get "help" from T_H cells. Healthy cells will be ignored while cells containing foreign proteins (e.g., cells infected by viruses) will be attacked by the immune system. It is these peptides that are recognized by T_H (MHC II) and T_C cells (MHC I).

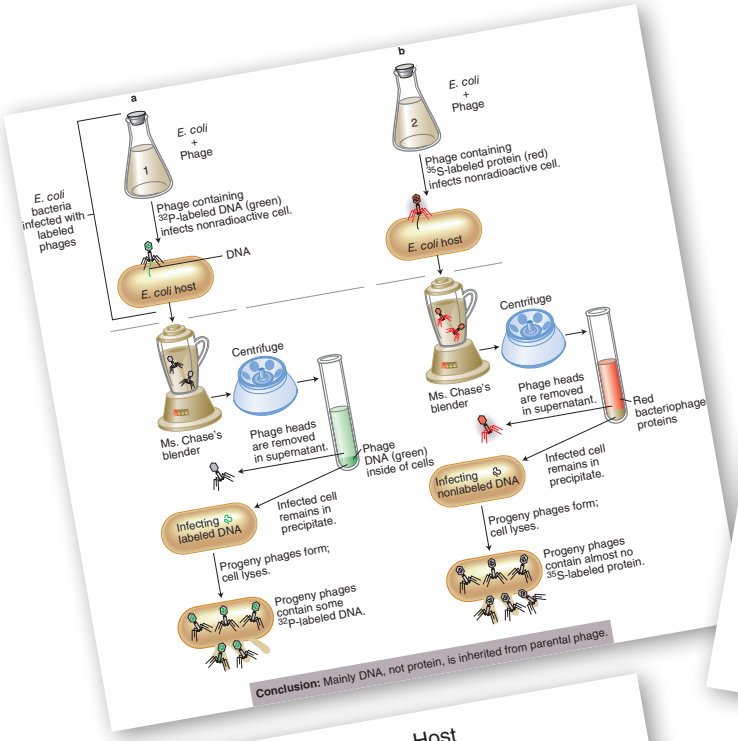


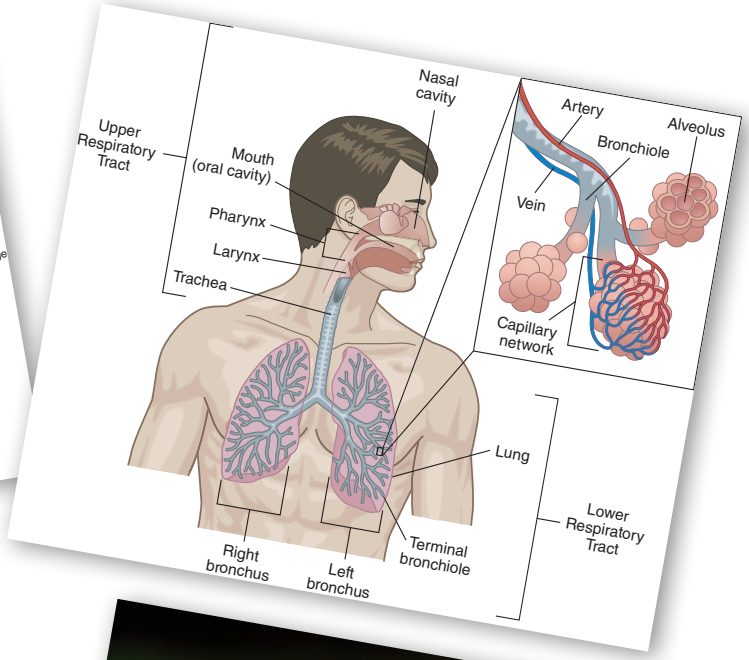


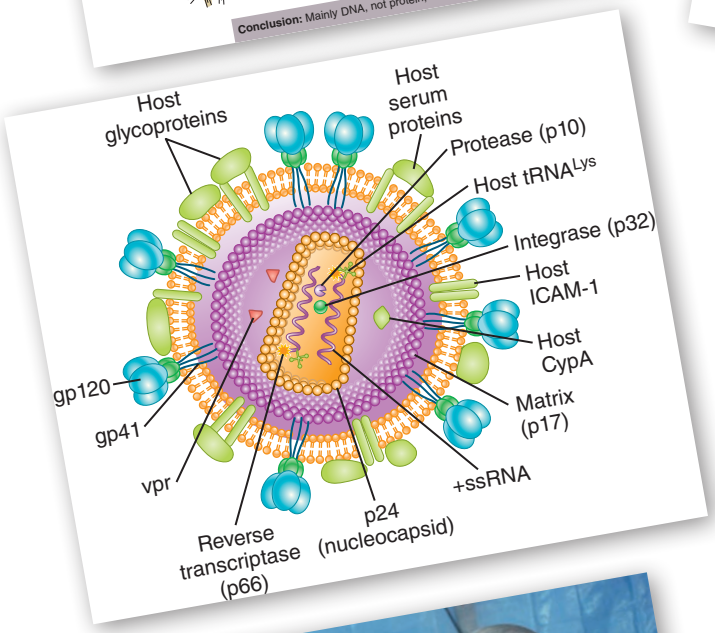
Antigen-presenting cell activate:
T_H (T helper cells)
T_C (cytotoxic T-lymphocytes)

FIGURE 1 Antigen-presenting cells activate T_H cells (T helper cell) and T_C cells (cytotoxic T lymphocytes).

High-Quality, Carefully Rendered Illustrations and Figures—Over 500 NEW and revised photos and illustrations are included in this edition, including a number of unique photographs taken by the author to depict research methods, historical perspectives, or current topics described in the text.

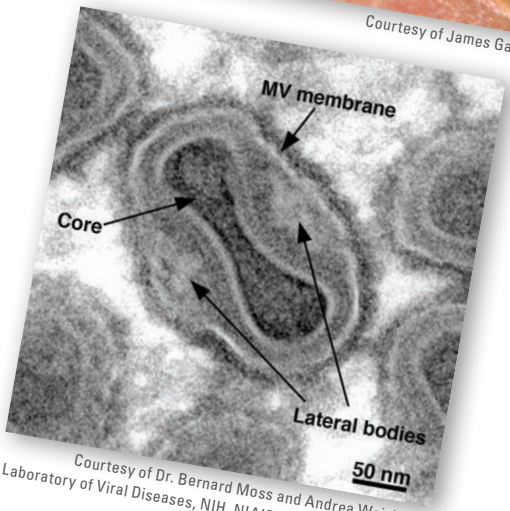






Courtesy of James Gathany/CDC.

Courtesy of the CDC/Sally Ezra.



Courtesy of Dr. Bernard Moss and Andrea Weisberg, Laboratory of Viral Diseases, NIH, NIAID, Bethesda, Maryland.

Summary

Martinus Beijerinck, a botanist, is credited with coining the term *virus* while studying TMV-infected tobacco plants during the late 1800s. Even though the first virus to be discovered was tobacco mosaic virus (TMV), plant viruses are not nearly as well understood as their animal counterparts. Plant viruses continue to be a major threat in the production of vegetable and ornamental crops worldwide. Their control remains a major challenge in the 21st century.

The infection of plant cells is not achieved by surface receptors—a major difference between viral infections of plants as opposed to animals. Plant viruses require a break in the cell wall for entry and are transmitted in a number of different ways, including mechanical means (i.e., human and environmental damage), soil transmission, vegetative propagation (grafting), piercing and chewing insects and other vectors, seed transmission, and pollen transmission.

The majority of plant viruses are transmitted by insect vectors (e.g., aphids, leafhoppers, plant-hoppers, beetles, mites, mealybugs, whiteflies, and thrips). Symptoms of viral plant diseases vary from mild to severe but rarely kill the plant. Symptoms may include dwarfing or stunting of plants, leaf curling, reduced yield, fruit distortion, chlorosis (yellowing), other color deviations (e.g., variegation of flower petals), "mosaic" patterns on leaves, ring-shaped spots on leaves, wilting and withering, necrosis (black or grayish brown discoloration due to the death of cells and tissues), or bark scaling.

In addition to symptomatic observations, methods used to detect and identify plant viruses are similar to those used in detecting animal viruses. Infectivity assays, ELISAs, electron microscopy, and RT-PCR or PCR are used to diagnose diseases caused by plant viruses. The major means of control (depending on the disease) include chemical or biological control of insect vectors, removal of alternate hosts (e.g., weeds), sanitation techniques (e.g., cleaning of farm implements and proper grafting techniques), use of certified virus-free seed or stock, growth of resistant crop varieties, and plant quarantines to prevent disease establishment in areas where it does not occur (material is grown or kept isolated for longer periods for observation to determine absence of disease or pest), and testing. These procedures are time-consuming and costly and require skilled professionals.

Advances in control of viral plant diseases are focused on creating natural (breeding) and engineered resistance to plant viruses.

The majority of plant viruses are naked, helical-shaped +ssRNA viruses. Instead of having segmented genomes like influenza A virus, some plant viruses have multipartite genomes in which the genome consists of more than one molecule of nucleic acid, but each genome molecule is packed into a separate virus particle. Thus, all discrete virus particles must enter the cell to establish a productive infection.

Viruses spread short distances (from cell to cell) with the aid of movement proteins that "channel" them through the plasmodesmata. Channeling occurs without causing cellular lysis. A systematic (long distance) infection of the plant occurs if plant viruses are transported longer distances through the vascular system by the phloem.

Plants do not have an "active" immune system analogous to humans, such as the production of antibodies to combat pathogens. Plants do, however, possess

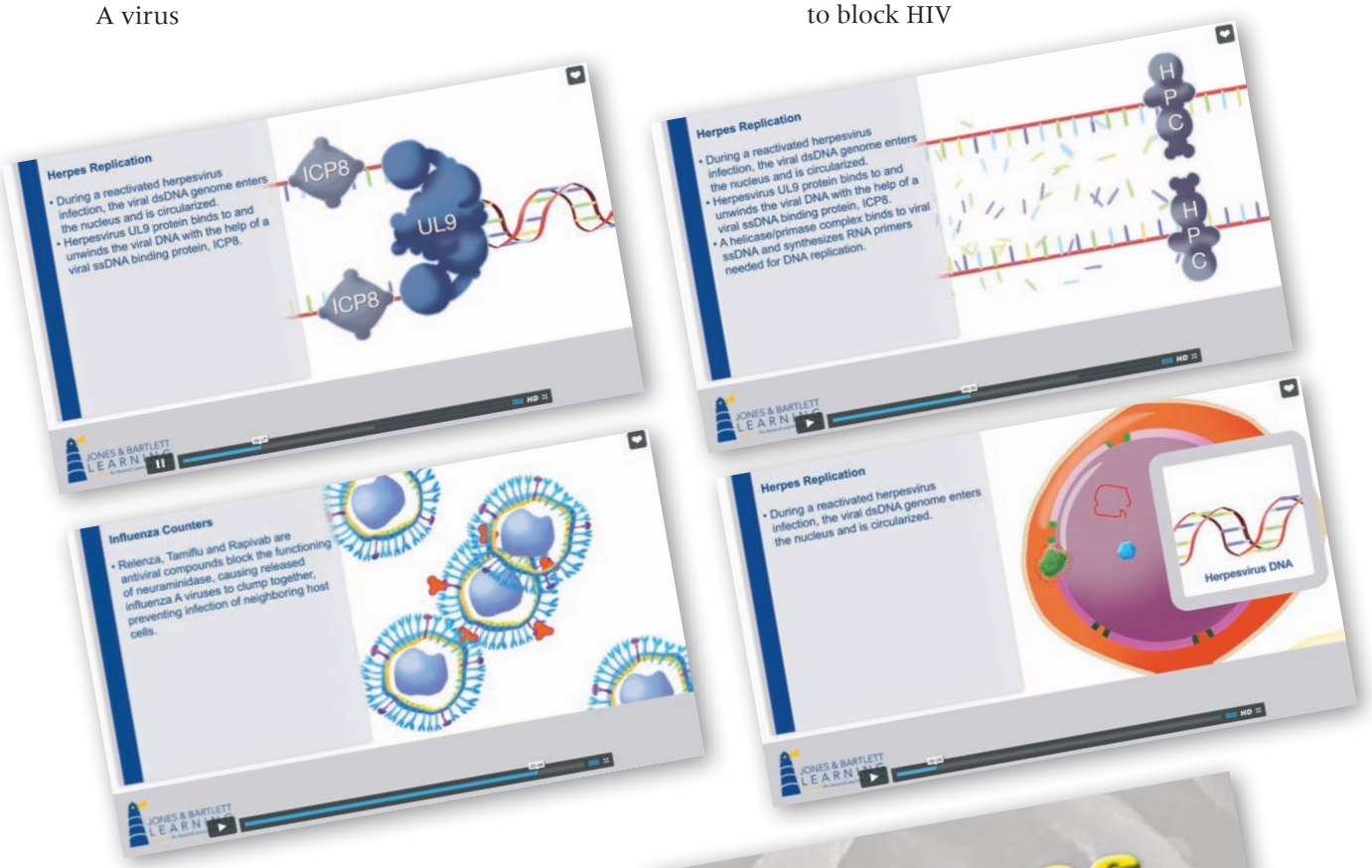
Chapter Summary—A synopsis of the key points is provided at the end of each chapter.

Resources—*Understanding Viruses* is grounded in evidence. Resources provided for reference have been separated by category into Primary Literature, Reviews, Popular Press, and Video Productions, so that students can easily find the type of information they are interested in delving into.

Additional Online Study Tools—Practice activities and prepopulated quizzes are available for self-study.

Animations—NEW to the third edition are animations for mechanisms of antiviral drugs, including:

- Mechanisms for Antiviral Drug: Acyclovir (DNA polymerase inhibitor)
- Mechanism for Antiviral Drug: Relenza/Tamiflu/Peramivir (Neuraminidase inhibitors) for Influenza A virus
- Mechanism for Antiviral Drug: Protease inhibitors of HIV
- Mechanism for Antiviral Drug: Protease inhibitor of Hepatitis C virus
- Mechanism for Antiviral Drug: ZMapp monoclonal antibody cocktail to inhibit Ebola virus
- Mechanism for Antiviral Drug: Integrase inhibitors to block HIV



Key Terms—Important terms are presented in bold in each chapter and defined in a comprehensive glossary for quick reference; throughout each chapter italicized terms and phrases are intended to focus attention on important concepts.

Viruses in the News Headlines—The top virus-related news stories are listed on the inside back cover.

Ebola Case Study—This NEW and unique in-depth analysis of the modern Ebola outbreak is perfect for classroom discussion. It is fully illustrated and includes over 50 Case Study Questions and a complete Resources section.

Appendix C

CASE STUDY: COMBATING THE WORST EPIDEMIC OF EBOLA VIRUS DISEASE IN HUMAN HISTORY

Patient Zero

During March 2014, blood samples collected from 20 patients hospitalized in Gueckedou, Macenta, and Kissidougou, Guinea, were shipped to Biosafety Level-4 (BSL-4) laboratories in Lyon, France, and Hamburg, Germany, for virology testing. Nearly all of the patients (84%) had died from a mysterious illness characterized by fever, severe diarrhea, and vomiting. **Reverse-transcriptase polymerase chain reaction (RT-PCR)** kits were used to screen the blood plasma for Old World arenaviruses and Lassa virus. *None of the samples were positive for Lasa virus.*

The viral RNA was extracted from patient blood plasma, and **commercial RT-PCR kits** were used to detect the nucleotide sequences of the conserved region of the Ebola virus *L* gene (which codes for Ebola virus RNA polymerase) using PCR primers designed to amplify genes of known Ebola virus species (**Sudan**, **Bundibugyo**, **Tai Forest**, **Reston**, **Lloviu**, **Marburg**, and **Ravn**). Additional **real-time RT-PCR** kits were used to amplify and detect the *GP* gene (which codes for Ebola virus surface glycoprotein [GP]) or the *NP* gene (which codes for the viral nucleoprotein) to detect Ebola virus. See **FIGURE 1** for the structure of Ebola virus. The commercial kits confirmed that 15 of the 20 patients were positive for Ebola virus based on detection of the *L* gene. Ebola viruses were detected in the serum sample from one patient using transmission electron microscopy. Serum from five patients that contained Ebola viruses were grown in cell cultures and isolated for further identification and analysis.

The Reservoir of Ebola Viruses

A **retrospective study** traced the Ebola virus infections to the first suspected case of the outbreak, 2-year-old Emilo Ouamiouo. The boy suffered from fever and vomiting and had black stool. The child died in Meliandou village, Gueckedou, Guinea, on December 6, 2013. A colony of thousands of Angolan free-tailed bats roosted in a hollow tree where Emilo and other children played in Meliandou. The boy's family hunted bats and then grilled and ate them. Past human Ebola outbreaks in wildlife such as had been associated with outbreaks in wildlife such as duikers (small antelope), gorillas, and chimpanzees or traced to hunters who butchered animals found dead in the rainforest. *Bats are the leading suspect as the natural Ebola* **reservoir**. Bats can survive Ebola infection. In a frustrating twist, the tree the children played at was burned to the stump just before researchers arrived to gather bats for samples for testing. Villagers said that when the tree was burning there was a "rain of bats." The hollow tree was only 50 meters (54 yards) from the house where the boy lived. The first individuals infected by Ebola viruses were women and children, rather than hunters. It is possible that the toddler was infected when playing in the tree with an infected bat or by ingesting a small quantity of bat droppings that contained Ebola viruses.

Epicenter of the Ebola Outbreak in West Africa

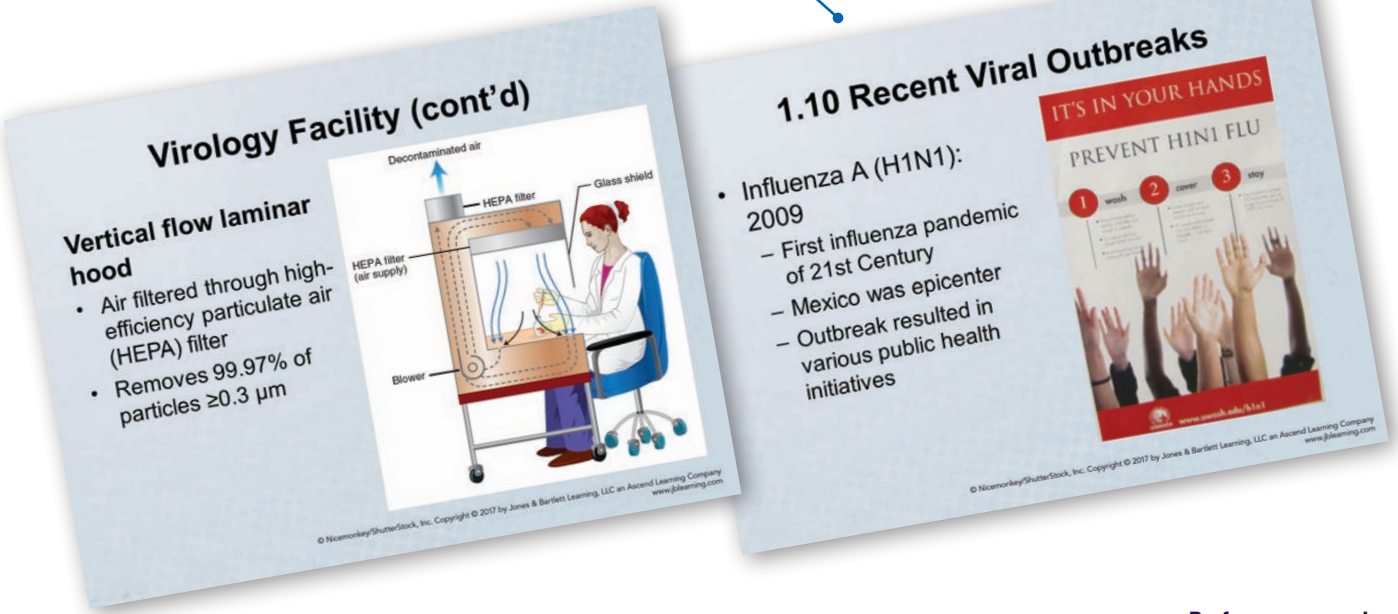
The child's sister, mother, and grandmother; a village midwife; and the nurse who cared for them became infected and suffered from similar symptoms, in addition to bleeding. *Between December 29, 2013, and January 25, 2014, all of them died.* The villagers were frightened

RNA transcription factor VP30
Matrix VP24
Glycoprotein (GP)
Nucleoprotein (NP)
RNA polymerase cofactor VP35
Envelope
Matrix VP40
RNA polymerase (L)

FIGURE AP 3-1 The structure of Ebola virus. It is an enveloped, helical-shaped, elongated/filamentous virus that contains ssRNA of negative polarity (–ssRNA). When visualized by electron microscopy, the viral particles look like thin spaghetti or long earthworms. The viral particles are 800–1,000 nm in length with a uniform diameter of 80 nm. The particles can get as long as 14,000 nm. The –ssRNA genome is encapsidated by a nucleoprotein, VP30 protein, and a viral RNA polymerase (L protein) complexed with VP35 protein to form a nucleocapsid. Embedded within the viral envelope are trimeric glycoprotein spikes. The matrix proteins are involved in morphogenesis and budding/release of new infectious particles from the host cell.

Teaching Tools

Lecture Slides in PowerPoint™ Format—The Lecture Slides provide lecture notes and images for each chapter of *Understanding Viruses, Third Edition*. Instructors with Microsoft PowerPoint software can customize the outlines, art, order of presentation, and add their own material.



Virology Facility (cont'd)

Vertical flow laminar hood

- Air filtered through high-efficiency particulate air (HEPA) filter
- Removes 99.97% of particles ≥0.3 µm

Decontaminated air
HEPA filter
Glass shield
HEPA filter (air supply)
Blower

© Nicemonkey/ShutterStock, Inc. Copyright © 2017 by Jones & Bartlett Learning, LLC an Ascend Learning Company www.jblearning.com

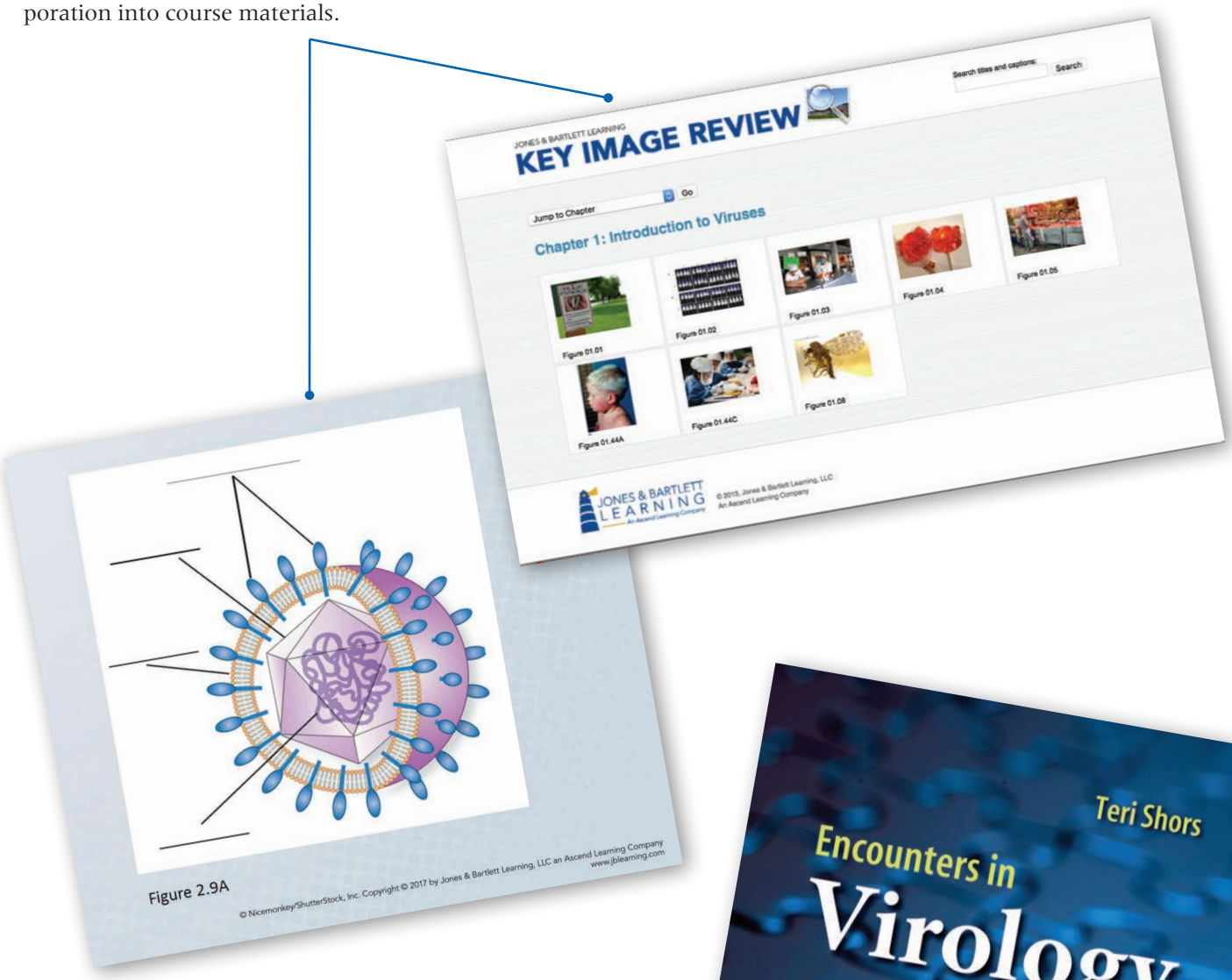
1.10 Recent Viral Outbreaks

- Influenza A (H1N1): 2009
  - First influenza pandemic of 21st Century
  - Mexico was epicenter
  - Outbreak resulted in various public health initiatives

IT'S IN YOUR HANDS
PREVENT H1N1 FLU
1 wash 2 cover 3 stay

© Nicemonkey/ShutterStock, Inc. Copyright © 2017 by Jones & Bartlett Learning, LLC an Ascend Learning Company www.jblearning.com

Image Bank—Access the visuals from the text, including unlabeled versions of many illustrations for easy incorporation into course materials.

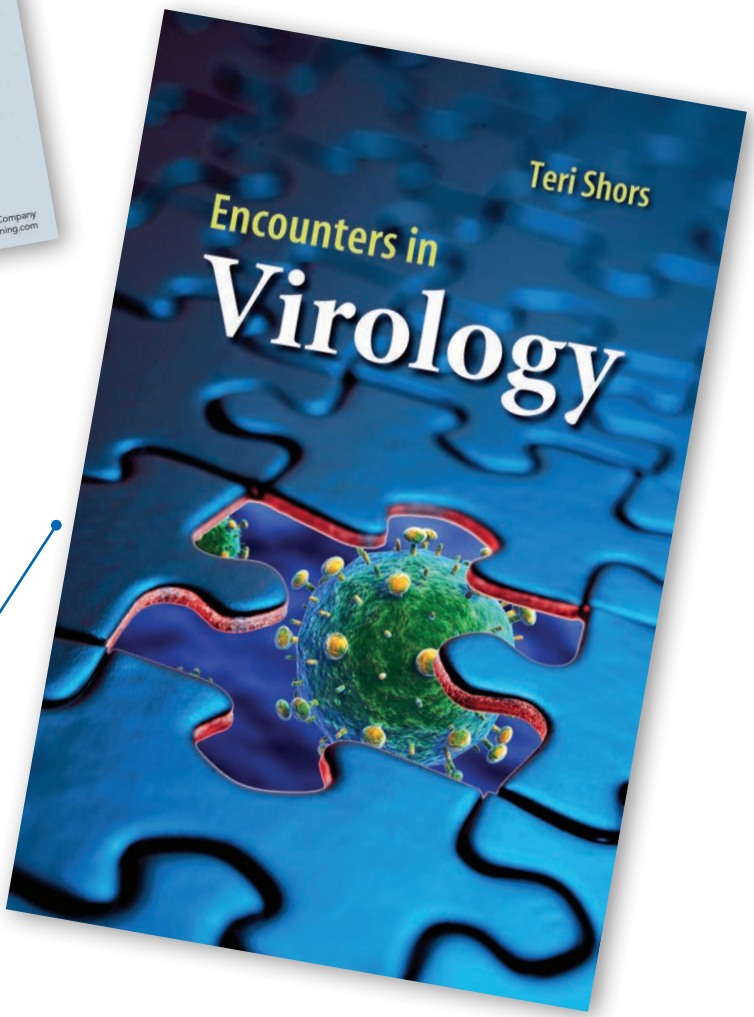


Instructor's Manual —A useful guide prepared by the Author that includes Teaching Tips and other suggestions about how to approach the material in this book for your course.

Test Bank—600 items are available for testing and assessment, in addition to 1,100+ questions and activities that are included in the online study and assessment tools.

Web Links—Hand-selected relevant sites in virology.

Encounters in Virology—Bonus case material for further application.



Acknowledgments

Creating a book for educational purposes involves many people who labor behind the scenes. First and foremost, I want to thank the editorial staff at Jones & Bartlett Learning, the publisher of this text, who were instrumental in getting the first edition of the textbook off the ground: Cathy Sether, Lou Bruno, Christine Myaskovsky, Kimberly Potvin, and Molly Steinbach. Without them, there would not have been subsequent editions. I had the opportunity to coauthor the third edition of *The Microbial Challenge*. Robert I. Krasner's initiative in 1980 led to the establishment of the Division for Microbiology Undergraduate Educators within the American Society for Microbiology. The textbook-writing experience gained with Robert I. Krasner prepared me to put forth a greatly improved *Understanding Viruses, Third Edition* manuscript.

The entire production team at Jones & Bartlett Learning worked tirelessly and with a sense of urgency to produce the third edition of *Understanding Viruses*. I am particularly grateful for Matt Kane's support of the revision; Audrey Schwinn's preparation of the manuscript for production and assistance with the preparation of art elements for the animations; and the technical assistance of copy editor Jennifer Coker, senior production editor Nancy Hitchcock, and proofreader Christina Palaia at Jones & Bartlett Learning.

I extend a very heartfelt thanks to Nancy Hitchcock who thoughtfully prioritized my tasks while I was juggling the book revision and teaching over 200 students during the spring semester. Nancy was extremely patient with my impatience. She was understanding and mindful of my schedule. Producing *Understanding Viruses* has been a major undertaking. New content was added up to the final minutes before being sent to the printer. The art package was extremely demanding. Nancy handled the production of the textbook with grace and her hair intact. Copy editor Jennifer Coker not only focused on the defined duties of a copy editor, but was also a learner of the information and raised queries that resulted in writing that is clear, to the point, and easier to read. She was indefatigable in her willingness to review new writing/content as it came in.

I am also indebted to other members of the talented production team: Troy Liston, Jamey O'Quinn, Joanna Lundeen, Kristin Parker, Mike O'Donnell, and Marta Mitsumori. I also extend gratitude for the team from Fabian & Baber, including Rhonda Fabian, Jerry Baber, Stephanie Browning, and Bridget Yachetti, who created a set of unique and meaningful animations to visually explain the diverse mechanisms of antiviral drugs.

The book would not have been possible without the many individuals who were willing to supply content for the figures. Scientific photographer James Gathany went out of his way to provide resource information and images not yet catalogued at the CDC's PHIL website. University of Wisconsin Oshkosh research technician Margaret Schuelke skillfully set up some of the virological assays in my research laboratory that were used as figures. Others who generously provided figures and/or resources to create figures for the textbook include Bernard Moss (Laboratory of Viral Diseases, NIH), Lorena Passarelli (Kansas State University), Jennifer M. Zaspel and Gareth Powell (Purdue Entomological Research Collection), Gene Drecktrah (UW Oshkosh Insect Collection), John Strous (Director of Medical Technology, UW Oshkosh), Shawn McAfee (Moraine Park Technical College), Howard (Beautiful Britain: Eyam Village and the Great Plague), Yujian Weng, Roger and Sylvia Gasser, and Renae M. Goos. Thanks to Brian Ledwell (UW Oshkosh) for his help with video capture and for incorporating digital technology into the classroom.

I extend gratitude to Michael T. Osterholm, Professor, Environmental Health Sciences, School of Public Health, and the Director of CIDRAP at the University of Minnesota, for his willingness to create a foreword for this text despite his incredible schedule. It speaks volumes for his dedication to virology/infectious disease education.

Peer evaluation was critical in revising and improving the content and accuracy of the textbook. Thank you for your input. I extend gratitude to the following peers for their evaluations and assistance with this edition of *Understanding Viruses*:

- Prakash H. Bhuta, PhD, Eastern Washington University
- Brian David Byrd, PhD, MSPH, Western Carolina University
- Julian Wade Farrior, PhD, Gwynedd Mercy College
- Jeannette M. Loutsch, PhD, University of Science and Arts of Oklahoma
- Patricio I. Meneses, PhD Fordham University
- Jessica Parilla, PhD, Georgia State University
- Carol Shoshkes Reiss, PhD, New York University

- Sarah M. Richart, PhD, Azusa Pacific University
- Paul A. Rowley, PhD, The University of Texas at Austin
- Gary Stanlake, PhD, Hardin-Simmons University
- Tzuen-Rong Jeremy Tzeng, PhD, Clemson University
- Xiaolu Wu, PhD, Pittsburg State University
- Eric Yager, PhD, Albany College of Pharmacy and Health Sciences

A very special thanks goes out to my former undergraduate mentor, colleague, and friend John Cronn. I appreciate his phone calls and emails to tell me about recent discoveries in *Science* or *Nature* that I might have missed and his wisdom about teaching and the academic life. Other important influential mentors along the way include Bernard Moss (chief of the Laboratory of Viral Diseases at the National Institutes of Health), Bertram Jacobs, Jean M. Schmidt, Vern Winston, Gordon Schrank, and the late Denise McGuire.

Other colleagues and instructors I would like to thank for various reasons are Linda Freed, Jim Armentrout, Mathew Kramer, Ethan Everett, Susan McFadden, Nancy Boury, David Dilkes, Sheldon Cooper, Todd Kostman, John Koker, Chip Sitzman, Fran Widmer, and Mary Seaman, The textbook evolved because of the challenging questions and enthusiasm of students in the classroom such as Jaime Antonio Castillo, Kaitlin Galow, Elainna Jentz, Boda Zhao, Yuqi She, Jaime Hernandez, Laura Jaeger, Eric Nygaard, Travis Pire, Ashley Utech, Kristen Razner, Natalie Raymond, Devin Matznick, Heather Sharpless, Patrick Fischer, Jeremy Kroll, Laura Hagen, Sitha Thor, Frances Delwiche, and Monica Dempsey.

Balancing time between research, teaching, and revising this manuscript was challenging at times. I would not have survived had it not been for lots of coffee, my camera, early morning walks through Menominee Park with Roger and Sylvia Gasser, the pail full of goodies that often included homemade soup hung on my back door by Roger and Sylvia after a long day of teaching, adventures with Eric Kropp, and Scott McGillivray's FaceBook posts. Once a week, Eric and I would search for wildflowers and wildlife and visit art museums. Eric tolerated my crazy schedule of getting up between midnight and 4:00 a.m. to work on the book and he would ask me how the book was progressing when everyone else was afraid to ask. Lastly, I must thank Leo and Sasha, the cats. They made sure that I was periodically distracted from my desk so that my blood would continue to circulate.

Teri Shors
Oshkosh, Wisconsin
May 2016

About the Author

Teri Shors has been a member of the Department of Biology at the University of Wisconsin Oshkosh since 1997; she was promoted to the rank of professor in 2010. Dr. Shors is a devoted teacher and researcher at the primarily undergraduate level and has been a recipient of university awards, including a distinguished teaching award, two endowed professorships, and most recently a Distinguished Alumni Award from the Department of Biological Sciences at St. Cloud State University in 2013. She has taught a variety of courses and laboratories and has made a strong contribution to the development of new courses in microbiology, virology (both classroom an online courses), and molecular biology.

Dr. Shors's graduate and postgraduate education is virology based and is reflected in her research. Before teaching at UW Oshkosh, she was a postdoctoral fellow in the Laboratory of Viral Diseases under the direction of Dr. Bernard Moss in the National Institute of Allergy and Infectious Diseases at the National Institutes of Health, Bethesda, Maryland. While her expertise centers upon the expression of vaccinia virus genes, she expanded her research into the potential of antiviral compounds in cranberries and other Wisconsin crops. The antiviral research was funded by a variety of granting agencies, including the WiSys Technology Foundation and a prestigious Merck/AAAS award. She has mentored many students engaged in independent research projects, including recent undergraduate honors theses on the Ebola outbreak in West Africa and the characterization of a biofilm present on an artesian well near Omro, Wisconsin.

Her passion lies in microbiology and virology education. In addition to authoring *Understanding Viruses, Third Edition,* she authored *Encounters in Virology* and coauthored *The Microbial Challenge, Third Edition* and *AIDS: The Biological Basis, Fifth Edition.* She has contributed to a variety of other texts and scientific papers. Initiative; creativity; humor; networking; using current events; incorporating the latest technology in her courses; and leading collaborative, cross-disciplinary studies are the hallmarks of her talents. Dr. Shors also enjoys walking, photography, creating photobooks, gardening, Halloween, museums, and traveling to new places. She is never idle and is a lifelong learner.