

Emerging and Re-emerging Infectious Diseases

developed under a contract from the
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National Institute of Allergy and Infectious Diseases



BSCS 

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Please contact NIH with questions about this supplement at supplements@science.education.nih.gov.

Contents

Foreword.	v
About the National Institutes of Health	vi
About Biological Sciences Curriculum Study.	vi
About the National Institute of Allergy and Infectious Diseases	vii
Introduction to <i>Emerging and Re-emerging Infectious Diseases</i>	1
Implementing the Module	5
What Are the Goals of the Module?	5
What Are the Science Concepts and How Are They Connected?	6
How Does the Module Correlate with the <i>National Science Education Standards</i> ?	6
How Does the BSCS 5E Instructional Model Promote Active, Collaborative, and Inquiry-Based Learning?	6
Engage	9
Explore/Explain	9
Elaborate/Evaluate	9
What's the Evidence for the Effectiveness of the BSCS 5E Model?	12
How Does the Module Support Ongoing Assessment?	13
How Can Controversial Topics Be Handled in the Classroom?	13
Using the Student Lessons	15
Format of the Lessons	15
Timeline for Teaching the Module.	16
Using the Web Site	17
Hardware and Software Requirements.	17
Getting the Most Out of the Web Site.	17
Collaborative Groups	17
State Standards Alignment.	18
Web Activities for People with Disabilities	18
Understanding Emerging and Re-emerging Infectious Diseases	19
Nature of Infectious Diseases.	19
Microbes That Cause Infectious Diseases	20
Occurrence of Infectious Diseases	22
Role of Research in Prevention	23
Host Defenses Against Infectious Diseases	24
Public Health Measures to Prevent Infectious Diseases	27
Treatment of Infectious Diseases	29
Emerging and Re-emerging Infectious Diseases	31
Infectious Diseases and Society	35

References	37
Additional Resources for Teachers	41
Glossary	43
Student Lessons	
Lesson 1— <i>Deadly Disease Among Us</i>	49
Lesson 2— <i>Disease Detectives</i>	61
Lesson 3— <i>Superbugs: An Evolving Concern</i>	71
Lesson 4— <i>Protecting the Herd</i>	85
Lesson 5— <i>Making Hard Decisions</i>	101
Masters	109

Foreword

This curriculum supplement, from the *NIH Curriculum Supplement Series*, brings cutting-edge medical science and basic research discoveries from the laboratories of the National Institutes of Health (NIH) into classrooms. As the largest medical research institution in the United States, NIH plays a vital role in the health of all Americans and seeks to foster interest in research, science, and medicine-related careers for future generations. NIH's Office of Science Education (OSE) is dedicated to promoting science education and scientific literacy.

We designed this curriculum supplement to complement existing life science curricula at both the state and local levels and to be consistent with the *National Science Education Standards*.¹ It was developed and tested by a team of teachers, scientists, medical experts, and other professionals with relevant subject-area expertise from institutes and medical schools across the country, representatives from the National Institute of Allergy and Infectious Diseases, and curriculum design experts from Biological Sciences Curriculum Study (BSCS) and Videodiscovery. The authors incorporated real scientific data and actual case studies into classroom activities. A three-year development process included geographically dispersed field tests by teachers and students. For the 2010 (third) printing, key sections of the supplement were updated, but the Student Lessons remain basically the same.

The structure of this module enables teachers to facilitate learning and stimulate student interest by applying scientific concepts to real-life scenarios. Design elements include a conceptual flow of lessons based on the BSCS 5E Instructional Model (see page 5), cutting-edge science content, and built-in assessment tools. Activities promote active and collaborative learning and are inquiry-based to help students develop problem-solving strategies and critical-thinking skills.

Each of our curriculum supplements comes with a complete set of materials for teachers, including extensive background and resource information, detailed lesson plans, masters for student worksheets, and a Web site with videos, interactive activities, updates, and corrections (as needed). The supplements are distributed at no cost to educators across the United States upon request. They may be copied for classroom use but may not be sold.

We welcome your feedback. For a complete list of curriculum supplements and ordering information, or to submit feedback, please visit <http://science.education.nih.gov>.

We appreciate the valuable contributions of the talented staff at Biological Sciences Curriculum Study (BSCS) and Videodiscovery, Inc. We are also grateful to the NIH scientists, advisors, and all other participating professionals for their work and dedication. Finally, we thank the teachers and students who participated in focus groups and field tests to ensure that these materials are both engaging and effective.

I hope you find our series a valuable addition to your classroom and wish you a productive school year. We welcome your feedback.

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About the National Institutes of Health

Founded in 1887, NIH is the federal focal point for health research in the United States. Today, NIH is one of the agencies within the Department of Health and Human Services. Its mission is science in pursuit of fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to extend healthy life and reduce the burdens of illness and disability. NIH works toward meeting the mission by providing leadership, direction, and grant support to programs designed to improve the health of the nation through research.

NIH's education programs contribute to ensuring the continued supply of well-trained basic research and clinical investigators, as well as the myriad professionals in the many allied disciplines who support the research enterprise. These efforts also help educate people about scientific results so that they can make informed decisions about their own—and the public's—health.

This curriculum supplement is one such education effort. It is a collaboration among the National Institute on Allergy and Infectious Diseases, the NIH Office of Science Education, Biological Sciences Curriculum Study, and Videodiscovery, Inc.

For more about NIH, visit <http://www.nih.gov>.

About Biological Sciences Curriculum Study

Headquartered in Colorado Springs, Colorado, BSCS was founded in 1958 as a curriculum study committed to an evidence- and inquiry-based approach to science education. BSCS instructional materials and professional development services are based on current research about teaching and learning for all science classrooms, kindergarten through college.

BSCS's materials are extensively field-tested in diverse settings across the country and evaluated for proven effectiveness. The BSCS 5E

Instructional Model and inquiry are hallmarks of its materials, placing students at the center of their learning.

The BSCS mission is to transform science teaching and learning through research and development that strengthens learning environments and inspires a global community of scientifically literate citizens. BSCS is a 501(c)3 nonprofit organization. For more information, please visit <http://www.bsos.org>.

The National Institute of Allergy and Infectious Diseases (NIAID) traces its origins to a small laboratory established in 1887 at the Marine Hospital in Staten Island, New York. In the 1880s, boatloads of immigrants were heading toward America, some of them unknowingly bringing with them cholera and other infectious diseases. No one knew what caused these diseases, and physicians relied on clinical signs alone to determine whether someone might be carrying an infectious agent. Scientists used the laboratory for research on these diseases, and it soon became an early part of the Public Health Service.

By 1948, the Rocky Mountain Laboratory and the Biologics Control Laboratory, both dating to 1902, joined the Division of Infectious Diseases and the Division of Tropical Diseases of the National Institutes of Health to form the National Microbiological Institute. Six years later, Congress gave the Institute its current name to reflect the inclusion of allergy and immunology research. Today, NIAID conducts and supports basic and applied research to better understand, treat, and ultimately prevent infectious, immunologic, and allergic diseases. For more than 50 years, NIAID research has led to new therapies, vaccines, diagnostic tests, and other technologies that have improved the health of millions of people in the United States and around the world.

NIAID is composed of four extramural divisions: the Division of AIDS; the Division of Allergy, Immunology, and Transplantation; the Division of Microbiology and Infectious Diseases; and the Division of Extramural Activities. In addition, NIAID scientists conduct intramural research in laboratories located in Bethesda, Rockville, and Frederick, Maryland, and in Hamilton, Montana.

Following is a brief description of the major areas of investigation.

Acquired immunodeficiency syndrome (AIDS). NIAID is responsible for conducting and supporting basic research on the pathogenesis of the human immunodeficiency virus (HIV), which causes AIDS; developing new drug therapies; conducting clinical trials of promising experimental drugs for HIV infection and related opportunistic infections and cancers; carrying out epidemiologic studies to assess the impact of HIV on the populations most severely affected by the epidemic; and developing and testing HIV vaccines.

Asthma and allergic diseases. Research on asthma and allergies has revealed much about their underlying mechanisms and contributed to the development of new ways to help affected individuals. NIAID has established a network of asthma, allergic, and immunologic diseases research centers to transfer results rapidly from fundamental studies in immunology and clinical studies of allergy to clinical practice. The Institute also supports the National Cooperative Inner-city Asthma Study to define factors that influence the disease's severity and to design and evaluate programs to reduce asthma episodes and deaths among African American and Hispanic children.

Emerging diseases. New diseases are arising worldwide and old diseases are re-emerging as infectious agents evolve or spread, and as changes occur in ecology, socioeconomic conditions, and population patterns. NIAID conducts and supports research on Lyme disease, hantavirus, multidrug-resistant tuberculosis, and other emerging diseases to develop new or improved diagnostics, treatments, and vaccines.

Enteric diseases. Worldwide, diarrheal diseases such as cholera and rotavirus infection are major causes of illness and death in infants and children. In contrast, viral hepatitis in its various forms can cause severe disease in older children and adults, although it produces few symptoms among younger age groups. NIAID supports basic research on how enteric agents cause illness as well as studies aimed at developing and testing vaccines to prevent enteric infections.

Genetics and transplantation. NIAID supports studies aimed at improving immunosuppressive therapies, further developing reagents needed for precise tissue matching, defining the genetic regulation of the immune response, and understanding the molecular mechanisms that control immune system genes. NIAID is participating in the first NIH cooperative clinical trial in kidney transplantation, designed to translate developments in basic research into new therapies to prevent graft rejection.

Immunologic diseases. The immune system is a complex network of specialized organs and cells that defends the body against attacks by foreign invaders. When functioning properly, the system fights off infections by such agents as viruses and bacteria. A malfunction, however, can unleash an enormous variety of diseases, from allergy to arthritis to cancer. NIAID research focuses on the basic biology of the immune system and mechanisms of immunologic diseases including autoimmune disorders.

Malaria and other tropical diseases. Diseases such as malaria, filariasis, trypanosomiasis, and leprosy disable and kill millions of people worldwide. NIAID's research efforts in tropical medicine are conducted by U.S. and foreign investigators receiving Institute support and by NIAID scientists in Bethesda, Maryland. NIAID supports a number of centers for tropical medicine research in countries where such diseases are endemic.

Sexually transmitted diseases (STDs). About 19 million Americans each year acquire infectious diseases other than AIDS through sexual contact, and almost half of those are among young people 15 to 24 years old. STDs such as gonorrhea, syphilis, chlamydia, genital herpes, and human papillomavirus can have devastating consequences, particularly for young adults, pregnant women, and newborn babies. NIAID-supported scientists in STD Cooperative Research Centers, NIAID laboratories, and other research institutions are developing better diagnostic tests, improved treatments, and effective vaccines.

Vaccine development. Effective vaccines have contributed enormously to improvements in public health in the United States during the past hundred years. Research conducted and supported by NIAID has led to new or improved vaccines for a variety of serious diseases, including rabies, meningitis, whooping cough, hepatitis A and B, chicken pox, and pneumococcal pneumonia. NIAID supports vaccine evaluation units for the testing of new vaccines in people at several U.S. medical centers.

Other areas of research include fungal diseases, hospital-associated infections, chronic fatigue syndrome, respiratory diseases, and antiviral and antimicrobial drug development.

You can find more information on NIAID's research efforts at <http://www3.niaid.nih.gov>.

Introduction to *Emerging and Re-emerging Infectious Diseases*

Objectives of the Module

Emerging and Re-emerging Infectious Diseases has two objectives: to introduce students to major concepts related to emerging and re-emerging infectious diseases and to convey to students the relationship between basic biomedical research and the improvement of personal and public health. The improvement of personal and public health is the central mission of the National Institutes of Health, the world's largest organization devoted to biomedical research and the funding agency for this module.

In medieval times, most people believed that supernatural forces created diseases to punish humankind for its sins. Nevertheless, as early as 1530, Gerolamo Frascatoro, an insightful Italian, suggested in a poem that syphilis and other diseases could be contagious—that is, they could be transmitted by direct contact with an infected person, contaminated materials, or infected air. The discovery of microorganisms by Anton van Leeuwenhoek in the late 1600s led some to speculate that these microscopic organisms might be the cause of disease. Although this “germ theory of disease” was first proposed in 1762, it was fully developed by Robert Koch in the 1870s as he studied anthrax, a disease of cattle and sometimes of humans.

Table 1. Discovery of bacterial causes of several diseases.

anthrax	1876	Koch
gonorrhea	1879	Neisser
tuberculosis	1882	Koch
plague	1894	Kitasato, Yersin
whooping cough	1906	Bordet, Gengou

Koch devised a set of steps, now called Koch's postulates, to prove that a particular bacterium causes a specific disease:

1. The organism should always be found in animals suffering from the disease;
2. the organism must be isolated from the animal's body and cultivated in pure culture;
3. the culture should induce the same disease when inoculated into a healthy animal; and
4. the organism should be reisolated and cultured from the healthy animal and found to be the same as the original organism.

Following Koch's initial work on anthrax, scientists identified the bacterial cause of many common diseases.

Despite great advances in determining the infectious agent involved in many bacterial diseases, the causes of many other diseases remained elusive. In 1898, Friedrich Loeffler and P. Frosch studied foot-and-mouth disease, a skin infection of animals. They discovered that the infectious agent for this disease was small enough to pass through filters that would screen out all known bacteria. Other experiments indicated that the causative agent was not a chemical toxin but a “minute living being.” In 1899, Martinus Beijerinck, a Dutch microbiologist who investigated the cause of tobacco mosaic disease in tobacco and tomato plants, proposed that the infectious agent was a “filterable virus” that must be incorporated into cells in order to reproduce. In 1900, Walter Reed discovered that yellow fever in humans is caused by a virus.

The work of these and other researchers led to an understanding of the viral basis of many diseases. The development of more sophisticated biochemical techniques in the early 1900s revealed the chemical simplicity of viruses

(consisting of just protein and nucleic acid), and the invention of the electron microscope in 1932 allowed viruses to be seen.

In addition to bacteria and viruses, physicians recognized that some infectious diseases are caused by fungi, protozoa, and helminths from the roundworm and flatworm phyla. Protozoa and helminths are sometimes collectively called parasites, meaning organisms that live at the expense of another organism (termed “the host”). Technically, infectious bacteria and viruses could also be considered parasites. In addition, some neurological disorders are due to infection by unusual proteins called prions.

Even as scientists began to understand the microbial cause of infectious diseases, medical workers were searching for ways to prevent or treat these diseases. For example, physicians had long known that survivors of many infectious diseases were immune from further infection by the disease-causing agent. For centuries, the Chinese had used variolization (introducing dried material from smallpox lesions into scratches on a healthy individual's skin) to induce a mild smallpox infection that would prevent the individual from contracting a severe or lethal case later in life. This procedure spread through Asia and was eventually introduced to the European community. Unfortunately, variolization occasionally caused severe and even lethal cases of smallpox.

In 1798, the rural English physician Edward Jenner made a curious observation. His patients who had contracted and recovered from cowpox, a disease similar to but much milder than smallpox, seemed to be immune not only to further cases of cowpox, but also to smallpox. By scratching the fluid from cowpox lesions into the skin of healthy individuals, he was able to immunize those people against smallpox. Louis Pasteur later developed vaccines for anthrax (caused by a type of bacterium) and rabies (caused by a virus) by treating the infectious agents for those diseases so that they lost their disease-producing abilities. Vaccination is now used to immunize people against many diseases.

Biologists also identified conditions and chemical agents that killed bacteria, leading to the prevention of many diseases. Pasteur used heat to sterilize culture media, eliminating unwanted microorganisms. The process of pasteurization, named in his honor, is now used to kill bacteria in a variety of beverages. Joseph Lister sprayed surgical rooms with aqueous phenol to reduce wound infections. People also began to recognize the importance of clean water and of treating sewage for preventing disease.

A key step forward in the fight against infectious disease was the discovery and development of drugs that could kill the microbe involved without killing the patient. Antibacterial drugs were discovered first. In the 1930s, Gerhard Domagk discovered that prontosil, a sulfonamide, could cure streptococcal infections in mice. In 1929, Alexander Fleming discovered that a substance produced by a *Penicillium* mold killed cultures of staphylococcal bacteria. He characterized the product and named it penicillin. Later, in the early 1940s, a group of British scientists directed by Howard Florey showed that penicillin was effective in controlling some infectious diseases and developed procedures for its mass production. The pharmaceutical industry flourished after World War II, and many additional antibacterial and antifungal drugs were discovered or synthesized.

Developing antiviral drugs has been more challenging. Because viruses reproduce inside host cells, it is difficult to find drugs that interfere with viral reproduction but are not toxic to host cells. Most of the drugs used today interfere with the enzymes involved in viral replication and do not affect (or affect only slightly) enzymes that are essential for the host cell. Acyclovir, used to treat genital herpes, and amantadine, used to prevent influenza A, are two examples of drugs that interfere with viral replication. AZT, the first drug to be widely used in the treatment of AIDS, also interferes with viral reproduction. In contrast, the newer protease inhibitors used to treat AIDS interfere with the process of virus packaging. Antifungal, antiprotozoan, and antihelminthic drugs have also been discovered; these drugs

frequently have serious side effects and must be administered carefully. (For a list of all current HIV/AIDS treatments, see <http://www.fda.gov/oashi/aids/virals.html>.)

Science and medicine have made dramatic advances over the past two centuries in understanding, preventing, and treating infectious diseases. Despite these advances, the past two decades have witnessed the emergence of a number of previously unrecognized diseases and the re-emergence of several previously well-controlled ones. This phenomenon is intriguing from a biological standpoint but alarming from a public health standpoint.

Concepts Covered in the Module

In this module, students explore the biological factors associated with disease emergence and re-emergence and consider the human activities that can increase or decrease the likelihood of outbreaks of infectious diseases. There are many concepts we could have addressed, but we chose, with the help of a variety of experts in this field, a relatively small number for your students to explore. Those concepts follow.

- Infectious diseases continue to be a major cause of human suffering and death, both in the United States and around the world. Emerging infectious diseases are diseases that have not occurred in humans before or that occurred only in small numbers in isolated places. Re-emerging infectious diseases are diseases that once were major health problems globally or in a particular country and then declined dramatically, but are again becoming health problems for a significant proportion of the population.
- A major cause of the emergence of new diseases is environmental change (for example, human encroachment into wilderness areas and increased human traffic through previously isolated areas).
- The re-emergence of some diseases can be explained by evolution of the infectious agent (for example, mutations in bacterial genes that confer resistance to antibiotics used to treat the diseases).

- The re-emergence of some diseases can be explained by the failure to immunize enough individuals, which results in a greater proportion of susceptible individuals in a population and an increased reservoir of the infectious agent. Increases in the number of individuals with compromised immune systems (due to the stress of famine, war, crowding, or disease) also explain increases in the incidence of emerging and re-emerging infectious diseases.
- Infectious diseases have a devastating impact nationally and globally, but a variety of strategies can alleviate suffering due to these diseases. Because resources are limited, allocating funds among projects that address different diseases raises complex ethical questions. Understanding the relevant biological principles can help in making these difficult decisions.

We hope the module's five lessons will carry these concepts to your students effectively. Although the lessons contain much interesting information about specific infectious diseases, we suggest that you focus your students' attention on the major concepts the module was designed to convey. The concluding steps in each lesson are intended to focus the students' attention on these concepts.

Implementing the Module

The five lessons in this module are designed to be taught either in sequence, as a supplement to your standard curriculum, or as individual activities that support or enhance your treatment of specific concepts in biology. The following pages offer general suggestions about using these materials in the classroom; you will find specific suggestions in the procedures provided with each lesson.

What Are the Goals of the Module?

Emerging and Re-emerging Infectious Diseases is designed to help students reach the following

major goals associated with biological literacy:

- to understand a set of basic scientific principles related to emerging and re-emerging infectious diseases,
- to experience the process of inquiry and develop an enhanced understanding of the nature and methods of science, and
- to recognize the role of science in society and the relationship between basic science and personal and public health.

Table 2. Conceptual flow of the lessons.

Lesson	Learning Stage	Major Concepts
Lesson 1 <i>Deadly Disease Among Us</i>	Engage	Infectious diseases continue to be a major cause of human suffering and death, both in the United States and around the world. Emerging infectious diseases are diseases that have not occurred in humans before or that occurred only in small numbers in isolated places. Re-emerging infectious diseases are diseases that once were major health problems globally or in a particular country and then declined dramatically, but are again becoming health problems for a significant proportion of the population.
Lesson 2 <i>Disease Detectives</i>	Explore/Explain	A major cause of the emergence of new diseases is environmental change (for example, changing methods of agriculture and animal husbandry; human encroachment into wilderness areas and increased human traffic through previously isolated areas).
Lesson 3 <i>Superbugs: An Evolving Concern</i>	Explore/Explain	The re-emergence of some diseases can be explained by evolution of the infectious agent (for example, changes in the influenza virus that allow it to evade immunity and cause serious illness).
Lesson 4 <i>Protecting the Herd</i>	Explore/Explain	The re-emergence of some diseases can be explained by the failure to immunize enough individuals, which results in a greater proportion of susceptible individuals in a population and an increased reservoir of the infectious agent. Increases in the number of individuals with compromised immune systems (due to the stress of famine, war, crowding, or disease) also explain increases in the incidence of emerging and re-emerging infectious diseases.
Lesson 5 <i>Making Hard Decisions</i>	Elaborate/Evaluate	Infectious diseases have a devastating impact nationally and globally, but a variety of strategies can alleviate suffering due to these diseases. Because resources are limited, allocating funds among projects that address different diseases raises complex ethical questions. Understanding the relevant biological principles can help in making these difficult decisions.

What Are the Science Concepts and How Are They Connected?

We have organized the lessons to form a conceptual whole that moves students from an introduction to emerging and re-emerging infectious diseases (*Deadly Disease Among Us*), to an investigation of some of the causes for the emergence and re-emergence of infectious diseases (*Disease Detectives, Superbugs: An Evolving Concern*, and *Protecting the Herd*), to a discussion of how people make decisions about allocating funds to combat infectious diseases (*Making Hard Decisions*). Table 2 illustrates the sequence of major concepts addressed by the five lessons.

Although we encourage you to use the lessons in the sequence outlined in Table 2, many of them can be taught individually to replace or enhance a more traditional approach to the same or related content. Table 3 provides recommendations for inserting the lessons into a standard high school curriculum in biology.

How Does the Module Correlate with the National Science Education Standards?

Emerging and Re-emerging Infectious Diseases supports teachers in their efforts to reform science education in the spirit of the National Research Council's 1996 *National Science Education Standards (NSES)*. Table 4 lists the specific content and teaching standards that this module primarily addresses.

How Does the BSCS 5E Instructional Model Promote Active, Collaborative, and Inquiry-Based Learning?

The lessons in this supplement use a research-based pedagogical approach called the BSCS 5E instructional model, or the BSCS 5Es. The BSCS 5Es are based on a **constructivist** theory of learning. A key premise of this theory is

that students are active thinkers who build (or construct) their own understanding of concepts out of interactions with phenomena, the environment, and other individuals. A constructivist view of science learning recognizes that students need time to

- express their current thinking;
- interact with objects, organisms, substances, and equipment to develop a range of experiences on which to base their thinking;
- reflect on their thinking by writing and expressing themselves and comparing what they think with what others think; and
- make connections between their learning experiences and the real world.

The three key findings related to student learning identified in *How People Learn* (Bransford et al., 2000), a comprehensive review of research on learning, support the pedagogical strategies promoted by implementing the BSCS 5Es:

- Students enter class with a variety of preconceptions that may later significantly interfere with learning if those preconceptions are not engaged and addressed,
- To develop competence in a given subject, students must build a strong foundation of factual knowledge within the context of a coherent conceptual framework.
- Students benefit from a metacognitive approach to learning that emphasizes goal setting and self-monitoring.

The BSCS 5Es sequence the learning experiences so that students can construct their own understanding of a science concept over time. The model leads students through five phases of active learning that are easily described using words that begin with the letter *E*: Engage, Explore, Explain, Elaborate, and Evaluate. Rather than just listening and reading, students are also analyzing and

Table 3. Correlation between lessons and topics in standard high school curricula.

Topics	Lesson 1	Lesson 2	Lesson 3	Lesson 4	Lesson 5
Infectious diseases (causes)	Yes	Yes	Yes	Yes	Yes
Society and infectious diseases	No	Yes	Yes	Yes	Yes
Antibiotics and antibiotic resistance	No	No	Yes	No	Yes
Natural selection	No	No	Yes	No	Yes
Vaccination	No	No	No	Yes	Yes

Table 4. Correlation to the National Science Education Standards.

A. The Content Standards

<ul style="list-style-type: none"> Identify questions and concepts that guide scientific investigations. Design and conduct scientific investigations. Use technology and mathematics to improve investigations and communications. Formulate and revise scientific explanations and models using logic and evidence. Recognize and analyze alternative explanations and models. Communicate and defend a scientific argument. Understanding scientific inquiry. 	<p>Lessons 2 and 3 Lesson 3 Lesson 4</p> <p>Lessons 2, 3, and 4</p> <p>Lessons 2, 3, and 4</p> <p>Lessons 4 and 5</p> <p>Lessons 2, 3, and 4</p>
<p>should develop understanding of the molecular basis of heredity.</p> <ul style="list-style-type: none"> In all organisms, the instructions for specifying the characteristics of the organism are carried in DNA. Changes in DNA (mutations) occur spontaneously at low rates. 	<p>Lesson 3</p> <p>Lesson 3</p>
<p>should develop understanding of biological evolution.</p> <ul style="list-style-type: none"> Species evolve over time. 	Lesson 3
<p>should develop understanding of the interdependence of organisms.</p> <ul style="list-style-type: none"> Human beings live within the world’s ecosystems. 	Lesson 2
<p>should develop abilities of technological design and understandings about science and technology.</p> <ul style="list-style-type: none"> Scientists in different disciplines ask different questions, use different methods of investigation, and accept different types of evidence to support their explanations. Science often advances with the introduction of new technologies. Creativity, imagination, and a good knowledge base are all required in the work of science and engineering. Science and technology are pursued for different purposes. 	<p>Lesson 2</p> <p>Lesson 5</p> <p>Lessons 1–5</p> <p>Lessons 1–5</p>
<ul style="list-style-type: none"> personal and community health natural and human-induced hazards science and technology in local, national, and global challenges 	<p>Lessons 1–5</p> <p>Lessons 1–5</p> <p>Lesson 5</p>
<ul style="list-style-type: none"> science as a human endeavor nature of scientific knowledge historical perspectives 	<p>Lessons 2 and 5</p> <p>Lessons 3, 4, and 5</p> <p>Lesson 1</p>

Table 4. Correlation to the National Science Education Standards. (continued)

B. The Teaching Standards

<p>Standard A: Teachers of science plan an inquiry-based science program for their students. In doing this, teachers</p>	<p>Correlation to <i>Emerging and Re-emerging Infectious Diseases</i></p>
<ul style="list-style-type: none"> • develop a framework of yearlong and short-term goals for students • select science content and adapt and design curricula to meet the interests, knowledge, understanding, abilities, and experiences of students • select teaching and assessment strategies that support the development of student understanding and nurture a community of science learners 	<p>Each lesson provides short-term objectives for students. Tables 2 (Conceptual Flow of the Lessons) and 8 (Suggested Timeline for Teaching the Module) also help teachers plan. Using the modules helps teachers update their curriculum in response to their students' interest in this topic. The focus on active, collaborative, and inquiry-based learning helps teachers meet this standard.</p>
<p>Standard B: Teachers of science guide and facilitate learning. In doing this, teachers</p>	<p>Correlation to <i>Emerging and Re-emerging Infectious Diseases</i></p>
<ul style="list-style-type: none"> • focus and support inquiries while interacting with students • orchestrate discourse among students about scientific ideas • challenge students to accept and share responsibility for their own learning • recognize and respond to student diversity and encourage all students to participate fully in science learning • encourage and model the skills of scientific inquiry, as well as the curiosity, openness to new ideas and data, and skepticism that characterize science 	<p>All of the lessons in the module encourage and support student inquiry. All of the lessons in the module promote discourse among students. All of the lessons in the module challenge students to accept and share responsibility for their learning. Combining the BSCS 5E Instructional Model with active, collaborative learning is an effective way of responding to the diversity of student backgrounds and learning styles. Annotations for the teacher that occur throughout the lessons provide many suggestions for how teachers can model these attributes.</p>
<p>Standard C: Teachers of science engage in ongoing assessment of their teaching and of student learning. In doing this, teachers</p>	<p>Correlation to <i>Emerging and Re-emerging Infectious Diseases</i></p>
<ul style="list-style-type: none"> • use multiple methods and systematically gather data about student understanding and ability • analyze assessment data to guide teaching 	<p>Each lesson has a variety of assessment components embedded within its structure. Annotations draw teachers' attention to these opportunities for assessment. Annotations provide answers to questions that can help teachers analyze student feedback. The annotations also suggest ways for teachers to change their approach to students, based on that feedback.</p>
<p>Standard E: Teachers of science develop communities of science learners that reflect the intellectual rigor of scientific inquiry and the attitudes and social values conducive to science learning. In doing this, teachers</p>	<p>Correlation to <i>Emerging and Re-emerging Infectious Diseases</i></p>
<ul style="list-style-type: none"> • display and demand respect for the diverse ideas, skills, and experiences of all students • nurture collaboration among students • structure and facilitate ongoing formal and informal discussion based on a shared understanding of rules of scientific discourse • model and emphasize the skills, attitudes, and values of scientific inquiry 	<p>The answers provided in the annotations for teachers model these qualities. All the lessons are designed to be completed by students working in collaborative groups. All the discussions in the activities model the rules of scientific discourse. The annotations for teachers provide many suggestions about how to model these skills, attitudes, and values.</p>

evaluating evidence, experiencing, and talking with their peers in ways that promote the development and understanding of key science concepts. These inquiry-based experiences include both direct experimentation and development of explanations through critical and logical thinking. Students often use technology to gather evidence, and mathematics to develop models or explanations.

The BSCS 5Es emphasize student-centered teaching practices. Students participate in their learning in ways that are different from those seen in a traditional classroom. Tables 5 and 6 exemplify what teachers do and what students do in the BSCS 5E Instructional Model.

The following paragraphs illustrate how we implemented the BSCS 5Es in *Emerging and Re-Emerging Infectious Diseases*.

Engage

The primary purpose of the Engage phase is to capture students' attention and interest. It also gives teachers a chance to find out what students already know or think they know about the topic and concepts to be developed. Students come to learning situations with prior knowledge, which may or may not be congruent with the concepts presented in this module.

The Engage lesson in this module, Lesson 1—*Deadly Disease Among Us*, is designed to make connections between past and present learning experiences and to anticipate upcoming activities. By completing it, students should become mentally engaged in the topic of infectious diseases and should begin to think about how the topic relates to their previous experiences. Successful engagement results in students who are intrigued by the concepts they are about to study in depth.

Explore/Explain

Lessons 2, 3, and 4 serve as the Explore and Explain phases of the model. Lesson 2 helps students discover that human activity in the environment is a major factor in the emergence of new diseases worldwide. Likewise, Lessons 3 and 4 help students understand the evolution of antibiotic resistance and the failure of immunization procedures as explanations for the re-emergence of diseases once thought conquered, or largely so.

Explore and Explain activities give students opportunities to develop their own understandings of important concepts and then to articulate their developing understanding to one another and to the teacher. These activities are also where you introduce formal labels for concepts and phenomena. Keep in mind, however, that these activities are still *student-centered*. That is, the students are developing their own explanations for the emergence and re-emergence of infectious disease. Here, your role is to guide students so that they have ample opportunity to develop their understanding. Students ultimately should be able to explain their understanding by bringing together their experiences, prior knowledge, and vocabulary.

Elaborate/Evaluate

During the Elaborate and Evaluate phases of the model, exemplified in this module by Lesson 5—*Making Hard Decisions*, students are challenged to extend and assess their understanding of infectious diseases. Through a new set of questions and experiences, students develop a deeper, broader understanding of the topic, obtain more information about areas of interest, and refine their scientific and critical-thinking skills.

A teacher's primary goal in the opening Elaborate phase is to help students articulate generalizations and extensions of concepts and understandings that are relevant to their lives. The final portion of the activity, where students present arguments for the proposals they have decided to recommend for funding, acts as the Evaluate portion. At this point, students see they can extend and apply their understanding of infectious disease to the real world. It is also important here that they receive feedback on the adequacy of their explanations and understandings.

Elaborate and Evaluate activities are complex and challenging, and Lesson 5 will stretch your students' abilities to listen, think, and speak.

To review the relationship of the BSCS 5E Instructional Model to the concepts presented in the module, see Table 2.

Table 5. The key components of the BSCS 5E Model: What the teacher does.

Stage	What the teacher does that's <i>consistent</i> with the 5E Model	What the teacher does that's <i>inconsistent</i> with the 5E Model
Engage	<ul style="list-style-type: none"> • Creates interest • Generates curiosity • Raises questions • Elicits responses that uncover what students know or think about the concept or subject 	<ul style="list-style-type: none"> • Explains concepts • Provides definitions and answers • States conclusions • Provides premature answers to students' questions • Lectures
Explore	<ul style="list-style-type: none"> • Encourages students to work together without direct instruction from teacher • Observes and listens to students as they interact • Asks probing questions to redirect students' investigations when necessary • Provides time for students to puzzle through problems • Acts as a consultant for students 	<ul style="list-style-type: none"> • Provides answers • Tells or explains how to work through the problem • Tells students they are wrong • Gives information or facts that solve the problem • Leads students step-by-step to a solution
Explain	<ul style="list-style-type: none"> • Encourages students to explain concepts and definitions in their own words • Asks for justification (evidence) and clarification from students • Formally provides definitions, explanations, and new labels • Uses students' previous experiences as the basis for explaining concepts 	<ul style="list-style-type: none"> • Accepts explanations that have no justification • Neglects to solicit students' explanations • Introduces unrelated concepts or skills
Elaborate	<ul style="list-style-type: none"> • Expects students to use formal labels, definitions, and explanations provided previously • Encourages students to apply or extend concepts and skills in new situations • Reminds students of alternative explanations • Refers students to existing data and evidence and asks, "What do you already know?" "Why do you think ... ?" 	<ul style="list-style-type: none"> • Provides definitive answers • Tells students they are wrong • Lectures • Leads students step-by-step to a solution • Explains how to work through the problem
Evaluate	<ul style="list-style-type: none"> • Observes students as they apply new concepts and skills • Assesses students' knowledge and/or skills • Looks for evidence that students have changed their thinking or behaviors • Allows students to assess their own learning and group-process skills • Asks open-ended questions such as, "Why do you think . . . ?" "What evidence do you have?" "What do you know about x?" "How would you explain x?" 	<ul style="list-style-type: none"> • Tests vocabulary words, terms, and isolated facts • Introduces new ideas or concepts • Creates ambiguity • Promotes open-ended discussion unrelated to concept or skill

Table 6. The key components of the BACS 5E Model: What the students do.

Engage	<ul style="list-style-type: none"> • Become interested in and curious about the concept/topic • Express current understanding of a concept or idea • Raise questions such as, “What do I already know about this?” “What do I want to know about this?” “How could I find out?” 	<ul style="list-style-type: none"> • Ask for the “right” answer • Offer the “right” answer • Insist on answers or explanations • Seek closure
Explore	<ul style="list-style-type: none"> • “Mess around” with materials and ideas • Conduct investigations in which they observe, describe, and record data • Try different ways to solve a problem or answer a question • Acquire a common set of experiences so they can compare results and ideas • Compare their ideas with those of others 	<ul style="list-style-type: none"> • Let others do the thinking and exploring (passive involvement) • Work quietly with little or no interaction with others (only appropriate when exploring ideas or feelings) • Stop with one solution • Demand or seek closure
Explain	<ul style="list-style-type: none"> • Explain concepts and ideas in their own words • Base their explanations on evidence acquired during previous investigations • Become involved in student-to-student conversations in which they debate their ideas • Record their ideas and current understanding • Reflect on and perhaps revise their ideas • Express their ideas using appropriate scientific language • Compare their ideas with what scientists know and understand 	<ul style="list-style-type: none"> • Propose explanations from “thin air” with no relationship to previous experiences • Bring up irrelevant experiences and examples • Accept explanations without justification • Ignore or dismiss other plausible explanations • Propose explanations without evidence to support their ideas
Elaborate	<ul style="list-style-type: none"> • Make conceptual connections between new and former experiences • Use what they have learned to explain a new object, event, organism, or idea • Use scientific terms and descriptions • Draw reasonable conclusions from evidence and data • Communicate their understanding to others 	<ul style="list-style-type: none"> • Ignore previous information or evidence • Draw conclusions from “thin air” • Use terminology inappropriately and without understanding
Evaluate	<ul style="list-style-type: none"> • Demonstrate what they understand about the concept(s) and how well they can implement a skill • Compare their current thinking with that of others and perhaps revise their ideas • Assess their own progress by comparing their current understanding with their prior knowledge • Ask new questions that take them deeper into a concept or topic area 	<ul style="list-style-type: none"> • Disregard evidence or previously accepted explanations in drawing conclusions • Offer only yes-or-no answers or memorized definitions or explanations as answers • Fail to express satisfactory explanations in their own words • Introduce new, irrelevant topics

When a teacher uses the BSCS 5E Instructional Model, he or she engages in practices that are very different from those of a traditional teacher. In response, students also participate in their learning in ways that are different from those seen in a traditional classroom. Tables 5 and 6, on pages 10 and 11, outline those differences.

What’s the Evidence for the Effectiveness of the BSCS 5E Model?

Support from educational research studies for teaching science as inquiry is growing (for example, Geier et al., 2008; Hickey et al., 1999; Lynch et al., 2005; and Minner et al., 2009). A 2007 study, published in the *Journal of Research in Science Teaching* (Wilson et al., 2010), is particularly relevant to the *Emerging and Re-emerging Infectious Diseases* supplement.

In 2007, with funding from NIH, BSCS conducted a randomized, controlled trial to assess the effectiveness of the BSCS 5Es. The study used an adaptation of the NIH supplement *Sleep, Sleep Disorders, and Biological Rhythms*, developed by BSCS in 2003 (NIH and BSCS, 2003). Sixty high school students and one teacher participated.

The students were randomly assigned to either the experimental or the control group. In the experimental group, the teacher used a version of the sleep supplement that was very closely aligned with the theoretical underpinnings of the BSCS 5Es. For the control group, the teacher used a set of lessons based on the science content of the sleep supplement but aligned with the most commonplace instructional strategies found in U.S. science classrooms (as documented by Weiss et al., 2003). Both groups had the same master teacher.

Students taught with the BSCS 5Es and an inquiry-based approach demonstrated significantly higher achievement for a range of important learning goals, especially when the results were adjusted for variance in pretest scores. The results were also consistent across time (both immediately after instruction and four weeks later). Improvements in student learning were particularly strong for measures of student reasoning and argumentation. Table 6 highlights some of the study’s key findings. The results of the experiment strongly support the effectiveness of teaching the BSCS 5Es.

Table 7. Differences in Performance of Students Receiving Inquiry-Based and Commonplace Instructional Approaches

Measure	Mean for Students Receiving Commonplace Teaching	Mean for Students Receiving Inquiry-Based Teaching	Effect Size
Total test score pretest (out of 74)	31.11	29.23	Not applicable
Total test score posttest	42.87	47.12	0.47
Reasoning pretest (fraction of responses at the highest level)	0.04	0.03	Not applicable
Reasoning posttest	0.14	0.27	0.68
Score for articulating a claim (out of 3)	1.58	1.84	0.58
Score for using evidence in an explanation (out of 3)	1.67	2.01	0.74
Score for using reasoning in an explanation (out of 3)	1.57	1.89	0.59

Source: C.D. Wilson et al. 2010. The relative effects and equity of inquiry-based and commonplace science teaching on students’ knowledge, reasoning, and argumentation. *Journal of Research in Science Teaching*, 47(3), 276–301.

Note: Effect size is a convenient way to quantify the amount of difference between two treatments. This study used the standardized mean difference (the difference in the means divided by the standard deviation, also known as Cohen’s *d*). The posttest scores controlled for the variance in students’ pretest scores. The reasoning posttest scores controlled for variance in students’ reasoning pretest scores at the highest level.

Evidence also suggests the BSCS 5Es are effective in changing students' attitudes on important issues. In a research study conducted during the field test for the NIH curriculum supplement The Science of Mental Illness (NIH and BSCS, 2005), BSCS partnered with researchers at the University of Chicago and the National Institute of Mental Health. The study investigated whether a short-term educational experience would change students' attitudes about mental illness. The results showed that after completing the curriculum unit, students stigmatized mental illness less than they had beforehand. The decrease in stigmatizing attitudes was statistically significant (Corrigan et al., 2007; Watson et al., 2004).

How Does the Module Support Ongoing Assessment?

Because we expect this supplement to be used in a variety of ways and at various points in each teacher's curriculum, we believe the most appropriate mechanism for assessing student learning occurs informally at various points within the lessons, rather than more formally, just once at the end of the module. Accordingly, we have integrated assessment components throughout the lessons. These embedded assessment opportunities include one or more of the following strategies:

- performance-based activities, such as participating in a structured discussion of a potentially controversial issue;
- oral presentations to the class, such as explaining analysis of data; and
- written assignments, such as answering questions or writing about a laboratory activity.

These strategies allow you to assess a variety of aspects of the learning process, such as students' prior knowledge and current understanding, problem-solving and critical-thinking skills, level of understanding of new information, communication skills, and ability to synthesize ideas and apply understanding to a new situation.



This assessment icon and an annotation that describes the aspect of learning being assessed appear in the margin beside the step in which each embedded assessment occurs.

How Can Controversial Topics Be Handled in the Classroom?

Teachers sometimes feel that the discussion of values is inappropriate in the science classroom or that it detracts from the learning of “real” science. The lessons in this module, however, are based on the conviction that there is much to be gained by involving students in analyzing issues of science, technology, and society. Society expects all citizens to participate in the democratic process, and our educational system must provide opportunities for students to learn to deal with contentious issues with civility, objectivity, and fairness. Likewise, students need to learn that science intersects with life in many ways.

In this module, students have a variety of opportunities to discuss, interpret, and evaluate basic science and health issues, some in the light of values and ethics. As students encounter issues about which they feel strongly, some discussions might become controversial. How much controversy develops will depend on many factors, such as how similar the students are with respect to socioeconomic status, perspectives, value systems, and religious preferences. In addition, the language and attitude of the teacher factor into the flow of ideas and the quality of exchange among the students.

The following guidelines may help teachers facilitate discussions that balance factual information with feelings.

- Remain neutral. Neutrality may be the single most important characteristic of a successful discussion facilitator.
- Encourage students to discover as much information about the issue as possible.
- Keep the discussion relevant and moving forward by questioning or posing appropriate problems or hypothetical situations. Encourage everyone to contribute, but do not force reluctant students into the discussion.
- Emphasize that everyone must be open to hearing and considering diverse views.
- Use unbiased questioning to help the students critically examine all views presented.
- Allow for the discussion of all feelings and opinions.

- Avoid seeking consensus on all issues. The multifaceted issues that the students discuss result in the presentation of divergent views, and students should learn that this is acceptable.
- Acknowledge all contributions in the same evenhanded manner. If a student seems to be saying something for its shock value, see whether other students recognize the inappropriate comment and invite them to respond.
- Create a sense of freedom in the classroom. Remind students, however, that freedom implies the responsibility to exercise that freedom in ways that generate positive results for all.
- Insist upon a nonhostile environment in the classroom. Remind students to respond to ideas instead of to the individuals presenting those ideas.

Using the Student Lessons

The heart of this module is the set of five lessons, which we hope will carry important concepts related to disease and public health to your students. To review the concepts in detail, refer to Table 2 in *Implementing the Module*.

Format of the Lessons

As you scan the lessons, you will find that each contains several major features.

At a Glance gives you a convenient summary of the lesson.

- The **Overview** provides a short summary of what students do.
- **Major Concepts** states the central idea(s) the lesson is designed to convey.
- **Objectives** list three to five specific understandings or abilities students should have after completing the lesson.
- **Prerequisite Knowledge** alerts you to the understandings and skills students should have before beginning the lesson.
- The **Basic Science–Public Health Connection** describes how the lesson illustrates the relationship between basic science and personal and public health. The mission of the NIH is to “uncover new knowledge that will lead to better health for everyone.” This mission statement recognizes that basic science and personal and public health are not separate issues; they are not even two sides of one issue. Rather, they are inextricably linked and form a powerful whole: Research into the basic processes of life leads inevitably to strategies for improving health, and questions about health trigger research into basic processes.
- The **Introduction** places the lesson in a context and provides a short overview of its key components.

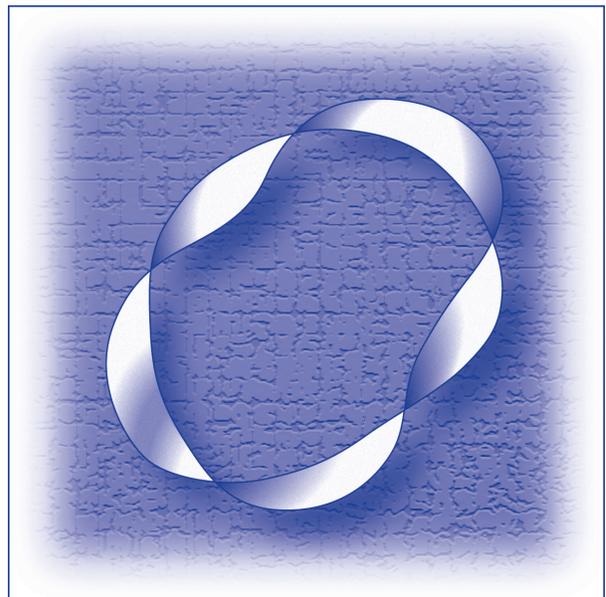
In Advance provides instructions for collecting the materials, photocopying, and other preparations needed for the activities in the lesson.

Procedure outlines the lesson’s steps and provides implementation suggestions and answers to questions. Annotations in the margins, identified by icons, provide specific hints about

helping students see connections between basic science and personal and public health,

assessing student understanding, and

Figure 1. A Möbius strip is a one-sided, one-edged loop. Test this by making a paper loop with five twists. With a marker, draw a continuous line around the strip, starting at the seam. Your line should pass along “both” sides of the paper before you return to your starting point, even though you do not lift your marker off the paper as you draw. Then, run your marker along the edge, again starting at the seam. You should see that the strip also contains only one edge. Loops with odd numbers of twists are Möbius strips; loops with even numbers of twists are not. In this module, we use a Möbius strip as a metaphor for the relationship between basic science and personal and public health.



focusing students' attention on the lesson's major concepts during its closing steps.

Other icons indicate

when to use the Web site (see "Using the Web Site" for instructions; a print-based alternative is provided for classes that don't have access to the Internet), and

the beginning of a print-based alternative version.

Potential Extensions describes ways you can extend or enrich the lesson.

The **Lesson Organizer** briefly summarizes the lesson. It outlines procedural steps for each activity and includes icons that notify you when you'll need masters, transparencies, and the Web site. You should use the lesson organizer only after you become familiar with the detailed procedures for the activities. It can be a handy resource during lesson preparation as well as during classroom instruction.

All the **Masters** required to teach the lessons are in a separate section at the end of the module.

Lessons 3, 4, and 5 (*Superbugs: An Evolving Concern*, *Protecting the Herd*, and *Making Hard Decisions*) use materials on the *Emerging and Re-emerging Infectious Diseases* Web site. For information about the site, see Using the Web Site on page 17. If you do not have enough computers equipped with Internet access, you can use the print-based alternatives.

Timeline for Teaching the Module

Table 8 outlines a plan for preparing for and completing the five lessons that follow. The plan assumes you will teach the lessons on consecutive days. It's important to review the timeline before you start teaching the module. Instructions for setting up computers are under Using the Web Site on page 17 and online at <http://science.education.nih.gov/supplements/diseases/teacher>; for laboratory preparation, on page 80; and for preparing other materials, under Materials and Preparation in each lesson.

Table 8. Suggested timeline for teaching the module.

3 weeks ahead	Reserve computers. Check performance of Web site. Order laboratory material for Lesson 3 (see page 80).
5–7 days ahead	Prepare medium and inoculate student cultures for Lesson 3 (pages 80–81). Copy masters and make transparencies. Collect materials.
2–3 days ahead	Lesson 3, Day 1
Day 1	Lesson 1 Lesson 3, Day 2
Day 2	Lesson 2
Day 3	Lesson 3, Day 3
Day 4	Lesson 4, Day 1
Day 5	Lesson 4, Day 2 (optional)
Day 6	Lesson 5

Using the Web Site

The *Emerging and Re-emerging Infectious Diseases* Web site is a tool that you can use to help organize your use of the module, engage student interest in learning, and orchestrate and individualize instruction. The site features simulations, illustrations, databases, and videos that articulate with the lessons. To access the curriculum's home page, go to <http://science.education.nih.gov/supplements/diseases/>. (If your classes don't have access to the Internet, you can use the print alternatives included with the lessons.)

Hardware and Software Requirements

The Web site can be accessed with any computer browser. Adobe Flash Player should be installed on the hard drive of each computer that will access the site. It's freely available at <http://get.adobe.com/flashplayer/>.

Getting the Most Out of the Web Site

Before you use this or any other piece of instructional software in your classroom, it may be valuable to identify some of the benefits you expect software to provide. Well-designed instructional multimedia software can

- motivate students by helping them enjoy learning—students want to learn more when content that otherwise might be uninteresting is enlivened;
- offer unique instructional capabilities that allow students to explore topics in greater depth—technology offers experiences that are closer to actual life than print-based media offer;
- support you in experimenting with new instructional approaches that allow students to work independently or in small groups—technology gives teachers increased credibility among today's technology-literate students; and
- increase your productivity—technology helps teachers with assessment, record keeping, and classroom planning and management.

The ideal use of the Web site requires one computer for each student group. However, if you have only one computer available, you still can use the Web site. For example, you can use a projection system to display the monitor image for the whole class. If you do not have access to the Web site, you can use the print-based alternative provided for each Web activity.

Collaborative Groups

We designed many of the activities in this module to be completed by groups of students working together. Although individual students working alone can complete many of the steps, this strategy will not stimulate the types of student-student interactions that are part of active, collaborative, inquiry-based learning. Therefore, we recommend that you organize collaborative groups of two to four students each, depending on the number of computers available. If necessary, up to six students may work as a group, although the students may not be as involved in the activity. Students in groups larger than this are likely to have difficulty organizing the student-computer interactions equitably. This can lead to one or two students' assuming the primary responsibility for the computer-based work. Although large groups can be efficient, they do not allow all students to experience the in-depth discovery and analysis that the Web site was designed to stimulate. Group members not involved directly may become bored or disinterested.

We recommend that you keep students in the same collaborative groups for all the activities in the lessons. This will allow each group to develop a shared experience with the Web site and with the ideas and issues that the activities present. A shared experience will also enhance your students' perceptions of the lessons as a conceptual whole.

If your student-to-computer ratio is greater than six students to one computer, you will need to change the way you teach the module from the instructions in the lessons. For example, if you have only one computer available you may want students to complete the Web-based work over an extended time period. You can do this several ways. The most practical one is to use your computer as a center along with several other centers at which students complete other activities. In this approach, students rotate through the computer center, eventually completing the Web-based work you have assigned.

A second way to structure the lessons if you have only one computer available is to use a projection system to display the computer monitor onto a screen for the whole class to see. Giving selected students in the class the opportunity to manipulate the Web activities in response to suggestions and requests from the class can give students some of the same autonomy in their learning they would have gained from working in small groups.

State Standards Alignment

To find out how this supplement's content aligns with your state's science, English language arts, and math education standards, go to <http://science.education.nih.gov/StateStandards>.

Web Activities for People with Disabilities

The Office of Science Education (OSE) provides access to the Curriculum Supplement Series for people with disabilities. The online versions of this series comply with Section 508 of the Rehabilitation Act. If you use assistive technology (such as a Braille reader or a screen reader) and have trouble accessing any materials on our Web site, please let us know. We'll need a description of the problem, the format in which you would like to receive the material, the Web address of the requested material, and your contact information.

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Understanding Emerging and Re-emerging Infectious Diseases

The term “disease” refers to conditions that impair normal tissue function. For example, cystic fibrosis, atherosclerosis, and measles are all considered diseases. However, there are fundamentally different causes for each of these diseases. Cystic fibrosis (CF) is due to a specific genotype that results in impaired transport of chloride ions across cell membranes, leading to the production of abnormally thick mucus. Thus, CF is most accurately called a *genetic* or *metabolic* disease. Atherosclerosis, which can lead to heart attacks and strokes, may be considered a disease of *aging*, because it typically becomes a problem later in life after plaques of cholesterol have built up and partially blocked arteries. In contrast, measles is an *infectious* disease because it occurs when an individual contracts an outside agent, the measles virus. An **infectious disease** is a disease that is caused by the invasion of a host by agents whose activities harm the host’s tissues (that is, they cause *disease*) and can be transmitted to other individuals (that is, they are *infectious*).

Nature of Infectious Diseases

Microorganisms that are capable of causing disease are called **pathogens**. Although microorganisms that cause disease often receive the most attention from the scientific community and the media, it is important to note that most microorganisms do *not* cause disease. In fact, many probably provide some protection against harmful microorganisms because they effectively compete with the harmful organisms for resources, preventing them from growing.

A true pathogen is an infectious agent that causes disease in virtually any susceptible host. Opportunistic pathogens are potentially infectious agents that rarely cause disease in individuals with healthy immune systems. Diseases caused by opportunistic pathogens are typically found among groups such as people whose immune systems are failing, cancer patients receiving chemotherapy (which adversely affects the immune system), or people

who have AIDS or are HIV-positive. An important clue to understanding the effect of HIV on the immune system was the observation of a rare type of pneumonia among young men caused by *Pneumocystis carinii*, an organism that causes disease only among the immunosuppressed.

The terms “infection” and “disease” are not synonymous. An **infection** results when a pathogen invades and begins growing within a host. **Disease** results only if and when, as a consequence of the invasion and growth of a pathogen, tissue function is impaired. Our bodies have defense mechanisms to prevent infection and, should those mechanisms fail, to prevent disease after infection occurs. Some infectious agents are easily transmitted (that is, they are very contagious) but they are not very likely to cause disease (that is, they are not very **virulent**). The polio virus is an example: It probably infects most people who contact it, but only about 5 to 10 percent of those infected actually develop clinical disease. Other infectious agents are very virulent but not terribly contagious. The terror surrounding Ebola hemorrhagic fever is based on the virulence of the virus (50 to 90 percent fatality rate among those infected); however, the virus itself is not transmitted easily by casual contact. The most worrisome infectious agents are those that are both very contagious and very virulent.

In order to cause disease, pathogens must be able to enter the host body, adhere to specific host cells, invade and colonize host tissues, and inflict damage on those tissues. Entrance to the host typically occurs through natural orifices, such as the mouth, eyes, or genital openings, or through wounds that breach the skin barrier to pathogens. Although some pathogens can grow at the initial entry site, most must invade areas of the body where they are not typically found. They do this by attaching to specific host cells. Some pathogens then multiply between host cells or within body fluids, while others, such as viruses and some

bacterial species, enter the host cells and grow there. Although the growth of pathogens may be enough to cause tissue damage in some cases, damage is usually due to the production of toxins or destructive enzymes by the pathogen. For example, *Corynebacterium diphtheriae*, the bacterium that causes diphtheria, grows only on nasal and throat surfaces. However, the toxin it produces is distributed to other tissues by the circulatory system, damaging heart, liver, and nerve tissues. *Streptococcus pyogenes*, the infectious agent associated with several diseases including strep throat and “flesh-eating disease,” produces several enzymes that break down barriers between epithelial cells and remove fibrin clots, helping the bacteria invade tissues.

Microbes That Cause Infectious Diseases

There are five major types of infectious agents: bacteria, viruses, fungi, protozoa, and helminths. In addition, a new class of infectious agents, the prions, has recently been recognized. A brief review of the general characteristics of each of these agents and examples of some diseases they cause follows.

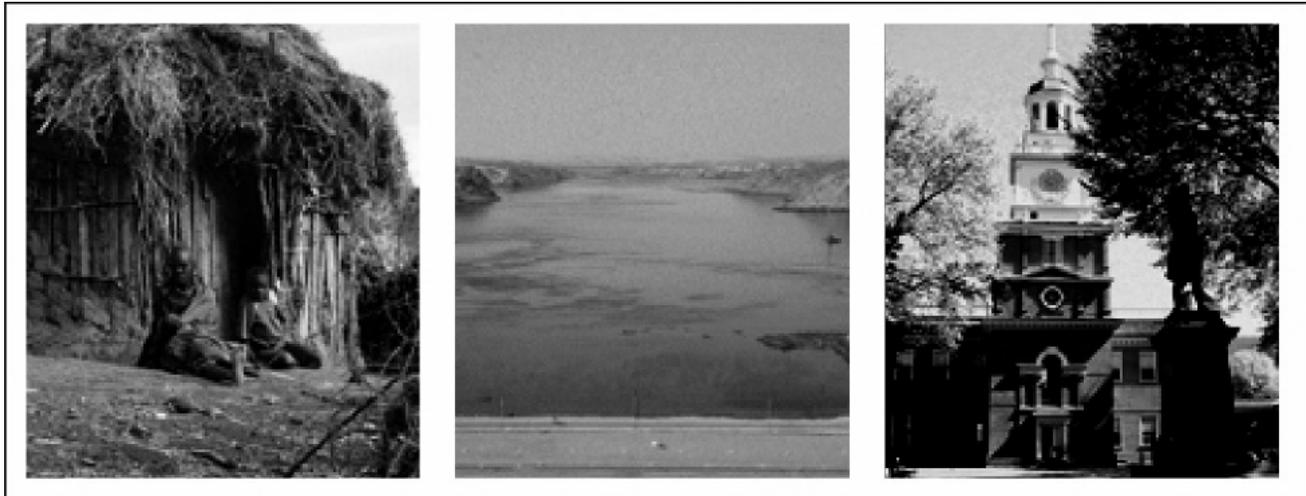
Bacteria. Bacteria are unicellular prokaryotic organisms; that is, they have no organized internal membranous structures such as nuclei, mitochondria, or lysosomes. Bacterial genomes consist of circular, double-stranded DNA. Their genomes associate with much less protein than

do eukaryotic genomes. Most bacteria reproduce by growing and dividing into two cells in a process known as binary fission. Despite these commonalities that group them together in the Bacteria domain, there is a wide range of diversity among the bacteria.

There is a variety of morphologies among bacteria, but three of the most common are bacillus (rod-shaped), coccus (spherical), and spirillum (helical rods). The energy sources for bacteria also vary. Some bacteria are photosynthetic and obtain their energy directly from the sun. Others oxidize inorganic compounds to supply their energy needs. Still other bacteria generate energy by breaking down organic compounds such as amino acids and sugars in a respiratory process. Some bacteria require oxygen (aerobes), while others are unable to tolerate it (anaerobes). Some bacteria can grow either with or without oxygen (facultative anaerobes).

Bacteria are frequently divided into two broad classes based on their cell wall structures, which influences their Gram stain reaction. Gram-negative bacteria appear pink after the staining procedure. Familiar pathogenic gram-negative organisms are *Salmonella typhi*, which causes typhoid fever, and *Yersinia pestis*, which causes plague. Gram-positive bacteria appear purple after the Gram stain procedure. Examples of pathogenic gram-positive bacteria are *Staphylococcus aureus*, which causes skin,

Figure 3. Emerging and re-emerging infectious diseases threaten all countries. Ebola hemorrhagic fever emerged in African villages; schistosomiasis is re-emerging in Egypt, largely as a consequence of the construction of the Aswan Dam; and legionellosis was identified after an outbreak of pneumonia among individuals attending a conference in Philadelphia.



respiratory, and wound infections, and *Clostridium tetani*, which produces a toxin that can be lethal for humans and is the causative agent of tetanus.

Viruses. Microbiologists have found viruses that infect all organisms, from plants and animals to fungi and bacteria. Viruses, however, are not organisms themselves because, apart from a host cell, they have no metabolism and cannot reproduce. A virus particle is composed of a viral genome of nucleic acid that is surrounded by a protein coat called a capsid. In addition, many viruses that infect animals are surrounded by an outer lipid envelope, which they acquire from the host cell membrane as they leave the cell. Unlike organisms, in which the genetic material is always double-stranded DNA, viral genomes may be double- or single-stranded DNA (a DNA virus), or double- or single-stranded RNA (an RNA virus).

In the general process of infection and replication by a DNA virus, a viral particle first attaches to a specific host cell via protein receptors on its outer envelope, or capsid. The viral genome is then inserted into the host cell, where it uses host cell enzymes to replicate its DNA, transcribe the DNA to make messenger RNA, and translate the messenger RNA into viral proteins. The replicated DNA and viral proteins are then assembled into complete viral particles, and the new viruses are released from the host cell. In some cases, virus-derived enzymes destroy the host cell membranes, killing the cell and releasing the new virus particles. In other cases, new virus particles exit the cell by a budding process, weakening but not destroying the cell.

In the case of some RNA viruses such as coronaviruses and hepatitis C virus, the genetic material can be used directly as messenger RNA to produce viral proteins, including a special viral RNA polymerase that copies the RNA template to produce the genetic material for new viral particles. Other RNA viruses, called retroviruses, use a unique enzyme called reverse transcriptase to copy the RNA genome into DNA. This DNA then integrates itself into the host cell genome. These viruses frequently exhibit long latent periods in which their genomes are faithfully copied and distributed to progeny cells each time the cell divides. The human immunodeficiency virus (HIV), which causes AIDS, is a familiar example of a retrovirus.

Just like other infectious agents, viruses cause disease by disrupting normal cell function. They do this in a variety of ways. Some viruses make repressor proteins that stop the synthesis of the host cell's proteins, RNA, and DNA. Viral activity may weaken cell membranes and lysosomal membranes, leading to cell autolysis. Some viral proteins are toxic to cells, and the body's immune defenses also may kill virus-infected cells.

Viruses are classified using a variety of criteria, including shape, size, and type of genome. Among the DNA viruses are the herpes viruses that cause chicken pox, cold sores, and painful genital lesions, and the poxvirus that causes smallpox. Significant RNA viruses that cause human disease include rhinoviruses that cause most common colds; myxoviruses and paramyxoviruses that cause influenza, measles, and mumps; rotaviruses that cause gastroenteritis; and the retroviruses that cause AIDS and several types of cancer.

Fungi. Fungi are eukaryotic, heterotrophic organisms that have rigid cellulose- or chitin-based cell walls and reproduce primarily by forming spores. Most fungi are multicellular, although some, such as yeasts, are unicellular. Together with bacteria, fungi fulfill the indispensable role of decomposers in the environment. Many fungi also infect plants and animals. Examples of diseases caused by fungi are ringworm and histoplasmosis (a mild to severe lung infection transmitted by bat or bird droppings). Yeasts of the *Candida* genus are opportunistic pathogens that may cause diseases such as vaginal yeast infections and thrush (a throat infection) among people who are immunocompromised or undergoing antibiotic therapy. Antibiotics reduce the bacterial population normally present in the throat and vagina, allowing the yeast to grow unchecked.

Protozoa. Protozoa are unicellular, heterotrophic eukaryotes that include the familiar amoeba and paramecium. Because protozoa do not have cell walls, they are capable of a variety of rapid and flexible movements. Protozoa can be acquired through contaminated food or water or by the bite of an infected arthropod such as a mosquito. Diarrheal disease in the United States can be caused by two common protozoan parasites, *Giardia*

lamblia and *Cryptosporidium parvum*. Malaria, a tropical illness that causes 300 million to 500 million cases of disease annually worldwide, is caused by several species of the protozoan *Plasmodium*.

Helminths. Helminths are simple, invertebrate animals, some of which are infectious parasites. They are multicellular and have differentiated tissues. Because they are animals, their physiology is similar in some ways to ours. This makes parasitic helminth infections difficult to treat because drugs that kill helminths are frequently toxic to human cells.

Many helminths have complex reproductive cycles that include multiple stages, many or all of which require a host. *Schistosoma*, a flatworm, causes the mild disease swimmer's itch in the United States; another species of *Schistosoma* causes the much more serious disease schistosomiasis, which is endemic in Africa and Latin America. Schistosome eggs hatch in freshwater, and the resulting larvae infect snails. When the snails shed these larvae, the larvae attach to and penetrate human skin. They feed, grow, and mate in the human bloodstream; the damage to human tissues caused by the accumulating schistosome eggs with their sharp spines results in disease symptoms including diarrhea and abdominal pain. Liver and spleen involvement are common. Another disease due to a helminth is trichinosis, caused by the roundworm *Trichinella spiralis*. This infectious agent is typically ingested in improperly cooked pork from infected pigs. Early disease symptoms include vomiting, diarrhea, and fever; later symptoms include intense muscle pain because the larvae grow and mature in those tissues. Fatal cases often show congestive heart failure and respiratory paralysis.

Prions. During the past three decades, evidence has linked some degenerative disorders of the central nervous system to infectious particles that consist only of protein. These "proteinaceous infectious particles" have been named prions (pronounced *pree-ons*). The known prion diseases include Creutzfeldt-Jakob disease (in humans), scrapie (in sheep), and bovine spongiform encephalopathy ("mad cow disease" in cattle); all known prion diseases frequently result in brain tissue that is riddled with holes. While

some prion diseases are inherited, others are apparently due to infection by eating infected tissue or inadvertently through medical procedures such as tissue transplants.

Occurrence of Infectious Diseases

Epidemiology is the study of the occurrence of disease in populations. Epidemiologists are concerned not only with infectious diseases, but also with noninfectious diseases such as cancer and atherosclerosis, and environmental diseases such as lead poisoning. These professionals work to prevent or minimize the impact of diseases in the population. Their work may include such activities as identifying unusually high incidences of a particular disease, determining the effectiveness of a vaccine, and calculating the cost effectiveness of various means of controlling disease transmission. Occasionally, epidemiologists act as "detectives" who track down the cause of a "new" disease, determine its reservoir and mode of transmission, and help organize various healthcare workers to bring the disease under control.

Disease reservoirs. The reservoir for a disease is the site where the infectious agent survives. For example, humans are the reservoir for the measles virus because it does not infect other organisms.

Animals often serve as reservoirs for diseases that infect humans. Infectious diseases that can be transmitted from animals to humans and from humans to animals, zoonoses, are thought to account for more than 60 percent of emerging infectious diseases today. The major reservoir for *Yersinia pestis*, the bacteria that causes plague, is wild rodents. There are also nonliving reservoirs. Soil is the reservoir for many pathogenic fungi as well as some pathogenic bacteria such as *Clostridium tetani*, which causes tetanus. More recent examples of zoonotic infectious diseases include hantavirus and severe acute respiratory syndrome (SARS). Scientists and epidemiologists are now studying the "one-health" concept, which emphasizes the unity of human and animal infectious diseases (Morens and Fauci, 2012).

Modes of transmission. Infectious agents may be transmitted through either direct or indirect contact. Direct contact occurs when an individual is infected by contact with the reservoir, for

example, by touching an infected person, ingesting infected meat, or being bitten by an infected animal or insect. Transmission by direct contact also includes inhaling the infectious agent in droplets emitted by sneezing or coughing and contracting the infectious agent through intimate sexual contact. Some diseases that are transmitted primarily by direct contact with the reservoir include ringworm, AIDS, trichinosis, influenza, rabies, and malaria.

Indirect contact occurs when a pathogen can withstand the environment outside its host for a long period of time before infecting another individual. Inanimate objects that are contaminated by direct contact with the reservoir (for example, a tissue used to wipe the nose of an individual who has a cold or a toy that has been handled by a sick child) may be the indirect contact for a susceptible individual. Ingesting food and beverages contaminated by contact with a disease reservoir is another example of disease transmission by indirect contact. The fecal-oral route of transmission, in which sewage-contaminated water is used for drinking,

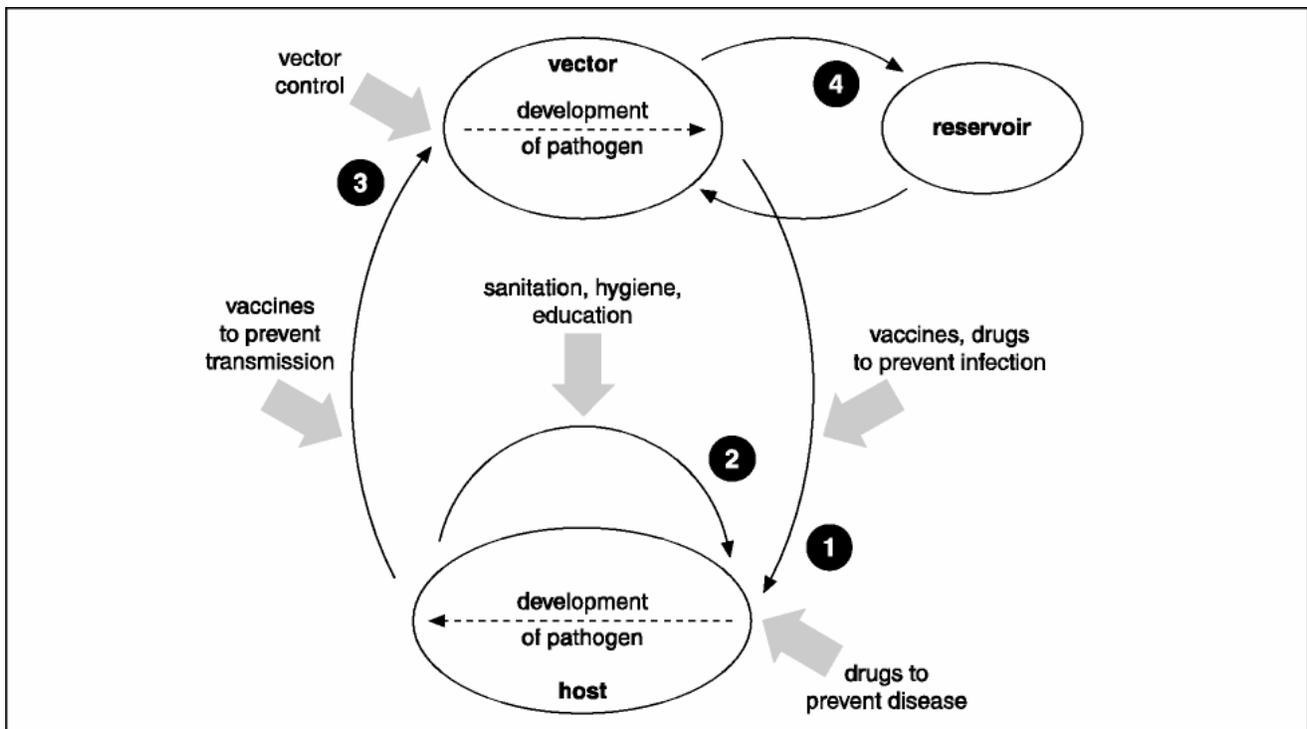
washing, or preparing foods, is a significant form of indirect transmission, especially for gastrointestinal diseases such as cholera, rotavirus infection, cryptosporidiosis, and giardiasis.

These modes of transmission are all examples of horizontal transmission because the infectious agent is passed from person to person in a group. Some diseases are also transmitted vertically; that is, they are transmitted from parent to child during the processes of reproduction (through sperm or egg cells), fetal development, or birth. Diseases in which vertical transmission occurs include AIDS, Group B strep infection, and herpes encephalitis (which occurs when an infant contracts the herpes simplex type II virus during vaginal birth).

Role of Research in Prevention

Infectious diseases can be prevented at a variety of points, depending on the infectious cycle for the particular disease (Figure 4). Basic research, such as that sponsored by NIH, reveals the specific infectious cycle and details regarding the activities of the pathogen that cause disease

Figure 4. The black arrows illustrate a generalized infectious cycle; the shaded arrows indicate points where infectious diseases can be prevented. (1) A host is infected by the reservoir or a vector for the pathogen. This individual may infect (2) other hosts in a population or (3) new vectors. (4) The pathogen may also cycle between the vector and a reservoir.



(for example, the particular cells, if any, that are attacked and the toxins produced by the pathogen that damage host tissues).

Understanding the infectious cycle is critical to identifying accessible targets for control strategies (Figure 4). For example, direct person-to-person transmission may be inhibited by proper hygiene and sanitary conditions as well as by education about disease prevention. Vector-borne diseases may be prevented by control measures that either kill the vector or prevent its contact with humans. Infection by a pathogen or development of a pathogen within a host may be prevented by vaccination. Finally, drugs may be used to prevent infection or suppress the disease process.

The tools, including drugs, vaccines, and vector-control methods, are already available to deal with some diseases. For other diseases, the methods for control are inadequate, undeveloped, or nonexistent. Scientists are trying to develop the new tools needed to banish these scourges of humankind. This requires basic research into the life processes of the pathogen and its interaction with the host in order to identify points within the life cycle where the pathogen is vulnerable to intervention, translational research to develop new tools (such as vaccines or antimicrobial drugs), and clinical research to test the safety and efficacy of these new tools.

Host Defenses Against Infectious Diseases

The human body has several general mechanisms for preventing infectious diseases. Some of these mechanisms are referred to as nonspecific defenses because they operate against a wide range of pathogens. Other mechanisms are referred to as specific defenses because they target particular pathogens and pathogen-infected cells.

Nonspecific mechanisms. Nonspecific mechanisms are the body's primary defense against disease. These mechanisms include anatomical barriers to invading pathogens, physiological deterrents to pathogens, and the presence of normal flora. An example of an anatomical barrier is the nasal opening to the respiratory system. This natural opening is a long, convoluted passage covered by mucous

membranes that trap airborne particles and prevent most of them from reaching the lungs. Other anatomical barriers are the skull and vertebral column, which protect the central nervous system—few pathogens are able to penetrate bone. The skin is also a major anatomical barrier to microorganisms. The surface layer of dead, hardened cells is relatively dry, and skin secretions make the surface somewhat acidic. When sweat evaporates, salt is left behind on the skin. All of these conditions (low moisture, low pH, and high salinity) prevent most microorganisms from growing and multiplying on the skin. The major medical challenge in treating burn patients is preventing and treating infections that result because of the absence of skin that ordinarily would prevent invasion of microorganisms.

Natural openings are also protected by a variety of physiological deterrents. For example, tears continuously flush debris from the eyes. Vaginal secretions are acidic, a hostile environment that discourages the growth of many pathogens. The eye, mouth, and nasal openings are protected by tears, saliva, or nasal secretions that contain lysozyme, an enzyme that breaks down bacterial cell walls. Blood, sweat, and some tissue fluids contain lysozyme as well.

In addition to lysozyme, the blood has many elements that defend the body from disease-causing organisms. The white blood cells include several types of phagocytic cells that detect, track, engulf, and kill invading bacteria and viruses, as well as infected host cells and other debris. These phagocytic cells are part of the nonspecific immune system. Blood plasma also includes clotting factors that initiate a clot at the injury site, preventing pathogens from invading the body further. Finally, the complement proteins in the blood participate in a cascade of molecular events that result in inflammation, the release of molecules that stimulate phagocytic cells, and the formation of a complex of proteins that binds to the surface of bacterial or infected host cells and lyses those cells.

The inflammatory response is another nonspecific defense mechanism that helps prevent infectious agents from spreading in the body. Inflammation

involves swelling, reddening, elevated temperature, and pain. Unfortunately, inflammation itself frequently causes tissue damage and, in severe cases, even death.

The protective role of the “normal flora” of microorganisms present on and in the body should not be overlooked. These organisms survive and grow on the skin and in the mouth, gastrointestinal tract, and other areas of the body but do not cause disease because their growth is kept under control by the host’s defense mechanisms and by the presence of other microorganisms. These organisms protect the host by successfully competing with disease-causing organisms, preventing the latter from invading host tissues. When the growth of the normal flora is suppressed (for example, due to antibiotic treatment), other “opportunistic” agents that normally do not grow in or on the body may be able to infect and cause disease.

Specific mechanisms of host resistance. When these nonspecific mechanisms fail, the body initiates a second, specific line of defense. This specific immune response enables the body to target particular pathogens and pathogen-infected cells for destruction. It depends on specialized white blood cells called lymphocytes and includes T-cells (produced from lymphocytes that matured in the thymus gland) and B-cells (produced from lymphocytes that matured in the bone marrow).

The two complementary components of the specific immune response are the cell-mediated response and the antibody-mediated response (Figure 5). The cell-mediated response involves T-cells and is responsible for directly destroying body cells that are infected with a virus or have become cancerous, or for activating other immune cells to be more efficient microbe killers. The antibody-mediated response involves both T-cells and B-cells and is critical for the destruction of invading pathogens as well as the elimination of toxins.

Both the cell-mediated and antibody-mediated responses are initiated after a particular type of phagocytic cell, a macrophage, engulfs a pathogen. Macrophages digest the pathogen and then display antigens from the pathogen on their surface. Antigens are specific molecules, such

as the proteins on the surface of pathogens, that elicit an immune response. This display helps the macrophages stimulate specific helper T-cells to release signal molecules called lymphokines. The lymphokines, in turn, stimulate the cell-mediated and antibody-mediated responses.

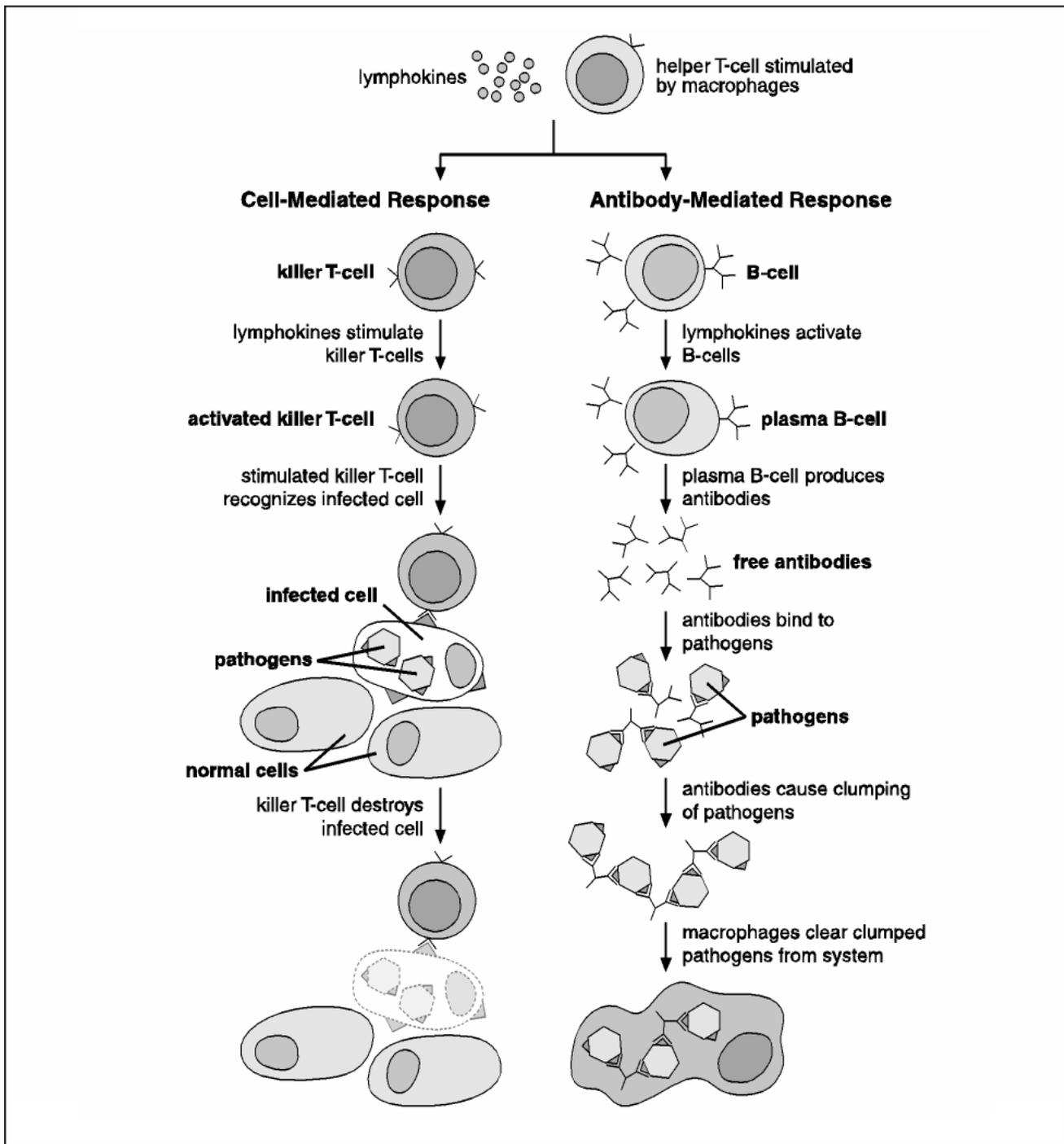
The cell-mediated response occurs when the lymphokines released from the helper T-cells stimulate other cell types to participate in the immune response. Lymphokine-stimulated killer T-cells attach to the pathogen-infected cells and destroy them, whereas lymphokine-activated phagocytic cells produce more toxic molecules that can kill the pathogen directly.

The antibody-mediated response occurs when the lymphokines activate specific B-cells to produce antibodies (proteins that specifically recognize and bind to antigens). These antibodies attach to antigens on the surface of the pathogens and signal attack by phagocytic cells and the complement system. Other B-cells go on to become memory B-cells, which respond quickly by producing more antibodies upon subsequent infection.

Immunity. When a host encounters an antigen that triggers a specific immune response for the second or later time, the memory lymphocytes recognize it and quickly begin growing and dividing, as well as producing high concentrations of lymphokines and antibodies. Because memory cells are present, this response happens much more quickly than in the initial encounter with the antigen. This rapid response explains why hosts are immune to developing many diseases a second time: The immune response occurs so quickly in a second encounter with the pathogen that the pathogen does not have enough time to reproduce to concentrations that result in disease before the host’s body has destroyed it. The memory response also explains the effectiveness of vaccination for preventing even the first occurrence of many diseases.

Vaccination. A vaccine is either a killed or weakened (attenuated) strain of a particular pathogen, or a solution containing critical antigens from the pathogen. The body’s immune system will respond to these vaccines as if they contain the actual pathogen, even though the

Figure 5. This diagram provides an overview of specific immunity.



vaccine is not capable of causing the disease. As a result of the specific immune response, memory lymphocytes will be present that respond rapidly when the actual pathogen is encountered. The resulting rapid activation of immune cells prevents disease.

New types of vaccines, the DNA vaccines, are in early-stage trials. These vaccines contain genes that encode proteins from pathogens. When these genes are inserted into host cells and are expressed in the form of pathogen proteins, an immune reaction may result.

The ultimate effectiveness of vaccination—eradication of the infectious agent—has been achieved only for smallpox. The World Health Organization has identified the polio and measles viruses among the next targets for global eradication.

For a variety of reasons, many diseases are not easily prevented by vaccination. Antibody response is generally the simplest to induce by vaccination, but some pathogens have ways to evade the immune response. Intracellular pathogens (such as viruses and some bacterial and protozoan pathogens) are not directly affected by antibodies because antibodies cannot pass inside cells. Moreover, during the disease process, some pathogens acquire an external coat composed of host-derived material while others disguise themselves by making molecules that resemble host molecules. Thus, the host's immune system does not identify them as foreign invaders. Still other pathogens mutate quickly, producing variants of their antigens that are not recognized by the host's immune system, even though the host survived a previous encounter with that pathogen. Cold and influenza viruses are examples of rapidly mutating pathogens. Scientists are working to improve vaccines against these pathogens.

Public Health Measures to Prevent Infectious Diseases

Developed countries have regulations that help protect the general public from infectious diseases. Public health measures typically involve eliminating the pathogen from its reservoir or from its route of transmission. Those measures include ensuring a safe water supply, effectively managing sewage treatment and disposal, and initiating food-safety, animal-control, and vaccination programs.

Safe water. Many pathogens that cause gastrointestinal diseases (for example, those that cause hepatitis A and typhoid fever) are transmitted via water. Travelers to developing countries are frequently advised to be immunized against these diseases. This is generally unnecessary in the United States and other developed countries because the water used for washing, drinking, and preparing food is purified before it goes into homes. Purification methods

include settling, filtration, and chlorination. The water for homes that use well water or springs is usually safe if guidelines about distance from sewage disposal facilities are followed; however, this water should be checked periodically. When breakdowns in a purification system occur, or when a system is overwhelmed (for example, due to unusual flooding), drinking water may not be safe and should be boiled or treated with chlorine before it is ingested.

Because gastrointestinal pathogens typically leave the body in the feces, public water must be guarded against contamination from sewage. Municipal water is usually tested for the presence of coliform organisms (nonpathogenic microorganisms that are part of the normal flora of the gastrointestinal tract) as indicators of sewage contamination. This procedure is necessary because when the water contains pathogens and is potentially dangerous, the pathogenic organisms are usually present in such small numbers that they are hard to detect.

Sewage treatment and disposal. Sewage includes wash water, water from toilets, and storm runoff. These fluids may carry the pathogens for many waterborne diseases, including giardiasis and hepatitis A. To ensure public safety, the U.S. government (and the governments of other developed countries) requires that sewage be treated to eliminate pathogens. The minimal acceptable level of treatment involves collection and sedimentation of sewage waters, separating solid matter (sludge) from the liquid (effluent) portion of sewage. The effluent is chlorinated to kill pathogens before it is released to rivers or lakes. The sludge is burned or dumped.

More advanced methods of treatment use a secondary treatment following this primary treatment. The effluent is transferred to tanks containing a population of microorganisms that decompose more than 90 percent of the organic wastes and eliminate pathogens by competition (this is another example of the important role of microorganisms in *preventing* disease). The resulting effluent is chlorinated before it is released to the environment. Some sewage-treatment plants include a tertiary treatment that involves additional chemicals that also eliminate pathogens.

Food-safety programs. The United States has many standards, inspection plans, and regulations about food preparation, handling, and distribution. Meatpacking facilities are inspected regularly so that diseased animals can be detected and eliminated, standards for processes such as meat cutting and refrigeration are observed, and residues from pesticides and antibiotics as well as contamination by bacteria and other parasites are detected. Restaurants and supermarkets are similarly inspected. Milk is pasteurized and dated for sale and is analyzed periodically for contamination. Industry standards for canning and preserving foods are maintained through periodic quality-control checks and, if contamination is found in representatives of any batches, public health officials recall the entire batch and alert the public through the media.

Animal-control programs. Animals are carriers of many diseases that also affect humans. Inspecting domestic herd animals for tuberculosis (due to the bacterium *Mycobacterium bovis*) and brucellosis (a disease that causes spontaneous abortion in domestic herd animals and abscesses of the liver, spleen, bone marrow, and lymph nodes in humans) has helped eliminate the threat of passing along the pathogens for those diseases to humans in contaminated milk and meat. Before their pets can be licensed, dog owners must show proof of rabies vaccination. Because most cases of rabies among people in the United States are due to bites from wild and stray animals, health officials are mandated to impound and destroy these animals. Many diseases, including bubonic plague, are spread by rodents, and rat control, especially in urban areas, is a major component of public health efforts. Insects also transmit many diseases (notable examples are malaria and West Nile virus). The spread of insect-borne diseases can be controlled by eliminating breeding areas for insects (for example, draining areas where stagnant water collects) and using pesticides. Many imported animals must be tested for specific diseases to prevent the introduction of those diseases into the country.

Vaccination programs. Most states now require that parents or guardians show proof of vaccination before their children can be enrolled in day-care facilities or public schools, although

some states allow certain exemptions, including exemptions based on religious beliefs. The value of immunization for an *individual's health* is obvious; however, it is also important for *public health*. If a certain proportion of a population (called the **threshold proportion**) is immune to a disease, the pathogen that causes that disease will be unable to reproduce itself at a high enough level to maintain itself in the population. This is because once the infected host recovers or dies, there will not be enough new, susceptible hosts for the pathogen to infect. Eventually, the pathogen cannot spread any further and could be eliminated from the population. Even if elimination of the pathogen does not occur, there will be relatively few cases of the related disease, and epidemics of the disease in the population will be avoided. This phenomenon is called **herd immunity**.

The threshold proportion varies depending on the disease and other conditions in the relevant population. Vaccination programs led by public health officials aim to achieve the immunization of at least the threshold number of individuals for the population.

Public health organizations. Cities and other local areas have public health agencies that enforce regulations, provide public health services

Figure 6. Vaccination programs are important components of public health systems.



such as vaccination programs, and monitor and report the incidence of particular diseases to state and federal agencies. State public health agencies are affiliated with laboratories and staff epidemiologists for investigating disease cases.

All of these agencies report data to the U.S. Public Health Service. NIH, the funding agency of this module, began in 1887 as the Laboratory of Hygiene; NIH is an agency of the U.S. Department of Health and Human Services (DHHS). It supports health-related research aimed at understanding, preventing, treating, and controlling infectious and other diseases of humankind. DHHS also operates the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, and the Food and Drug Administration (FDA). CDC staff investigate disease outbreaks, publish a summary of current epidemiological reports, and sponsor a variety of education programs, research projects, and reference laboratories. FDA monitors the safety of our food, medicines, and many other products that we use daily. Finally, the World Health Organization (WHO), among other efforts, coordinates multinational vaccination campaigns.

Treatment of Infectious Diseases

While literally meaning “destroyer of life,” the term “antibiotic” has become the most commonly used word to refer to a chemical substance used to treat bacterial infections. The term “antimicrobial” has a somewhat broader connotation, generally referring to anything that inhibits the growth of microbes. Technically, the term antimicrobial does not encompass the “antihelminthic” drugs because worms are not microscopically small. Antimicrobials can be either microbistatic (inhibiting the replication of the microbe) or microbicidal (actually killing the target microorganism). In the former case, a combination of therapy and immunity may be required to finally terminate the infection.

Treatment of bacterial diseases. Because bacteria are prokaryotes, it has been relatively easy to find and develop antibacterial drugs that have minimal side effects. These drugs target structural features and metabolic characteristics of prokaryotes that are significantly different from those in eukaryotic cells. Drugs used to treat bacterial diseases can be grouped into

categories based on their modes of action. In general, these drugs inhibit cell wall synthesis, protein synthesis, nucleic acid synthesis, or other enzyme-catalyzed reactions.

The penicillins and cephalosporins all interfere with the synthesis of the peptidoglycan layer in prokaryotic cell walls. Because eukaryotes have neither the peptidoglycan components nor the enzymes that synthesize them, these drugs do not affect the host cells. A second class of drugs, including chloramphenicol, the tetracyclines, and erythromycin, bind to prokaryotic ribosomes and inhibit protein synthesis. Prokaryotic ribosomes are structurally different from eukaryotic ribosomes, so these drugs have minimal effect on eukaryotic cells. Nevertheless, some of them may be toxic to some human tissues when they are used in high doses or for prolonged periods of time.

Rifampicin is one of the antibiotics frequently used for treating tuberculosis. This drug inhibits prokaryotic RNA synthesis. DNA synthesis in prokaryotes may be inhibited by the fluoroquinolones. In contrast, the sulfonamides stop bacterial infections by inhibiting other enzymes. Sulfonamides interfere with the synthesis of folic acid, a vitamin necessary for nucleic acid synthesis. Most bacteria must synthesize their own folic acid because their membranes are impermeable to external folic acid. Mammalian cells are not affected by sulfonamides because they are unable to make their own folic acid and have evolved mechanisms for transporting external folic acid across their membranes.

Treatment of viral diseases. Bacteria replicate independently of their hosts and have unique properties that are often the target of antibacterial drugs. In contrast, drugs that effectively inhibit viral infections are highly toxic to host cells because viruses use the host’s metabolic enzymes in their reproduction. For this reason, most illnesses due to viruses are treated symptomatically until the host’s immune system controls and eliminates the pathogen (or the host dies). Antiviral drugs that are used typically target virus-specific enzymes involved in viral nucleic acid synthesis. One of the most familiar of these drugs is acyclovir, which is used to treat outbreaks of genital herpes. Amantadine is an antiviral drug sometimes used to prevent or

moderate influenza among those at high risk of severe illness from the disease.

In addition to antiviral drugs that inhibit the replication of the HIV genome (such as AZT), AIDS patients today are also prescribed proteases that interfere with the packaging of the HIV genome into virus particles. (For a list of all current HIV/AIDS treatments, see <http://www.fda.gov/oashi/aids/virals.html>.)

Treatment of fungal and parasitic diseases.

The development of drugs to treat fungal, protozoan, and helminthic diseases is challenging because agents that kill or inhibit the growth of these eukaryotic organisms are also highly toxic to mammalian cells. Because fungi and protozoa are rapidly proliferating cells, drugs against these organisms tend to target key components of their replicative or biosynthetic pathways. Common antifungals inhibit sterol syntheses (the azole derivatives) or disrupt the cell membrane (polyenes like amphotericin B). Most antihelminthic drugs target adult worms, which are no longer growing and do not replicate. These drugs are often aimed at inhibiting fundamental processes, such as energy production and muscle function (for example, the benzimidazoles and avermectins), or at targets involved in egg production or larval development.

Malaria, a protozoan disease, was successfully treated for many years with chloroquine, widely available over the counter. In recent decades, *Plasmodium* species that are resistant to this drug have appeared and spread to areas where malaria is a common threat. In those areas, a combination of the drugs sulfonamide and pyrimethamine is frequently used to treat the disease.

Resistance to antimicrobial agents. One of the ongoing problems scientists and medical workers face in the fight against infectious diseases is the development of resistance to the agents used to control them. The phenomenon of resistance has been known since almost the beginning of antibiotic use. For example, penicillin was introduced for clinical use in treating bacterial infections in the 1940s. As early as 1943, Alexander Fleming, the discoverer of penicillin, observed that some bacteria were resistant to

the drug and warned that indiscriminate use of penicillin would lead to the proliferation of resistant pathogenic bacteria. By 1946, medical staff at a London hospital estimated that 14 percent of the staphylococcal strains isolated from their patients were resistant to penicillin. Today, more than 90 percent of these bacteria are resistant. In an environment of widespread penicillin use, selection for resistant bacteria occurred; that is, the pathogenic organisms evolved.

The same process has occurred for many other antimicrobial drugs. Alarming, many pathogens are simultaneously acquiring resistance to multiple drugs. For example, some strains of *Mycobacterium tuberculosis* are resistant to all of the currently available drugs used for treatment.

Mechanisms of antimicrobial resistance.

Antibiotic resistance appears as a result of changes in genes or the acquisition of genes that allow the pathogen to evade the action of antimicrobial drugs. Resistance mechanisms include structural changes in or around the target molecule that inhibit the drug's ability to bind to it; reduced permeability of the cell membrane to the drug and actively pumping the drug out of the cell after it has entered; and production of enzymes that inactivate the antibiotic after it has been taken up by the cell. Microbes that produce larger-than-normal amounts of the target molecule may be "less susceptible" (as opposed to resistant) to a drug, meaning it takes a higher drug level to adversely affect that microbe.

Transfer of antimicrobial-resistance genes.

Bacteria have many methods for developing resistance. Antibiotic resistance initially arises as mutations to existing genes; however, many (probably most) bacteria *acquire* these genes rather than experience the mutation themselves. Resistance genes are transferred to other members of the same species and across species by a variety of bacterial genetic-exchange mechanisms. Many gram-negative bacteria, including *Escherichia coli* and *Salmonella* species, can transfer extrachromosomal genetic material called plasmids via the process of *conjugation*. Bacteria endowed with the plasmids have numerous pili along their surfaces; one of these extends to a plasmid-lacking bacterium as a conjugation tube.

The plasmid then replicates, and one copy travels through the conjugation tube into the recipient bacterium. One large class of plasmids is called resistance plasmids because they carry genes that confer antibiotic resistance. Many resistance plasmids carry genes for resistance to multiple antibiotics; thus, one conjugation event can simultaneously transfer resistance to several antibiotics.

Some species of bacteria are capable of taking up free-floating bits of DNA from their environments in a process known as *bacterial transformation*. If they take up a DNA fragment containing an antibiotic-resistance gene, they may become resistant to that antibiotic. Another mechanism of genetic exchange in bacteria is *transduction*. When a virus infects a bacteria cell, the virus takes over the cell's metabolism, directing synthesis of the virus' genetic material and production of the components of the viral particle. Simultaneously, the host bacterial DNA is degraded. In the last stage of virus production, its genetic material is encapsulated in a protein coat. Occasionally, a piece of the host bacterial DNA may be packaged in a viral particle. The resulting "transducing particle," like a normal viral particle, has the ability to attach to a recipient bacterium and transfer its genetic material into the cell. However, in this case, the transferred genetic material may be a bacterial gene that provides resistance to an antibiotic.

Finally, many transposons carry antibiotic-resistance genes. Transposons are sequences of DNA that are capable of inserting themselves randomly into genomes. Because they do not appear to rely on specific genetic sequences of the target insertion site, they can readily move across species.

Although mutations that result in antibiotic resistance, and, less so, bacterial genetic exchange, are rare events, they need occur only once. In an environment of heavy antibiotic use, the forces of natural selection will favor the propagation of resistant variants of a pathogen. The human body is a rich environment for the growth of large numbers of bacteria and for the interaction of a variety of pathogenic and nonpathogenic bacteria. Thus, there is optimal opportunity for rare mutational and genetic-exchange events.

Other pathogens have more limited options for drug resistance. Strains of pathogens develop that are naturally less susceptible to a particular drug due to a normally occurring mutation. In the face of continuing drug use, this strain rapidly grows out of the population being spread through the usual transmission process. In recent decades, for example, *Plasmodium* strains that are resistant to chloroquine have spread malaria throughout Africa, South America, and Southeast Asia.

Emerging and Re-emerging Infectious Diseases

Fifty years ago many people believed the age-old battle of humans against infectious disease was virtually over, with humankind the winners. The events of the past three decades have shown the foolhardiness of that position. At least a dozen "new" diseases have been identified (such as AIDS, Legionnaire's disease, and hantavirus pulmonary syndrome), and traditional diseases that appeared to be "on their way out" (such as malaria and tuberculosis) are resurging. Globally, infectious diseases remain the leading cause of death, and they are the third leading cause of death in the United States. Clearly, the battle has not been won.

Emerging infectious diseases are diseases that 1) have not occurred in humans before (this type of emergence is difficult to establish and is probably rare); 2) have occurred previously but affected only small numbers of people in isolated places (AIDS and Ebola hemorrhagic fever are examples); or 3) have occurred throughout human history but have only recently been recognized as distinct diseases due to an infectious agent (Lyme disease and gastric ulcers are examples). Table 7 lists several examples of infectious diseases that have emerged in the past three decades.

A review of Table 7 reveals that environmental changes are related to the emergence of many infectious diseases. For example, Lyme disease, hantavirus pulmonary syndrome (HPS), and Lassa fever all emerged when humans began encountering the arachnid vector (for Lyme disease) or rodent host (for HPS and Lassa fever) of the causative agents in greater numbers than ever before. Factors related to the emergence of infectious diseases such as Legionnaire's disease and hemolytic uremic syndrome include changing technologies:

Table 7. Examples of emerging infectious diseases.

Year Recognized	Disease	Infectious Agent	Contributing Factors
new viral strains emerge periodically	pandemic influenza	influenza virus	pig-duck agriculture (possibly)
1937	West Nile infection	West Nile virus	complex interactions between the virus, birds and other animals, mosquitoes, and the environment
1967	Marburg hemorrhagic fever	Marburg virus	unknown natural reservoir; nosocomial transmission; possible aerosol transmission
1969	Lassa fever	Lassa virus	urbanization and other conditions that favor the rodent host; nosocomial transmission
Before 1976	salmonellosis (salmonella poisoning)	<i>Salmonella enteritidis</i> (bacterium)	globalization of food trade, improper preparation of eggs for eating
1976	Ebola hemorrhagic fever	Ebola virus	unknown natural reservoir; nosocomial transmission; possible aerosol transmission
1977	Legionnaire's disease	<i>Legionella pneumophila</i> (bacterium)	cooling and plumbing systems
1977	cyclospora	<i>Cyclospora cayetanensis</i> (unicellular parasite)	increased use of staining methods for detecting enteric parasites
1978 (linked to the disease)	CDAD (<i>Clostridium difficile</i> associated disease)	<i>C. difficile</i> (bacterium)	prolonged use of antibiotics
1981	MRSA infection	methicillin-resistant <i>Staphylococcus aureus</i> (bacterium)	decades of often unnecessary antibiotic use
1982	hemolytic uremic syndrome	<i>Escherichia coli</i> 0157:H7 (bacterium)	mass-food-production systems
1982	Lyme disease	<i>Borrelia burgdorferi</i> (bacterium)	conditions favoring the tick vector and deer, such as reforestation near homes
1983	AIDS	human immunodeficiency virus	migration to cities, global travel, transfusions, organ transplants, intravenous drug use, multiple sexual partners
1983	gastric ulcers	<i>Helicobacter pylori</i> (bacterium)	newly recognized as due to infectious agent
mid-1980s	VRE infection	vancomycin-resistant enterococci (bacteria)	decades of often unnecessary antibiotic use; nosocomial transmission
1989	hepatitis C	hepatitis C virus (HCV)	undetectable in blood supplies until about 1992
early 1990s	salmonellosis (salmonella poisoning)	<i>Salmonella</i> serotype Typhimurium DT104 (bacteria)	poorly understood; food-producing animals probably involved
1993	hantavirus pulmonary syndrome	hantavirus	environmental changes favoring contact with rodent hosts

Year Recognized	Disease	Infectious Agent	Contributing Factors
disease first described in 1996	new variant Creutzfeldt-Jakob disease	prions (misfolded proteins)	unknown
1996	VISA infection	vancomycin intermediate-resistant <i>S. aureus</i> (bacterium)	decades of often unnecessary antibiotic use
1998	Nipah encephalitis	Nipah virus	ecological, environmental interaction of fruit bats, date palm fruit, pigs, and humans
2002	VRSA infection	vancomycin-resistant <i>S. aureus</i> (bacterium)	decades of often unnecessary antibiotic use
2003	SARS (severe acute respiratory syndrome)	SARS-associated coronavirus	may have been an animal virus that recently acquired the ability for human-human transmission

Sources: Morse, S.S. 1995. Factors in the emergence of infectious diseases. *Emerging Infectious Diseases* [Serial online], 1(1). Available <http://www.wnc.cdc.gov/EID/>. June 1999; Satcher, D. 1995. Emerging infections: Getting ahead of the curve. *Emerging Infectious Diseases* [Serial online], 1(1). Available <http://www.wnc.cdc.gov/EID/>. June 1999; Morse, S.S. (Ed.). 1993. Examining the origins of emerging viruses. *Emerging viruses*. New York: Oxford University Press; ProMED. 1994. About ProMED. Available <http://www.fas.org/promed/about/index.html>. June 1999. Web sites: <http://www.niaid.nih.gov/topics/westnile/>; <http://www.ncbi.nlm.nih.gov>.

Note: "Year Recognized" is the year the infectious agent was identified.

air conditioning systems for the former disease and mass food production for the latter.

Re-emerging infectious diseases are diseases that once were major health problems globally or in a particular country and then declined dramatically, but are again becoming health problems for a significant proportion of the population (malaria and tuberculosis are examples). Many specialists in infectious diseases include re-emerging diseases as a subcategory of emerging diseases. Table 8 lists examples of re-emerging infectious diseases.

A review of Table 8 reveals some explanations for the re-emergence of infectious diseases. Tuberculosis has re-emerged due to evolution of the causative bacteria. The pathogen has acquired resistance to the antibiotics used to treat tuberculosis (either through mutation or genetic exchange), and the long-term use of antibiotics (both within one individual and across the population) has selected for the pathogen's proliferation. Malaria has also become drug-resistant, and the vector mosquito has acquired resistance to pesticides as well. The re-emergence of diseases such as diphtheria and whooping cough (pertussis) is related to inadequate vaccination of the population. When

the proportion of immune individuals in a population drops below a particular threshold, introduction of the pathogen into the population leads to an outbreak of the disease.

Despite the challenges of emerging and re-emerging infectious diseases, the results of basic research, such as that sponsored by NIH, show that there is reason for hope. AIDS was first described in 1981, and it took two years to identify the retrovirus that causes AIDS, which was named the human immunodeficiency virus. In contrast, less than four months elapsed between the description of hantavirus pulmonary syndrome (HPS) in 1993 and the identification of the previously unknown viral agent, now called Sin Nombre virus. One difference between these two cases is that the years that intervened between the advent of AIDS and the advent of HPS saw the development of the polymerase chain reaction, a powerful research technique that allows rapid identification of causative agents. Recommendations for avoiding and/or treating new infectious diseases become possible when new techniques, developed through basic research, are applied to the problem of disease emergence.

Other examples of the benefits of basic research include the development of HIV protease inhibitors

Table 8. Examples of re-emerging infectious diseases.

Disease	Infectious Agent	Contributing Factors
chikungunya	chikungunya virus	viral genome mutation enabled infection of new mosquito vectors and expanded transmission
cholera	<i>Vibrio cholerae</i> 0139 (bacterium)	evolution of new strain of bacteria combining increased virulence and long-term survival in the environment
cryptosporidiosis	<i>Cryptosporidium parvum</i> (protozoan)	inadequate control in water supply; international travel; increased use of child-care facilities
dengue fever	dengue virus	urbanization, international travel, and inadequate vector-control measures
diphtheria	<i>Corynebacterium diphtheriae</i> (bacterium)	interruption of immunization program due to political changes
H5N1 influenza	influenza H5N1 virus	living close to H5N1-infected poultry
malaria	<i>Plasmodium</i> species (protozoan)	drug resistance; favorable conditions for mosquito vector
meningitis, necrotizing fasciitis (flesh-eating disease), toxic-shock syndrome, and other diseases	Group A <i>Streptococcus</i> (bacterium)	uncertain
pertussis (whooping cough)	<i>Bordetella pertussis</i> (bacterium)	refusal to vaccinate based on fears the vaccine is not safe; other possible factors: decreased vaccine efficacy or waning immunity among vaccinated adults
polio (infant paralysis)	poliovirus	–
rabies	rabies virus	breakdown in public health measures; changes in land use; travel
Rift Valley fever (RVF)	RVF virus	–
rubeola (measles)	measles virus	failure to vaccinate; failure to receive second dose of vaccine
schistosomiasis	<i>Schistosoma</i> species (helminth)	dam construction; ecological changes favoring snail host
trypanosomiasis	<i>Trypanosoma brucei</i> (protozoan)	human population movements into endemic areas due to political conflict; diagnosis is very difficult, and current treatments have severe secondary effects
tuberculosis	<i>Mycobacterium tuberculosis</i> (bacterium)	antibiotic-resistant pathogens; immunocompromised populations (malnourished, HIV-infected, poverty-stricken)
West Nile encephalitis	West Nile virus	complex interactions between the virus, birds and other animals, mosquitoes, and the environment; emergence in U.S. and other regions likely due to global travel
yellow fever	yellow fever virus	insecticide resistance; urbanization; civil strife

Sources: Krause, R.M. 1992. The origin of plagues: Old and new. *Science*, 257: 1073–1078; Measles—United States, 1997. 1998, April 17. *Morbidity and Mortality Weekly Report*, 47(14): 273–276; Pertussis vaccination: Use of acellular pertussis vaccines among infants and young children. 1997, March 28. *Morbidity and Mortality Weekly Report*, 46(RR-7); ProMED. 1994. About ProMED. Available from <http://www.fas.org/promed/about/index.html>. June 1999. Centers for Disease Control and Prevention Web site: <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6115a1.htm>. July 2013.

Note about rubeola: After the initial decline of measles cases after the licensing of the vaccine in 1963, there was a resurgence of measles—to some 50,000 cases—from 1989 to 1991. Since then, the incidence of measles declined to a median of 60 cases per year between 2000 and 2010, and then increased to 222 in 2011.

by researchers funded by NIH and others. These drugs, when used in combination with other anti-HIV drugs, are responsible for the dramatic decrease in deaths from AIDS in the United States. One active area of research at NIH is the development of new types of vaccines based on our new understanding of the immune system. In addition, basic research on the immune system and host-pathogen interactions has revealed new points at which vaccines could work to prevent diseases.

Finally, basic research on the ecology of disease organisms—their reservoirs, modes of transmission, and vectors, if any—reveals points at which preventive measures can be used to interrupt this cycle and prevent the spread of disease. For example, research supported by NIAID delineated the mechanism of Lyme disease transmission and how disease results: The tick vector was identified and the life cycle of the causative bacterium was traced through deer and rodent hosts. Understanding this ecology has led to predictions about the regions where and years when the threat of Lyme disease is greatest, as well as recommendations to the public for avoiding infection. These examples and others demonstrate that investment in basic research has great long-term payoffs in the battle against infectious diseases.

Infectious Diseases and Society

What are the implications of using science to improve personal and public health in a pluralist society? As noted earlier, one of the objectives of this module is to convey to students the relationship between basic biomedical research and the improvement of personal and public health. One way to address this question is by attending to the ethical and public policy issues raised by our understanding and treatment of infectious diseases.

Ethics is the study of good and bad, right and wrong. It has to do with the actions and character of individuals, families, communities, institutions, and societies. During the past two and one-half millennia, Western philosophy has developed a variety of powerful methods and a reliable set of concepts and technical terms for studying and talking about the ethical life. Generally speaking, we apply the terms “right” and “good” to those actions and qualities that foster the interests of

individuals, families, communities, institutions, and society. Here, an “interest” refers to a participant’s share or participation in a situation. The terms “wrong” or “bad” apply to those actions and qualities that impair interests.

Ethical considerations are complex and multifaceted, and they raise many questions. Often, there are competing, well-reasoned answers to questions about what is right and wrong and good and bad about an individual’s or group’s conduct or actions. Thus, although science has developed vaccines against many diseases, and professional medical recommendations encourage their widespread use, individuals are permitted (in most, but not all, states) to choose not to be vaccinated. (Figure 7)

Typically, answers to these questions all involve an appeal to values. A **value** is something that has significance or worth in a given situation. One of the exciting events to witness in any discussion in ethics in a pluralist society is the varying ways in which the individuals involved assign value to things, persons, and states of affairs. Examples of values that students may appeal to in discussions of ethical issues

Figure 7. Most states allow exemptions to immunization law.

Date of Birth _____	
STATEMENT OF EXEMPTION TO IMMUNIZATION LAW	
IN THE EVENT OF AN OUTBREAK, EXEMPTED PERSONS WILL BE SUBJECT TO EXCLUSION FROM SCHOOL AND QUARANTINE.	
MEDICAL EXEMPTION: The physical condition of the above named person is such that immunization would endanger life or health, or is medically contraindicated due to other medical conditions.	
Signed _____ (Physician)	Date _____
RELIGIOUS EXEMPTION: Parent or guardian of the above named person or the person himself/herself adheres to a religious belief opposed to immunizations.	
Signed _____ (Parent, guardian, emancipated student/consenting minor)	Date _____
PERSONAL EXEMPTION: Parent or guardian of the above named person or the person himself/herself adheres to a personal belief opposed to immunizations.	

include autonomy, freedom, privacy, protecting another from harm, promoting another's good, justice, fairness, economic stability, relationships, scientific knowledge, and technological progress.

Acknowledging the complex, multifaceted nature of ethical discussions is not to suggest that "anything goes." Experts generally agree on the following features of ethics. First, ethics is a process of rational inquiry. It involves posing clearly formulated questions and seeking well-reasoned answers to those questions. For example, developing countries and isolated rural areas suffer particularly severely from many infectious diseases because conditions of crowding and poor sanitation are ideal for the growth and spread of pathogens. The same is true for many inner-city environments. These places provide a constant reservoir of disease-causing agents. We can ask questions about what constitutes an appropriate ethical standard for allocating healthcare funds for curtailing the spread of infectious diseases. Should we expend public research dollars to develop drugs whose cost will be out of reach for developing countries? Is there any legal and ethical way for the United States to prevent over-the-counter sales of antibiotics in other countries, a practice that may enhance the evolution of antibiotic-resistant pathogens? Well-reasoned answers to ethical questions constitute **arguments**. Ethical analysis and argument, then, result from successful ethical inquiry.

Second, ethics requires a solid foundation of information and rigorous interpretation of that information. For example, one must have a solid understanding of infectious disease to discuss the ethics of requiring immunizations and reporting of infectious diseases. Ethics is not strictly a theoretical discipline but is concerned in vital ways with practical matters. This is especially true in a pluralist society.

Third, because tradeoffs among interests are complex, constantly changing, and sometimes uncertain, discussions of ethical questions often lead to very different answers to questions about what is right and wrong and good and bad. For example, we acknowledge that individuals have a right to privacy regarding their infectious disease status. Yet, some argue that AIDS patients who knowingly infect others should have their right to privacy overridden so that partners may be notified of the risk of contracting AIDS.

It is our hope that completing the activities in this module will help students see how understanding science can help individuals and society make reasoned decisions about issues relating to infectious diseases and health. Science provides evidence that can be used to support ways of understanding and treating human disease, illness, deformity, and dysfunction. But the relationships between scientific information and human choices, and between choices and behaviors, are not linear. Human choice allows individuals to choose against sound knowledge, and choice does not necessarily lead to particular actions.

Nevertheless, it is increasingly difficult for most of us to deny the claims of science. We are continually presented with great amounts of relevant scientific and medical knowledge that is publicly accessible. As a consequence, we can think about the relationships among knowledge, choice, behavior, and human welfare in the following ways:

**knowledge (what is known and not known)
+ choice = power**

**power + behavior = enhanced human welfare
(that is, personal and public health)**

One of the goals of this module is to encourage students to think in terms of these relationships, now and as they grow older.

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Additional Resources for Teachers

The following resources may provide additional background information about emerging and re-emerging infectious diseases for you and your students.

RESOURCES ON THE INTERNET

National Institute of Allergy and Infectious Diseases (NIAID)

<http://www.niaid.nih.gov/>

NIAID, the institute that helped support the development of this module, maintains this Web site. The site provides information on NIAID's activities, press releases about recent scientific advances related to allergy and infectious diseases, and a rich collection of online publications about a variety of infectious diseases, the immune system, women's health issues, and many other topics.

This page lists infectious diseases and links to more information about them:

<http://www.niaid.nih.gov/publications/pdf/curriculum.pdf>

ProMED: The Program for Monitoring Emerging Diseases

<http://www.fas.org/promed/>

The Federation of American Scientists (FAS) sponsors the Program for Monitoring Emerging Diseases (ProMED), a policy initiative that calls for global monitoring of emerging diseases.

The Web site provides links to ProMED email archives, WHO outbreak news, recommended reading, and other Internet resources.

Centers for Disease Control and Prevention

<http://www.cdc.gov/>

The Centers for Disease Control and Prevention (CDC), a component of the U.S. Department of Health and Human Services, operates this Web site. It contains information about CDC activities and recent press releases, fact sheets on more than 150 diseases, injuries, and disabilities in the United States and around the world. It also links to many offices and programs of interest, such as a children's site by CDC called BAM! (Body and Mind). BAM! has a variety of information pages for kids including one called "Disease Detectives." The Teacher's Corner within the BAM! site provides a link to EXCITE (Excellence in Curriculum Integration through Teaching Epidemiology), a collection of teaching materials on the science of epidemiology.

The CDC site also has a link to CDC's electronic journal, *Emerging Infectious Diseases*, a valuable resource for anyone interested in research in this field: <http://www.cdc.gov/eid/index.htm>.

World Health Organization

<http://www.who.int/>

This Web site provides information about the activities and disease-eradication goals of the World Health Organization (WHO). It also offers press releases about recent world health news; fact sheets on infectious and noninfectious diseases, environmental issues that affect public health, family and reproductive health, and health policies and statistics around the world; and a catalog of more than 700 WHO publications organized by subject.

BOOKS AND ARTICLES

A Distant Mirror: The Calamitous 14th Century, by Barbara Wertheim Tuchman (1987; Ballantine Books; ISBN 0345349571).

America's Vital Interest in Global Health (1997; National Academy Press).

Emerging Infections: Microbial Threats to Health in the United States (1992; National Academy Press).

Infections and Inequalities: The Modern Plagues, by Paul Farmer (1999; University of California Press; ISBN 0520215443).

Man and Microbes: Disease and Plagues in History and Modern Times, by Arno Karlen (1996; Touchstone Books; ISBN 0684822709).

Microbiology: Principles and Explorations, 7th ed., by Jacquelyn G. Black (2008; Wiley, John & Sons, Inc.; ISBN: 9780470279823).

Plagues and Peoples, by William H. McNeill (1998; Anchor; ISBN 0385121229).

Rats, Lice, and History: Being a Study in Biography, Which, After Twelve Preliminary Chapters Indispensable for the Preparation of the Lay Reader, Deals with the Life History of Typhus Fever, by Hans Zinsser (1984; Little Brown & Co; ISBN 0316988960).

Who Gave Pinta to the Santa Maria?: Torrid Diseases in a Temperate World, by Robert S. Desowitz (1997; WW Norton & Co; ISBN 039304844).

Glossary

acquired immunodeficiency syndrome

(AIDS): Infectious disease syndrome that is caused by the human immunodeficiency virus (HIV). Characterized by the loss of a normal immune response and increased susceptibility to opportunistic infections and some cancers.

acquired immunity: Specific immunity that develops after exposure to a particular antigen or after antibodies are transferred from one individual to another.

acyclovir: Synthetic drug with antiviral activity against herpes simplex virus. Often used to treat genital herpes.

aerobe: Organism that can grow in the presence of atmospheric oxygen.

airborne transmission: Transmission of an infectious organism in which the organism is truly suspended in the air and travels a meter or more from the source to the host. Chicken pox, flu, measles, and polio are examples of diseases that are caused by airborne agents.

allergen: Substance that can induce an allergic reaction or specific susceptibility.

amantadine: Antiviral compound sometimes used to treat influenza type A infections.

amebiasis: Infection with amoebas. Usually refers to an infection by *Entamoeba histolytica*. Symptoms are highly variable, ranging from an asymptomatic infection to severe dysentery.

amphotericin B: Antibiotic used to treat systemic fungal infections and also used topically to treat candidiasis.

anaerobe: Organism that can grow in the absence of atmospheric oxygen.

anthrax: Infectious disease of animals caused by ingesting the spores of *Bacillus anthracis*. Can occur in humans.

antibacterial: Agent that kills bacteria or inhibits their growth.

antibiotic: Microbial product, or its derivative, that kills or inhibits the growth of susceptible microorganisms.

antibody: Glycoprotein produced in response to an antigen. Antibodies have the ability to combine with the antigen that stimulated their production.

antibody-mediated immunity: Immunity that results from the presence of antibodies in blood and lymph.

antigen: Foreign (nonself) substance to which lymphocytes respond.

antimicrobial agent: Agent that kills or inhibits the growth of microorganisms.

antiseptic: Chemical applied to tissue to prevent infection by killing or inhibiting the growth of pathogens.

antitoxin: Antibody to a microbial toxin. An antitoxin binds specifically with the toxin, neutralizing it.

arenavirus: Type of RNA virus. Lassa fever is caused by an arenavirus.

autogenous infection: Infection that results from a patient's own microflora.

B-cell: Type of lymphocyte derived from bone marrow stem cells that matures into an immunologically competent cell under the influence of the bone marrow. Following interaction with an antigen, a B-cell becomes a plasma cell, which synthesizes antibodies.

bacillus: Rod-shaped bacterium.

bactericide: Agent that kills bacteria.

binary fission: Asexual reproduction in which a cell separates into two cells.

biologic transmission: Disease transmission in which an infectious organism undergoes some morphologic or physiologic change during its passage through the vector.

botulism: Form of food poisoning caused by a neurotoxin produced by *Clostridium botulinum*. Sometimes found in improperly canned or preserved food.

broad-spectrum drug: Chemotherapeutic agent that is effective across a wide range of different types of pathogens.

candidiasis: Infection caused by a fungus of the genus *Candida*. Typically involves the skin.

carrier: Infected individual who is a potential source of infection for other people.

cell-mediated immunity: Immunity that results from T-cells contacting foreign or infected cells and destroying them.

chemotherapeutic agent: Compound used in the treatment of disease that kills or inhibits the growth of microorganisms and does so at concentrations low enough to avoid doing damage to the host.

chicken pox: Highly contagious skin disease caused by the varicella-zoster virus. Acquired by droplet inhalation into the respiratory system.

cholera: Infectious disease caused by *Vibrio cholerae* bacteria.

coccus: Bacterium that is roughly spherical in shape.

common cold: Acute, self-limiting, and highly contagious viral infection of the upper respiratory tract.

communicable disease: Disease associated with an agent that can be transmitted from one host to another.

complement system: Group of circulating plasma proteins that plays a major role in an animal's immune response.

compromised host: Host with lowered resistance to infection and disease for any reason (for example, malnutrition, illness, trauma, or immunosuppression).

conjugation: Form of gene transfer and recombination in bacteria that requires direct cell-to-cell contact.

conjugative plasmid: Plasmid that carries the genes for sex pili and can transfer copies of itself to other bacteria during conjugation.

contact transmission: Transmission of an infectious agent by direct contact of the source or its reservoir with the host.

Creutzfeldt-Jakob disease: Chronic, progressive, fatal disease of the central nervous system caused by a prion.

diphtheria: Acute, highly contagious childhood disease caused by *Corynebacterium diphtheriae* bacteria.

disinfectant: Agent that kills, inhibits, or removes microorganisms that may cause disease.

DPT (diphtheria-pertussis-tetanus) vaccine:

Vaccine containing three antigens that is used to immunize people against diphtheria, whooping cough, and tetanus.

endemic disease: Disease that is commonly or constantly present in a population, usually at a relatively constant low level.

epidemic: Sudden increase in occurrence of a disease above the normal level in a particular population.

epidemiologist: Person who specializes in epidemiology.

epidemiology: Study of the factors determining and influencing the frequency and distribution of disease, injury, and disability in a population.

eukaryotic cell: Cell that has its genetic material (DNA) enclosed by a nuclear membrane.

facultative anaerobe: Microorganism that does not require atmospheric oxygen but grows better in its presence.

fungicide: Agent that kills fungi.

genital herpes: Sexually transmitted disease caused by the herpes simplex type II virus.

giardiasis: Intestinal disease caused by the protozoan *Giardia lamblia*.

Gram stain: Differential staining procedure that allows categorization of bacteria into two groups (gram-positive and gram-negative) based on their ability to retain crystal violet when decolorized with an organic solvent such as ethanol.

hantavirus: Type of RNA virus. Hantavirus pulmonary syndrome and Korean hemorrhagic fever are caused by viruses in the genus *Hantavirus*.

harborage transmission: Disease transmission in which an infectious agent does not undergo morphologic or physiologic change during its time inside the vector.

hepatitis A (infectious hepatitis): Type of hepatitis that is transmitted by fecal-oral contamination. It affects mostly children and young adults, especially under conditions of overcrowding and poor sanitation. Caused by the hepatitis A virus.

hepatitis B (serum hepatitis): Type of hepatitis caused by the hepatitis B virus (HBV). Transmitted through body fluids.

herd immunity: Resistance of a population to the spread of an infectious organism due to the immunity of a high proportion of the population.

host: Body of an organism that harbors another organism. The host provides a microenvironment that supports the growth and reproduction of the parasitic organism.

human immunodeficiency virus (HIV): Retrovirus associated with the onset of AIDS.

immune: Protected against a particular disease by either nonspecific or specific biological defenses, including the presence of specific antibodies.

immune response: Response of the body to contact with an antigen that leads to the formation of antibodies and sensitized lymphocytes. Designed to render harmless the antigen and the pathogen producing it.

immunity: General ability of a host to resist developing a particular disease.

immunology: Science concerned with understanding the immune system and the many factors that are involved with producing both acquired and innate immunity.

index case: First disease case in an epidemic within a population.

infection: Invasion of a host by an agent, with subsequent establishment and multiplication of the agent. An infection may or may not lead to disease.

infectious agent: Living or quasi-living organism or particle that causes an infectious disease. Bacteria, viruses, fungi, protozoa, helminths, and prions are infectious agents.

infectious disease: Change from a state of health to a state in which part or all of a host's body cannot function normally because of the presence of an infectious agent or its products.

inflammation: Localized protective response to tissue injury or destruction. In an acute form, it is characterized by pain, heat, redness, and swelling in the injured area.

influenza (flu): Acute viral infection of the respiratory tract caused by one of three strains of influenza virus (A, B, and C).

intermediate host: Host that serves as a temporary but essential environment for the completion of a parasite's life cycle.

Koch's postulates: Set of rules for proving that a microorganism causes a specific disease.

Koplik's spot: Lesion of the oral cavity caused by the measles virus.

Legionnaire's disease: Pulmonary form of disease caused by infection with *Legionella pneumophila* bacteria.

Lyme disease: Tick-borne disease caused by the spirochete *Borrelia burgdorferi*.

lymphocyte: Type of white blood cell. Lymphocytes transmit chemical signals that help coordinate the immune system.

malaria: Infectious disease caused by the *Plasmodium* protozoa. Characterized by fever and chills that occur at regular intervals.

measles: Highly contagious skin disease caused by a virus in family Paramyxoviridae. The virus enters the body through the respiratory tract or the conjunctiva. Measles is endemic throughout the world.

microbiota (microbial flora): Microorganisms that are normally associated with a particular tissue or organ.

morbidity rate: Number of individuals who become ill with a particular disease within a susceptible population during a specified time period.

mortality rate: Ratio of the number of deaths from a particular disease to the total number of cases of the disease.

nonspecific immunity: General defense mechanisms that provide animals with protection from infection and disease but are not targeted at a particular pathogen.

nosocomial infection: Infection produced by a pathogenic agent that a patient acquires during hospitalization or treatment inside another healthcare facility.

opportunistic organism: Organism that is usually harmless but can be pathogenic in a compromised host.

pandemic: Increase in the occurrence of a disease in a large and geographically widespread population. Sometimes called a worldwide epidemic.

parasite: Organism that lives on or within another organism (the host). The relationship benefits the parasite and harms the host.

pasteurization: Process of heating milk and other liquids to destroy microorganisms that can cause spoiling or disease.

pathogen: Disease-producing agent.

pathogenicity: Ability to cause disease.

penicillins: Group of antibiotics that are often used to treat infections by gram-positive bacteria.

peptidoglycan: Large polymer that provides much of the strength and rigidity of bacterial cell walls.

period of infectivity: Time during which the source of an infectious agent is disseminating the agent (is infectious).

plague: Acute, infectious disease with a high mortality rate; caused by *Yersinia pestis* bacteria.

plasmid: Circular, double-stranded DNA molecule that can exist and replicate independently of the host cell chromosome or be integrated with it. Although a plasmid is stably inherited, it is not required for bacterial cell growth and reproduction.

poliomyelitis: Acute, contagious viral disease of the central nervous system that can lead to paralysis.

population: Group of organisms of the same species.

prevalence rate: Total number of people infected at one time in a population, regardless of when the disease began.

prion: Infectious particle that is responsible for certain slow-acting diseases such as scrapie in sheep and goats, and Creutzfeldt-Jakob disease in humans. Prions have a protein component, but scientists have not yet detected a nucleic acid component.

prokaryotic cell: Cell that lacks a membrane-delimited nucleus and other membrane-bound organelles. Bacteria are prokaryotic cells.

rabies: Acute infectious disease of the central nervous system caused by an RNA virus of the rhabdovirus group.

reservoir: Site, alternate host, or carrier that harbors pathogenic organisms and serves as a source from which other individuals can be infected.

retrovirus: RNA virus that carries the enzyme reverse transcriptase and forms a DNA copy of its genome during its reproductive cycle.

schistosomiasis: Helminth infection acquired from contact with water containing infected snails.

smallpox: Highly contagious, often fatal disease caused by a poxvirus. Smallpox has been eradicated throughout the world.

source: Location or object from which a pathogen is immediately transmitted to a host.

specific immune response: Collection of several immunological events in which lymphocytes recognize the presence of a particular antigen and act to eliminate it.

spirillum: Rigid, spiral-shaped bacterium.

spirochete: Flexible, spiral-shaped bacterium.

sporadic disease: Disease that occurs occasionally and at random intervals in a population.

superinfection: Bacterial or fungal infection that is resistant to the drug(s) being used to treat it.

T-cell: Lymphocyte derived from bone marrow stem cells that matures into an immunologically competent cell under the influence of the thymus. Involved in cell-mediated immune reactions.

TB skin test: Tuberculin hypersensitivity test to detect a current or past infection with *Mycobacterium tuberculosis* bacteria.

tetanus: Often fatal disease caused by the anaerobic, spore-forming bacterium *Clostridium tetani*. Characterized by muscle spasms and convulsions.

toxin: Microbial product or component that at low concentrations can injure a cell or organism.

transduction: Transfer of genes between bacteria by bacteriophages.

transformation: Mode of gene transfer in bacteria in which a piece of DNA in the environment is taken up by a bacterium and integrated into the bacterium's genome.

transposon: DNA segment that carries the genes required for transposition and can move from one place to another in the genome. Often carries genes unrelated to transposition as well.

tuberculosis: Infectious disease resulting from infection by a species of *Mycobacterium*. Infection is usually by inhalation, and the disease usually affects the lungs, although it can occur elsewhere in the body.

vaccination: Administration of a vaccine to stimulate an immune response.

vaccine: Preparation of killed microorganisms; living, weakened (attenuated) microorganisms; inactive or attenuated virus particles; inactivated bacterial toxins; or components (protein, carbohydrate, or nucleic acid) of the microorganism that are administered to stimulate an immune response. Vaccines protect an individual against the pathogenic agent or substance in the future.

vector: Living organism that transfers an infective agent from one host to another.

vector-borne transmission: Transmission of an infectious pathogen between hosts by way of a vector.

virulence: Degree or intensity of pathogenicity of an organism as indicated by mortality rate from the related disease and/or ability to invade tissues and cause disease.

virus: Infectious agent composed of a protein coat and a single type of nucleic acid. Lacks an independent metabolism and reproduces only within a host cell.

VRSA: Vancomycin-resistant *Staphylococcus aureus*.

whooping cough (pertussis): Infectious disease of the respiratory tract caused by *Bordetella pertussis*.

zoonosis: A disease that can be transmitted to humans from animals or from animals to humans.

Deadly Disease Among Us



Overview

Students complete a short “surprising statistics” quiz on the impact of infectious diseases, then classify several diseases as “emerging,” “re-emerging,” or “endemic.”

At a Glance

Major Concepts

Infectious diseases continue to be a major cause of human suffering and death, both in the United States and around the world. Emerging infectious diseases are diseases that have not occurred in humans before or that occurred only in small numbers in isolated places. Re-emerging infectious diseases are diseases that once were major health problems globally or in a particular country and then declined dramatically, but are again becoming health problems for a significant proportion of the population.

Objectives

After completing this lesson, students will

- recognize that infectious diseases are a continuing problem among all human populations,
- be able to define and give examples of emerging infectious diseases, and
- be able to define and give examples of re-emerging infectious diseases.

Prerequisite Knowledge

Students should be familiar with bacteria and viruses and understand that infectious diseases are due to infection of the body by an external agent.

Basic Science–Public Health Connection

This opening lesson introduces emerging and re-emerging infectious diseases as a public health issue that can be examined using the methods of science (for example, collecting and organizing data into categories).

Introduction

In developing countries where much of the population lives in conditions of extreme poverty, infectious diseases remain the leading cause of death. In the United States, prevention and control of infectious diseases have been so successful in the past half century that many people view infectious diseases as either a thing of the past or minor illnesses easily treated and cured, except among the very young, very old, or seriously ill.

In recent years, however, Americans have been shocked by the emergence of a variety of “new” infectious diseases. For example, *Escherichia coli* strain O157:H7 caused vomiting and severe diarrhea among children swimming in public pools in Atlanta, Georgia, in 1998, and among 58 people across nine states in 2011 who ate romaine lettuce tainted with the bacteria. A previously unrecognized virus (a hantavirus) caused a frequently fatal respiratory illness among apparently healthy young people in the Southwest. New diseases have emerged in developing countries as well. Ebola hemorrhagic fever, which was first described in 1976 in Zaire (now the Democratic Republic of the Congo), has particularly horrifying symptoms and a fatality rate of 50 to 90 percent. West Nile virus, first isolated in Uganda, is now found in other African countries, West Asia, Europe, and the Middle East. And AIDS, which emerged simultaneously in the United States and Africa in the early 1980s, has become a global pandemic.

Likewise, many diseases thought to be adequately controlled appear to be making a comeback. In developed countries, public health measures such as sanitation, sewage treatment, vaccination programs, and access to good medical care—including a wide range of antibiotics—have virtually eliminated “traditional” diseases such as diphtheria, whooping cough, and tuberculosis. However, many of these diseases are becoming a public health problem once again, as immunization programs and other public health standards are enforced less vigorously and, especially, as antibiotic-resistant pathogens evolve. In fact, medical workers have identified strains of pneumonia-causing *Staphylococcus aureus* that are resistant to all of the currently available drug treatments, and physicians and public health workers are concerned that we are about to re-enter the preantibiotic era for treating such diseases, especially with inexpensive drugs. Among the diseases “re-emerging” as a consequence of microbial resistance are tuberculosis and gonorrhea, a leading cause of death from infectious diseases worldwide and a major cause of infertility, respectively.

This lesson engages students in the seriousness of infectious diseases by helping them become aware of the widespread impact of such diseases. Students discover that some diseases are relatively new to humankind (emerging diseases), while others that had been nearly eliminated in developed countries are now beginning to increase in incidence (re-emerging diseases). They also learn that many diseases have been a perennial problem in human populations, never significantly declining (endemic diseases).

In Advance

Photocopies and Transparencies	Equipment and Materials
<ul style="list-style-type: none">• 1 transparency of Master 1.1 for the class• 1 copy of Master 1.2 for the class• 1 transparency of Master 1.3 for the class	<ul style="list-style-type: none">• 1 overhead projector• red transparency pen• (Optional) computers with access to the Internet

Preparation

Make the disease cards: copy Master 1.2, and cut the copy apart to form individual cards. Glue each card to a 5 × 7 index card.

Note to teachers: Lesson 3 includes a bacterial growth experiment. If you are teaching the lessons on consecutive days, students will need to complete Steps 5 to 8 on Master 3.1b, *Bacterial Growth Experiment*, during this class session. See Master 3.1b for details. (Students should have completed Steps 1 to 4 in 2 to 3 days before this class; see suggested timeline, page 16.)

1. Introduce the module and this lesson by asking students, “What disease do you think is the greatest threat to students in this class? What disease do you think is the greatest threat to the world’s population?” Solicit several responses and entertain a brief discussion about the diseases students perceive as threats and why.

List students’ responses on the board or a transparency.

Heart disease was the top killer globally in 2008. AIDS and cancer are likely to be two of the top threats students perceive. According to the World Health Organization (WHO), in 2008 HIV/AIDS was the sixth-highest killer worldwide, while cancer of the trachea, bronchus, or lung was the seventh-highest killer. Also in the top 10 killers globally were stroke and other cerebrovascular disease (2nd), pneumonia (3rd), chronic obstructive pulmonary disease (4th), diarrheal diseases such as cholera (5th), tuberculosis (8th), diabetes mellitus (9th). (8th), diabetes mellitus (9th).

2. Tell students that, as a class, they will take a quiz on some past and current causes of death and illness. Explain that you do not expect them to know the answers to these questions, but ask them to make well-reasoned guesses based on what they do know. Then, display a transparency of Master 1.1, *Causes of Death Quiz*, solicit students’ answers to each item, and provide the correct answers.

Procedure



If you can project the video “Infectious Disease Then and Now” from the Web site to the whole class, you can substitute this video for the quiz. Go to <http://science.education.nih.gov/supplements/diseases>, and click on “Web Portion of Student Activities” and then on “Lesson 1— Infectious Disease Then and Now.” The video covers roughly the same content and may take less time than the quiz. Both the quiz and the video serve an Engage role for this lesson and the module.

Question 1. Which of the following diseases has been recognized since antiquity?

(c) Guinea worm disease, or dracunculiasis, is mentioned in biblical texts. Although it is unfamiliar to Americans, it is not uncommon on the Arabian peninsula and sub-Saharan Africa. The disease is caused by a parasitic roundworm that is ingested in a larval form. The larvae migrate through the tissues where they mate and grow. A year after the larvae are ingested, a mature female migrates to subcutaneous regions, typically in the legs and feet. The worm may reach a yard in length. Its migrations cause great pain and inflammation, a burning itch, and subcutaneous ulcers. One form of treatment is to wet the skin to stimulate the worm to stick its head out and catch the head in a split stick. The worm is then slowly extracted, over the course of several weeks, by rolling it around the stick (if it is pulled too quickly, the worm will break in two, causing greater problems). This treatment may be the origin of the caduceus symbol that represents the medical profession. Students will learn as they complete this lesson that Legionnaire's disease and Ebola fever were first recognized as distinct diseases in 1976, and AIDS first came to worldwide attention in the early 1980s.

Question 2. In the 1700s and 1800s, a terrible, wasting disease killed thousands of European and American city dwellers. What disease was this?

(d) Tuberculosis (TB) killed 1 of every 4 Americans in the 1800s. The disease is still a leading killer globally, although it had decreased dramatically in the United States until the AIDS epidemic. The immune system of most people who contract the bacterium that causes tuberculosis successfully prevents its growth, and active disease never develops. Any condition that compromises the immune system, such as HIV infection, will allow the bacteria to grow, resulting in active tuberculosis.

Question 3. What infectious disease causing severe fever and chills plagued settlers in the Southern and Midwestern United States during the 1800s and early 1900s?

(c) Malaria is thought to have been introduced to the United States from Europe and Africa in the 16th and 17th centuries. The incidence of malaria in this country probably peaked around 1875. In a review of U.S. malaria outbreaks, J. Zucker estimated that more than 600,000 cases occurred in 1914. Improved socioeconomic conditions, mosquito-control measures, and availability of effective drugs later led to the virtual elimination of this disease in the United States, although localized outbreaks are still occasionally reported.

Question 4. Most deaths among U.S. servicemen in 1918 were due to what cause?

(b) Flu caused most of these deaths. The global influenza epidemic of 1918 is estimated to have killed 30 million people. The movement of troops during World War I, accompanied by crowding, poor nutrition, and generally poor living conditions, probably contributed to the rapid spread of the flu around the world. The 1918 flu was particularly virulent and, unlike typical flu epidemics, caused death more frequently among young adults than among children and elderly people.

Question 5. In 1994, a terrible disease nearly killed an 18-year-old high school student in California. Which of the following diseases was it?

(d) Tuberculosis (TB). The student contracted TB from a classmate at her high school, who had an active, misdiagnosed case of the disease. An additional 11 students at her school developed active cases of TB, and several hundred more had positive skin tests, indicating that they had been exposed. The student tells her story in Lesson 3, *Superbugs: An Evolving Concern*.

Question 6. According to the World Health Organization, which of the following diseases caused more deaths in 1998 and 2008 than the others?

(d) Pneumonia was the third-highest killer in 1998, behind heart disease and cerebrovascular disease. By 2008, the leading cause of death was heart disease, followed by stroke and other cerebrovascular disease.

3. Explain that the quiz emphasized the impact of infectious diseases on people's health and well-being. Point out that even though medical advances in the last century have resulted in far fewer deaths from infectious diseases than at any other time in history, those diseases are still the leading cause of death worldwide and the third leading cause of death in the United States. Explain that in this lesson, students will learn about some infectious diseases that cause problems in the world today.

You may need to distinguish *infectious* diseases from *noninfectious* diseases. Ask students to review the *Causes of Death Quiz* and identify some of the infectious and noninfectious diseases listed there. If necessary, point out that noninfectious diseases such as most cancers, heart disease, and cystic fibrosis cannot be “caught,” and that infectious diseases such as AIDS and tuberculosis are caused by living (or quasi-living, in the case of viruses and prions) agents that can be transmitted from one individual to another.

Identifying a disease as “infectious” or “noninfectious” has recently become more complex than it used to be. Researchers have discovered that infectious agents may play a role in some diseases that were

previously considered noninfectious, chronic conditions. For example, there is evidence that most gastric ulcers are caused by *Helicobacter pylori* bacteria, and that there's a link between toxoplasmosis and schizophrenia. Similarly, infection by *Chlamydia pneumoniae* and periodontal disease may contribute to the development of cardiovascular disease, leading some people to question whether heart disease might be infectious.



Circulate among the groups while they categorize their diseases in Steps 5, 8, and 10 for an informal assessment of students' skills in organizing information.

4. **Organize students in groups of three and distribute five *Disease Cards* made from Master 1.2 to each group.**

Distribute the cards in such a way that each disease is reviewed by at least one group.

5. **Explain that scientists find it useful to group diseases in different ways, depending on the problems they want to address. As an example, display the first classification criterion on Master 1.3a, *Disease Classifications*, and direct the groups to review their disease cards and sort them into piles that represent different categories of infectious agents.**

An important science process skill is identifying commonalities and differences and devising classification systems. In this step, students have the opportunity to practice this skill, and in Steps 7, 9, and 10, they consider the usefulness of classifying diseases in various ways.



The discussion in Steps 7 and 9 are opportunities to point out the contribution of basic research to the development of effective treatments and preventive measures for many diseases. For example, research on the life cycle of *Schistosoma* identified snails as an intermediate host, revealing an important point for preventive measures. Scientists also recently discovered a drug that kills adult schistosomes, reducing the possibility of severe liver disease and interrupting the organism's reproductive cycle. Continuing research likely will lead to effective treatment and preventive measures in the future for diseases like AIDS that are currently incurable.

6. **Solicit headings for the categories identified from several groups and write them on the appropriate place on Master 1.3a. Then, ask the other groups to name one or more diseases they classified in the categories and write these into the appropriate rows. Ask students to describe the symptoms of each disease as they do so.**
7. **Ask students to suggest reasons why scientists might find it useful to classify diseases based on the type of infectious agent.**

If students need help with this, ask them to review the treatment for each of the diseases within a category and each disease's symptoms. Students should notice that diseases caused by the same type of infectious agent tend to have similar types of treatment strategies, and that similar symptoms occur in diseases caused by different types of agents. It is useful to classify diseases by the type of infectious agent because that is a better indicator of the type of treatment that may be effective than is a list of symptoms.

8. **Reveal the next classification criterion, on Master 1.3b, and ask students to re-sort their disease cards based on this criterion (the mechanism of transmission for each disease).**

9. Repeat Steps 6 and 7 for this criterion.

It is useful to classify diseases by the way they are transmitted because a disease's mode of transmission may suggest an effective preventive measure. For example, the spread of diseases such as AIDS and Ebola hemorrhagic fever that are transmitted by intimate contact can be stopped or reduced through education and elimination of some behaviors (such as burial practices in which family members disembowel the deceased in nonsterile conditions) and institution of other behaviors (such as proper disease-control measures in hospitals). The spread of vector-borne diseases such as malaria can be prevented by measures that treat people, reduce the size of the vector population, or limit contact between humans and the vector.

10. Reveal the last classification criterion, history of the occurrence of the disease, on Master 1.3c, and ask students to re-sort their cards. Then, repeat Steps 6 and 7.

Students likely will identify two categories: “new” (for example, AIDS, Ebola, and Legionnaire’s disease) and “old” (for example, strep throat, guinea worm disease, pneumonia, polio, and tuberculosis).

If this is the case, add these headings to the first two rows on Master 1.3c and list the diseases named by students. Then challenge them to re-examine the “old” diseases they listed and to subdivide that category. Help them by asking a question such as, “Is there any difference in the history of the ‘old’ disease tuberculosis and the ‘old’ disease pneumonia?” When students make the appropriate distinction, add the new headings for the second and third rows on Master 1.3c and relist the diseases accordingly.

Students should note that whereas all the old diseases are described as “present from antiquity,” the incidence of some of them has increased recently (in particular, the incidence of some has increased recently after declining in the past). The categories from the subdivided “old” category could be renamed “Old and Increasing,” “Old and Remaining Constant,” and “Old and Changing/Evolving.”

11. Supply the headings “Emerging” for the apparently new diseases, “Re-emerging” for diseases that have recently increased in incidence after a decline, and “Endemic” for diseases that have remained relatively constant in incidence. Write these labels at the heads of the appropriate rows.

The disease cards provide examples of all three types of diseases, as shown in Figure 9.

Both polio and guinea worm disease have declined dramatically and, we hope, are on their way to global eradication. Cholera and influenza are more complicated examples that are less easily classified. On the basis of the information on their cards, students will likely classify cholera as



This step focuses students’ attention on the major concept of this activity and the module: Infectious diseases are an increasing health concern in part due to emerging and re-emerging diseases.

a re-emerging disease and influenza as an endemic disease. Depending on the sophistication of your students and the time available, you may simply accept their initial categorization or you may choose to share the additional information below and ask them where they would categorize these two diseases. In either case, note that the categorization of infectious diseases into these three areas is somewhat subjective, and different researchers may categorize them differently based on the weight they give to various characteristics.

Cholera may be classified as either re-emerging, because of increasing incidence due to the spread of the disease to Africa, or emerging, because of the appearance of the new serotype *Vibrio cholerae* O139. This new serotype evades the immunity developed to previous cholera strains, so it can infect a population that had developed immunity.

Influenza is probably most accurately classified as an emerging disease because, although the flu occurs every year, each strain of the influenza virus is genetically distinct. In this sense, it is a constantly emerging pathogen.

You may also want to elaborate on the definition of emerging diseases by noting that this category includes 1) diseases that are truly “new” among humans (few, if any, examples fall into this subcategory); 2) diseases that probably affected a few individuals even hundreds and thousands of years ago but have just recently affected enough of the population that they are noticed (AIDS and Ebola hemorrhagic fever are examples for this subcategory); and 3) diseases that affected people hundreds and thousands of years ago but have just recently been recognized as due to an infectious pathogen (gastric ulcers caused by *Helicobacter pylori* is an example that falls into this subcategory). Many researchers include re-emerging diseases as a subcategory of emerging diseases.

Figure 9. History of occurrence.

Category	Diseases
Emerging Diseases	AIDS, cholera, CJD, Ebola hemorrhagic fever, influenza, Legionnaire’s disease, Lyme disease
Re-emerging Diseases	tuberculosis, malaria, schistosomiasis
Endemic Diseases	pneumonia, polio, guinea worm disease, plague, strep throat

12. Conclude the lesson by telling students that public health workers are becoming increasingly concerned about the emergence of “new” diseases and the re-emergence of some “old” diseases. These biologists have found it useful to classify infectious diseases as emerging, re-emerging, or endemic because there tend to be different factors related to each category. Tell students that they will explore factors related to disease emergence and re-emergence in upcoming lessons.

Internet sites maintained by both the Centers for Disease Control and Prevention (<http://www.cdc.gov/>) and the World Health Organization (<http://www.who.org/>) include sections with information on infectious (and noninfectious) diseases. Assign students to use these and other resources to create additional disease cards and to classify those diseases as emerging, re-emerging, or endemic.

Potential Extensions

Lesson 1 Organizer

What the Teacher Does	Procedure Reference
<p>Ask students these questions:</p> <ul style="list-style-type: none"> • What disease do you think is the greatest threat to students in this class? • What disease do you think is the greatest threat to the world’s population? <p>Solicit several responses and briefly discuss why students view these diseases as threats.</p>	<p>Page 51 Step 1</p>
<p>For classes without Internet access, Steps 2 and 3</p> <ul style="list-style-type: none"> • Tell students they will take a brief oral quiz. Explain that you don’t expect them to know the answers; they should make well-reasoned guesses based on what they know now. • Display a transparency of Master 1.1. Ask students to share their guesses and reasons for each question before you provide correct answers. <i>Correct answers are: 1c, 2d, 3c, 4b, 5d, 6d</i> • Explain that the quiz emphasized the impact of infectious diseases. Point out that infectious diseases are still the leading cause of death worldwide and the third leading cause of death in the United States. Tell students that they will learn about some infectious diseases that cause problems in the world today. 	<p>Pages 51–54 Step 2 and 3</p>  
<p>Alternate, online procedure for Steps 2 and 3</p> <ul style="list-style-type: none"> • Show the video segment <i>Infectious Disease Then and Now</i> from the Web site instead of having students do the quiz. • Answer any student questions, and point out that infectious diseases have an impact on people’s health and well-being. Point out that they are still the leading cause of death worldwide and the third leading cause of death in the United States. Tell students that they will learn about some infectious diseases that cause problems in the world today. 	<p>Pages 51 Steps 2 and 3</p> 
<p>Organize students into groups of three. Give each group five disease cards made from Master 1.2.</p>	<p>Page 54 Step 4</p> 
<p>Explain that scientists group diseases by what problem they are investigating. Display a transparency of Master 1.3a, and ask groups to sort their disease cards into categories of infectious agents.</p>	<p>Page 54 Step 5</p> 

What the Teacher Does	Procedure Reference
Fill in the transparency of Master 1.3a by asking groups for suggestions. First, ask groups to identify headings for the categories. Then ask them to name specific diseases in each category and describe symptoms.	Page 54 Step 6
Ask students to suggest reasons why scientists might find it <i>useful</i> to classify diseases based on type of infectious agent.	Page 54 Step 7
Display a copy of Master 1.3b and ask students to re-sort their disease cards based on the mechanism of transmission for each disease. Repeat Steps 6–7 for this criterion.	Pages 54–55 Steps 8 and 9 
Reveal the last classification criterion, history of the occurrence of the disease (Master 1.3c), and ask students to re-sort their disease cards. Repeat Steps 6–7 for this criterion.	Page 55 Step 10 
Label the rows on Master 1.3c with the headings <ul style="list-style-type: none"> • “Emerging” for the apparently new diseases, • “Re-emerging” for diseases that have recently increased in incidence after a decline, and • “Endemic” for diseases that have remained relatively constant in incidence. 	Page 56 Step 11
Conclude the lesson by telling students that public health workers are increasingly concerned about the emergence of new diseases and the re-emergence of some “old” diseases. Biologists classify diseases in this way because there tend to be different factors related to these categories. Inform students that they will explore some of these factors for emerging and re-emerging diseases in upcoming lessons.	Page 57 Step 12

Note: Shaded text highlights the steps for classes with access to the Internet.



= For classes without access to the Internet.



= Involves copying a master.



= Involves making a transparency.



= Involves using the Internet.

Disease Detectives



Overview

Students assume the roles of public health experts to investigate the cause of a mystery disease.

Major Concepts

A major cause of the emergence of new diseases is environmental change (for example, human encroachment into wilderness areas and increased human traffic through previously isolated areas).

Objectives

After completing this lesson, students will

- recognize the variety of evidence that epidemiologists must collect to determine the origin, infectious agent, and route of transmission of an infectious disease;
- be able to give examples of how an infectious agent can be transmitted to humans; and
- be able to explain how environmental changes can result in the emergence of infectious diseases.

Prerequisite Knowledge

Students should know that infectious diseases are diseases that result from the presence of an external agent or its products. Students should also know that antibodies are produced by the body in response to invasion by a foreign organism or molecule and that the presence of particular antibodies indicates a previous encounter with the foreign agent that triggered their production. They should also understand that purified antibodies to a particular organism or molecule can be used to detect that organism or molecule in tissue samples from victims of an infectious disease.

Basic Science–Public Health Connection

This lesson demonstrates how scientists use ecological, biochemical, and medical research to investigate infectious disease outbreaks. The lesson also illustrates how the results of such research can help stop epidemics and lead to public health recommendations and the development of drugs and vaccines to limit future epidemics of the disease.

At a Glance

Introduction

When local healthcare workers recognize a cluster of strange disease cases with similar characteristics, they bring it to the attention of national public health officers. Epidemiologists collect a variety of evidence including demographic evidence (such as geographic location, age and other defining characteristics of victims, and mortality rate), laboratory evidence from victims' tissues, and evidence about environmental factors that might be involved. Their goal is to protect public health by identifying the disease as rapidly as possible and recommending appropriate actions to prevent it from becoming an epidemic.

A recent example of the effectiveness of this strategy was the identification of hantavirus pulmonary syndrome (HPS) as an emerging disease. Cases of this apparently new disease were first recognized in May 1993. Within four months, the infectious agent had been identified as a “new” variety of hantavirus, the reservoir of the virus had been determined to be deer mice, and the route of transmission (inhalation of viral particles from the rodents' feces and urine) had been deciphered. Strategies for avoiding contact with the virus were developed, and early diagnosis and support therapy were recommended to reduce mortality due to the disease.

Three “mystery diseases” (unnamed for the students, but based on HPS, Lyme disease, and Lassa fever) are the initial focus of this lesson. HPS was first recognized in 1993; Lyme disease first came to the attention of public health workers in 1975 as an unusual number of cases of juvenile rheumatoid arthritis in children in Lyme, Connecticut; and Lassa fever was first identified in an outbreak in Nigeria in 1969. Cases of HPS were originally clustered in the Four Corners region of the U.S. Southwest, and the majority of cases to date have been found there. Lyme disease is the most commonly diagnosed tick-borne disease in the United States, with the majority of cases clustering in the Northeast, although cases have occurred in 48 of the 50 states. Lassa fever outbreaks occur in West Africa.

Investigating these diseases leads students to recognize that all three of them “emerged” as a result of environmental changes and/or movement of humans into areas inhabited by the organism that serves as a reservoir for the pathogen. Lesson 3, *Superbugs: An Evolving Concern*, and Lesson 4, *Protecting the Herd*, help students understand two factors involved in the re-emergence of infectious diseases.

In Advance

Photocopies and Transparencies	Equipment and Materials
<ul style="list-style-type: none">• 1 copy for each student of Masters 2.1 and 2.11• 1 copy for each group of Masters 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8• 1 copy for <i>half</i> the groups of Master 2.9• 1 copy for the other half of groups of Master 2.10• 1 transparency of Master 2.11	<ul style="list-style-type: none">• 1 overhead projector• blank transparencies• (Optional) Computers with access to the Internet

Preparation

Make the investigation files: copy Masters 2.2, 2.3, and 2.4 and assemble them into file folders that you label “Physician’s File,” “Laboratory Scientist’s File,” and “Field Researcher’s File.” You may want to use a different-colored folder for each type of file. Make enough sets of these files so that no more than three or four students (one student from each of three or four different groups) study the documents in the file together. For example, for a class of 30 students (10 groups), prepare three sets of each type of file.

1. Introduce the lesson by asking students to suppose that a friend developed a strange rash and then a fever accompanied by severe vomiting and diarrhea. Their friend was hospitalized for a week before finally recovering. Then, they hear about a student in another class who had similar symptoms, and they learn that this student’s cousin was also sick with fever, vomiting, and diarrhea. A few days later, they hear a television report about a strange illness affecting five students at a nearby high school. The symptoms described sound just like those experienced by their friend. Ask students to suggest questions they might ask about how to protect themselves from this illness. Write these questions on the board or a transparency.

If students ask, explain that the symptoms do not indicate a particular disease but are used to get students thinking. Complete this step quickly, accepting and listing four or five reasonable questions from students, such as, “Do all the sick people have the same disease?” “What is the cause of the disease?” and “Do the victims have anything in common that can tell us how the disease is transmitted?” It is important to leave these questions on the board or the overhead projector so that students can refer to them as they complete the lesson.

Procedure

2. Tell students that public health officers are responsible for answering these types of questions when a cluster of unusual cases of disease occurs. Explain that in this lesson, students will follow in the footsteps of public health officers to answer some of the questions they listed about a mystery disease. Give a copy of Master 2.1, *Three Mysterious Diseases*, to each student, and ask four volunteers to read the script to the class.

If you have students who are interested and talented in drama, you may want to give them the scripts the previous day and ask them to read them dramatically to the class.

If students ask what you mean by “unusual cases of disease,” explain that it could mean a variety of unexpected occurrences including symptoms that are rare in general, symptoms that are rare in the population in which they are now occurring, or unusual severity of illness or fatality rates.



If you can project the video for the whole class, you can use the “Three Mysterious Diseases” videos on the Web site to introduce the lesson. Go to <http://science.education.nih.gov/supplements/diseases>, and click on “Web Portion of Student Activities” and then “Lesson 2—Three Mysterious Diseases.”

3. Group students into teams of three and tell them they will spend the next 30 minutes investigating the first mystery disease. Ask them to assign each group member one of the following roles: physician, laboratory scientist, or field researcher. Explain that each of these experts will look for clues that will help each group answer the questions the class listed in Step 1.

We suggest that you use the same groups as in Lesson 1.

4. Identify a station in the room for each of the three experts. Place copies of the relevant master (Masters 2.2, 2.3, or 2.4) at each station. Give each group one copy of Master 2.5, *Notes from the Physician’s Investigation*; Master 2.6, *Notes from the Laboratory Scientist’s Investigation*; and Master 2.7, *Notes from the Field Researcher’s Investigation*. Direct students to go to the appropriate station and review and discuss the clues they find there about the disease with their colleague “experts” from the other groups. Ask them to record significant information on the forms you distributed. Tell students they will have 15 to 20 minutes to complete their research.

Move among the groups during this time, answering their questions and using probing questions to direct their attention to significant details in their information. Students in the field researcher groups may wonder why there is no interview transcript from “J. McDonald.” Draw their attention to the “Other Comments” on McDonald’s “Investigation of Victim’s Home” report, in which she indicates that the victim’s mother and aunt refused to be interviewed.

Tip from the field test: To save time and reduce confusion, place three or four copies of Masters 2.5, 2.6, and 2.7 at the appropriate stations before class. Then tell students they will find a copy of the form they need to complete at the station.

5. Reconvene the original groups and give one copy of Master 2.8, *Mystery Disease 1 Final Report*, to each student. Allow group members 10 minutes to pool their information and complete the report form.

Again, move among the groups, answering their questions and directing their attention to significant details. Students may have particular difficulty with the final task, which asks whether the disease is emerging, re-emerging, or endemic. Help them come to the conclusion that this is an emerging disease by asking questions such as, “Was there evidence that this disease is common in the Southwest?” “Was there evidence that it was *not* one of these common diseases?” “What did you decide was the cause of the disease?” “Has this infectious agent been known to cause a disease with the ARDS symptoms?” and “What is the evidence that this is an ‘old’ disease? . . . that it is a ‘new’ disease?”

6. Distribute Master 2.9, *Mystery Disease 2 Final Report*, to half the groups and Master 2.10, *Mystery Disease 3 Final Report*, to the remaining half. Explain to students that a group of experts similar to those in their groups pooled information from their investigations to complete these reports. Ask students to study the report forms while you distribute one copy of Master 2.11, *Mystery Diseases Summary Table*, to each student.
7. Direct students to complete the table on Master 2.11 for the two diseases for which they have report forms.
8. Display a transparency made from Master 2.11, and ask several groups to report one piece of information as you complete the first row of the table. Ask the remaining groups whether they have additional information and whether they disagree with any of the information provided by the other groups. Follow the same procedure for the other two mystery diseases.

All three diseases are classified as emerging diseases and although students are not given this information, all three have probably occurred for hundreds if not thousands of years. Nevertheless, only recently have cases occurred in sufficient numbers that they were recognized as specific diseases. The infectious agents for the three diseases are transmitted by

- Mystery Disease 1—contact with deer mouse (*Peromyscus maniculatus*) urine and feces
- Mystery Disease 2—bite from deer ticks (*Ixodes dammini*)
- Mystery Disease 3—contact with rat (*Mastomys natalensis*) urine and feces, and close contact with victims of the disease



Collect students' *Final Reports* and review them to evaluate how well students were able to identify the evidence that supported or refuted a claim about the disease. Identify areas where students could improve and discuss them with the class when you return their papers.



This is a good time to note how technological advances have improved our ability to identify the infectious agents for mysterious diseases. Identification of the spirochete type of bacterium as the cause of Lyme disease required nearly seven years, whereas molecular biology techniques available in 1993 meant that the infectious agent for HPS was identified within a month. Continuing NIAID-supported research on the Lyme disease spirochete has led to improved diagnosis of the disease and the development of a new vaccine to prevent it.



In Step 10, students are challenged to synthesize in their own words the discussion from Step 9. Completing the sentences requires them to state and elaborate on the lesson's major concept.

The environmental factors involved are

- Mystery Disease 1—climatic conditions favoring large deer mice populations and human encroachment into areas inhabited by deer mice
- Mystery Disease 2—climatic conditions favoring large acorn harvests and human movement into wooded areas
- Mystery Disease 3—conditions that reduce competition from *R. rattus*, including human efforts to reduce the *R. rattus* population

9. **Allow students to examine the summary table and then ask them to list any common features they note about the three mystery diseases. Lead a class discussion by asking, “Can you see one overall factor that resulted in the emergence of all three of these diseases?” and “What does this suggest about things people need to consider as we develop land for residential and business purposes?”**

Common features of the three mystery diseases, as revealed on Master 2.11, are that all the diseases are emerging, the transmission of the infectious agent involves a nonhuman animal, and environmental factors strongly help explain their occurrence. Guide students to the understanding that environmental and ecological factors, combined with the movement of humans into previously uninhabited areas, help explain the relatively sudden appearance of these “new” diseases.

You may want to reveal the names of the three mystery diseases at this time:

- Mystery Disease 1—hantavirus pulmonary syndrome (HPS)
- Mystery Disease 2—Lyme disease
- Mystery Disease 3—Lassa fever

Explain to students that these diseases were first recognized in 1993 (HPS), 1975 (Lyme disease), and 1969 (Lassa fever). Although the symptoms and “clues” presented in the mystery disease cases would immediately implicate HPS, Lyme disease, or Lassa fever if physicians saw them today, in 1993, 1975, or 1969, these three diseases were “new” to healthcare workers, just as they were to students in this lesson.

10. **Ask students to complete individually, in writing, the sentences at the bottom of Master 2.11, *Mystery Diseases Summary Table*.**
11. **Collect students' assignments from Step 10 and close the lesson by noting several responses (anonymously) and engaging the students in a discussion of the issues that should be considered to avoid or minimize the risks of emerging diseases.**

Completing the lesson should lead students to recognize that changing environmental conditions create opportunities for new or previously rare diseases to affect large numbers of people. Students are likely

to respond to the second question by a blanket statement such as, “People should stay out of uninhabited areas.” Challenge them to think more deeply by asking questions such as, “Should you or anyone else be allowed to tell people where they can live?” “What if people in a developing country have an opportunity to dramatically increase their income, as well as their country’s productivity, by developing an area previously uninhabited by people? Do the advantages of economic development outweigh the risks of emerging diseases? What do you need to consider to make this evaluation?” and “How might medical and ecological research efforts help resolve these dilemmas?”

You may want to give students the example of the Aswan Dam in Egypt. Schistosomiasis is a disease that causes diarrhea, abdominal pain, and liver problems. Chronic infections may lead to liver failure and may also affect the central nervous system. The disease is caused by a helminth that has a complex life cycle, including stages in both snails and the human bloodstream. Because snails thrive in still waters such as those found in irrigation canals and artificial lakes, the incidence of schistosomiasis frequently increases following construction of dams. Although this was known before the Aswan Dam was built, the officials involved in the decision felt that the economic advantages of the dam outweighed the disease consequences. Before the dam was built, about 1 percent of the schoolchildren in the area had schistosomiasis. After the dam was built, the incidence of schistosomiasis among children in some villages near the artificial lake rose to 100 percent. Since then, Egypt has spent part of the profits from the Aswan Dam on a major, ongoing chemotherapy campaign against schistosomiasis.

This example also shows that the incidence of “old” diseases may be affected by environmental changes. Schistosomiasis is not a “new” disease, but the increased incidence of the disease makes it a candidate for a re-emerging disease. Other factors related to disease re-emergence are explored in the next two lessons.

Several popular books on emerging infectious diseases make exciting reading and provide further illustration of scientists’ work in identifying and limiting the risks of emerging diseases. Assign students to read and report on books such as *The Hot Zone*, by Richard Preston (which describes outbreaks of Ebola hemorrhagic fever), *The Coming Plague*, by Laurie Garrett (which describes the efforts of scientists and policymakers regarding a variety of emerging and re-emerging diseases, including HPS, Lassa fever, malaria, and Legionnaire’s disease), and *Restless Tide: The Persistent Challenge of the Microbial World*, by Richard M. Krause.

Potential Extensions

Lesson 2 Organizer

What the Teacher Does	Procedure Reference
Ask students to imagine the scenario in Step 1 on page 63. Ask students to suggest questions they might ask about how to protect themselves from the illness. Write students' questions on the board.	Page 63 Step 1
For classes with Internet access, Step 2 Show the <i>Three Mysterious Diseases</i> video clips from the Web site. (Students may still appreciate having the copy of Master 2.1 for reference.)	Page 64 Step 2  
For classes without Internet access, Step 2 Tell students that public health officers answer these types of questions when a cluster of unusual cases of disease occurs. Explain that students will play the role of a public health officer to answer the questions they have about a mystery disease. Give each student a copy of Master 2.1 . Ask for volunteers to read the script aloud to the class.	Page 64 Step 2  
Group students into teams of three. Ask groups to assign a role to each student. Allow 30 minutes for groups to investigate the first mystery disease. Experts should look for clues to help answer the questions from Step 1.	Page 64 Step 3
Place copies of Masters 2.2, 2.3, or 2.4 at three stations (Physician's File, Laboratory Scientist's File, or Field Researcher's File). Ask students from the original groups to meet with the same experts from the other groups at the appropriate station. Allow 15 to 20 minutes for these new groups to review information in their files and discuss the clues about the disease. Ask groups to record significant information on a copy of the master appropriate for their expert role (Master 2.5, 2.6, or 2.7).	Page 64 Step 4 
Ask the "experts" to return to their original groups. Give each student a copy of Master 2.8 . Allow 10 minutes for group members to pool their information and complete the report.	Page 65 Step 5 
Give Master 2.9 to half the groups and Master 2.10 to the other half. Ask students to study the report forms.	Page 65 Step 6 

What the Teacher Does	Procedure Reference
Give each student a copy of Master 2.11 . Ask students to complete the table for the two diseases for which they have report forms.	Page 65 Steps 6 and 7 
Display a transparency of Master 2.11 . Ask several groups to report one piece of information to complete the first row of the table. Ask other groups if they have other information or disagree with any information provided by other groups. Complete the table using this approach.	Page 65 Step 8 
Discuss the summary table with students by asking the following questions: <ul style="list-style-type: none"> • Are there any common features you can list about the three mystery diseases? What are they? • Can you see one overall factor that resulted in the emergence of all three of these diseases? • What does this suggest about things people need to consider as we develop land for residential and business purposes? 	Page 66 Step 9
Have students work individually to complete the sentences at the bottom of Master 2.11 .	Page 66 Step 10
Collect Master 2.11 . Close the activity by noting several responses (anonymously). Engage students in a discussion of issues that should be considered in order to avoid or minimize the risks of emerging diseases.	Page 66 Step 11

Note: Shaded text highlights the steps for classes with access to the Internet.

 = For classes without access to the Internet.

 = Involves copying a master.

 = Involves making a transparency.

 = Involves using the Internet.

Superbugs: An Evolving Concern



Overview

Students investigate the growth of bacteria in the presence of antibiotics and use the results to explain a case of antibiotic-resistant tuberculosis.

Major Concepts

The re-emergence of some diseases can be explained by the evolution of the infectious agent (for example, mutations acquired in bacterial genes that confer resistance to antibiotics used to treat the diseases).

Objectives

After completing this lesson, students will

- be able to explain how antibiotic treatment results in populations of bacteria that are largely resistant to the antibiotic and
- describe inappropriate and/or questionable uses of antibiotics.

Prerequisite Knowledge

Students should be familiar with bacterial growth and with evolution by natural selection.

Basic Science–Public Health Connection

In this lesson, students learn that the evolution of antibiotic resistance among bacteria observed in laboratory experiments occurs in the natural environment as well, and that such evolution has serious consequences for the effectiveness of treatments for some diseases.

In 1943, penicillin was introduced as the “magic bullet” for curing many infectious diseases. By 1946, however, approximately 14 percent of *Staphylococcus aureus* strains isolated at a London hospital were resistant to penicillin. Today, scientists estimate that more than 95 percent of all *S. aureus* strains are penicillin-resistant.

After the introduction of penicillin, additional antibiotics were rapidly isolated and developed, including streptomycin and the tetracyclines. Today, more than 100 antibiotics are available. Nevertheless, some strains of at least three bacterial species (*Enterococcus faecium*, *Mycobacterium tuberculosis*, and *Pseudomonas aeruginosa*) are resistant to all the antibiotics

At a Glance

Introduction

available to treat these species, and healthcare workers fear that the time is rapidly approaching when more deadly organisms escape the effects of all known antibiotics.

The primary reason for the increase in antibiotic resistance is the excessive use of antibiotics. When mutant genes arise that make a bacterium less sensitive to an antibiotic, that bacterium survives and produces descendants in an environment rich in antibiotics. That is, the process of natural selection operates. Multiple mutations may be necessary for fully resistant bacteria. However, once resistant genes appear, bacteria have a variety of mechanisms for exchanging those (and other) genes both within and across species. These mechanisms include conjugation, transformation, transduction, and transposon-mediated exchange. This exchange allows for “accelerated evolution” of bacterial species (accelerated in the sense that random mutations that result in antibiotic resistance need not occur in every individual bacterium, or even in every species of pathogen, but can simply be acquired from another organism).

This lesson invites students to explore one reason for the re-emergence of some infectious diseases: the evolution of antibiotic resistance among pathogens. In Lesson 4, *Protecting the Herd*, students explore another reason for the re-emergence of infectious diseases.

In Advance

Photocopies and Transparencies	Equipment and Materials
<ul style="list-style-type: none"> • 1 copy per student of Masters 3.1, 3.2, 3.4 • 1 copy per student for the print-based version only of Master 3.3 • 1 copy per group of Master 3.5 	<ul style="list-style-type: none"> • (Optional) Computers with access to the Internet • All items needed for the lab (see page 80)

Students complete this lesson during several (five to seven) class periods. You will need to prepare the materials for the laboratory exercise. Ordering information and preparation directions are on pages 80–81, immediately following the lesson.



For classes with access to the Internet:

Information about the safe use of microorganisms in classrooms, including lists of organisms considered safe for students at various levels of school, can be found at <http://www.science-projects.com/safemicrobes.htm>. Leaders in infectious disease research, including scientists from NIH, contributed to the Web site. *Pseudomonas fluorescens*, the organism used in the laboratory exercise in this lesson, is included on the list of microorganisms considered appropriate for students in grade 9 or higher. Nevertheless, experts acknowledge that people who are immunocompromised may be at risk for infection by organisms that do not affect healthy individuals.

We recommend that you read a statement such as the following to your classes before beginning the lesson:

Pseudomonas fluorescens, the bacterium used in the laboratory exercise you will begin soon, does not cause disease in healthy people. However, people who have weakened immune systems should not have contact with most microorganisms or with people who handle those organisms. Your immune system may be weakened if you are undergoing antibiotic therapy, if you are taking immunosuppressive drugs or drugs for cancer treatment, or if you have AIDS or are HIV-positive. If you have a weakened immune system for these or any other reasons, let me know, and I will give you an alternative experience that is safer for you.

Students who should not participate in the laboratory exercise can view a video demonstration of it on the Web site, as described in the following paragraphs. They can rejoin the class on Day 3 of the lesson, after the other students have recorded their results and discarded their bacterial cultures.

If you do not have the time or facilities to conduct the laboratory exercise, you will need only one day to complete this lesson. Complete Steps 1 to 3, Day 1, and then have students view a video demonstration of the laboratory exercise, *Bacterial Growth Experiment*, on the *Emerging and Re-emerging Infectious Diseases* Web site. Students will need copies of Master 3.1 to help them follow the steps in the demonstration. Then, move to Day 3 of the lesson.

To set up computers, go to <http://science.education.nih.gov/supplements/diseases> and choose “Web Portion of Student Activities.”

Note to teachers: If you don't have enough computers equipped with Internet access to conduct Steps 4 and 5 on Day 3, you can use the print-based alternative (page 78).

DAY 1 (5 to 7 days before Day 3 of the lesson)

Procedure

1. **Remind students of the theory of evolution.** Explain that theories in science are well-accepted explanations about some natural phenomenon and are backed up with a great deal of scientific evidence. The greater the evidence and the more diverse the evidence, the stronger the theory. The evidence comes from scientists who generate hypotheses and conduct experiments to test their hypotheses.

Students should be able to state the basic elements of the theory of evolution: 1) there is variation among the individuals in a population; 2) some of these differences can be inherited; 3) some individuals will be better adapted to their environment than others; 4) the better-adapted individuals will reproduce more successfully; and 5) thus, the heritable characteristics that make individuals better adapted will increase in frequency in the population.

2. Organize students into groups of three and challenge the groups to use their understanding of evolution by natural selection to write a hypothesis about what will happen in a population of bacteria after growing for several generations in the presence of an antibiotic.

If students have difficulty with this, stimulate their thinking by asking questions such as, “What effect does an antibiotic usually have on bacteria? Do you know of cases in which that effect did not occur? What does that suggest about variations that exist in the bacteria population? Which bacteria survived? What trait did they pass on to other progeny?”

3. Convene a class discussion in which you ask several groups to share the hypotheses they developed. Challenge the class to work together to refine them into one hypothesis similar to the following:
If a bacterial culture is grown in a medium containing an antibiotic, then after several generations, all the bacteria in the culture will be resistant to the antibiotic.
4. Tell students that they will conduct an experiment to test this hypothesis, and explain that they will also consider the implications of their results for controlling infectious diseases in an activity the following week. Then, distribute Master 3.1, *Bacterial Growth Experiment*, and instruct students to complete Steps 1 through 4 with their group members.

Emphasize that for safety reasons as well as the success of their experiments, students must use aseptic techniques. If students are not familiar with aseptic techniques for handling bacterial cultures, you will need to demonstrate them.



Alternatively, you can have your students view the “Day 1” video segment of *Bacterial Growth Experiment* online, which shows students using aseptic techniques as they prepare the initial cultures in the experiment (<http://science.education.nih.gov/supplements/nih1/diseases/activities/activity3.htm>).

DAY 2 (2 to 3 days before Day 3 of the lesson)

1. Direct groups to complete Steps 5–8 on Master 3.1.

DAY 3

1. Tell students that today they will analyze the results of the bacterial growth experiment they have been running and will use those results to help explain what happened to a high school student who had tuberculosis.

2. Organize students into groups and instruct them to collect their bacterial growth plates. While they do this, give each student a copy of Master 3.2, *Discussion Questions for the Bacterial Growth Experiment*. Tell the groups to draw (or describe) their results on the flow chart on Master 3.1c first, then refer to those results as they discuss and write answers to the discussion questions on Master 3.2.

Depending on students' microbiology background, you may need to explain that when a single, microscopic bacterium is placed on an agar plate, it will grow and divide into two progeny cells. Each progeny cell will grow and divide, and so on, until thousands and thousands of individual bacteria are growing right in that spot. At this point, the growth becomes visible to us as a colony of bacteria. Each colony came from a single original bacterium on the plate. When approximately 10,000 or more bacteria are plated, each individual bacterium is close enough to a neighboring bacterium that the colonies they produce merge together, and we observe confluent growth, or a "lawn," of bacteria across the plate.

Move among the groups as they discuss each question and help lead students to the following understandings.

Question 1. Compare the bacterial growth on the two plates from the parental culture (Plates 1 and 2). Which has more growth? Explain why. How do you explain the presence of bacteria on the plate containing kanamycin?

The nutrient agar plate (Plate 1) should show a lawn of bacteria, or confluent growth, whereas the plate containing kanamycin should show only 50 to 100 colonies. Students should explain that the antibiotic prevented the growth of most of the bacteria on Plate 2. A simple, straightforward answer is all students need to provide for the last question: The bacteria that grew on Plate 2 were resistant to the antibiotic.

Question 2. Compare the growth on Plates 3 and 4, which you prepared from culture A (without kanamycin). How does the growth on the plates with and without kanamycin appear? What does this tell you about the bacteria grown in culture A?

The plate without kanamycin (Plate 3) should show a lawn of bacterial growth, whereas the plate with kanamycin (Plate 4) should show 50 to 100 colonies. The results on Plate 3 indicate that a lot of bacteria were growing in the sample plated from culture A. Comparing the results on that plate with the results on Plate 4 indicates that some of the bacteria in the culture (for example, 50 out of 10,000 or more) were resistant to the antibiotic, but most were not.

Question 3. Compare the growth on Plates 5 and 6, which you prepared from culture B (with kanamycin). How does the growth on the plates with and without kanamycin appear? What does this tell you about the bacteria grown in culture B?

Both plates should show a lawn of bacterial growth. This indicates that most or all of the bacteria growing in this culture were resistant to kanamycin.

Question 4. Compare the growth of cultures A and B on Plates 4 and 6 (with kanamycin). Explain how culture B could have so many more resistant bacteria than culture A, even though they both came from the same parental culture.

If, after a minute or two of discussion, students cannot offer an explanation, suggest that they use their understanding of natural selection to explain the difference in the results on the plates for the two cultures. They should be able to explain that the environment in culture B (which contained kanamycin) selected for the growth of those bacteria that were resistant to kanamycin. By the time students plated a sample from that culture, all of the bacteria in the sample were resistant, so they all grew on the plate with kanamycin, resulting in a lawn of bacterial growth (Plate 6). Culture A did not contain kanamycin, so there was no selection for kanamycin resistance, and most of the bacteria students plated from that culture were not resistant. Thus, most did not grow on the plate with kanamycin (Plate 4).

Question 5. How do you explain the presence of some resistant bacteria in the parental culture and culture A?

To answer this question, students must recognize that bacteria become resistant (for example, through mutation) *before* natural selection operates. In other words, the bacteria in the parental strain did not “know” that some of them would be placed in growth medium with kanamycin and “respond” by becoming resistant. Instead, in the parental strain, a few bacteria were already present that were resistant to kanamycin, even though no kanamycin was present. Similarly, a few bacteria in culture A were resistant to kanamycin, even though no antibiotic was present. When the resistant and nonresistant bacteria from the parental culture were placed in medium containing kanamycin (culture B), only the resistant bacteria survived and reproduced, passing their kanamycin resistance trait on to their progeny. Soon, virtually all the bacteria in the culture—the progeny of the original resistant bacteria—were resistant to kanamycin, as observed on the students’ plates.

3. Convene a brief class discussion in which you clarify any confusion you noted as you circulated among the groups and/or invite students to ask questions about the results of their experiments.

Steps 4 and 5 for classes with access to the Internet:



4. Tell students that they will watch a young woman named Debi French discuss her battle with tuberculosis. Then, they will use the results of their bacterial growth experiments to help explain what happened in her struggle with the disease. Ask groups to take their copies of the flow chart and *Discussion Questions* with them to the computer stations.

Emphasize that the bacterium in their experiment (*P. fluorescens*) is not the kind that causes tuberculosis (*M. tuberculosis*). *P. fluorescens* does not cause disease in healthy people. Furthermore, the antibiotic kanamycin is not used clinically, so the resistant bacteria cultured in this exercise do not compromise medical treatments. Emphasize, however, that all bacterial cultures in your class are decontaminated before disposal and that aseptic conditions must be followed in all work with microorganisms.

5. Distribute a copy of Master 3.4, *Debi's Story: Explaining What Happened*, to each student and tell them to click on *Debi's Story* to start the video. Indicate that students have 20 minutes to answer the questions on *Debi's Story*.

You may want to emphasize to students that this is a true story, and that Debi herself tells her story on the video.

Organizing student groups at individual computer stations to view Debi French's story will allow students to complete this part of the lesson at their own pace. An alternative, if you have the equipment to project the video from the Web site onto a large screen for whole-class viewing, is to show the first part of the video to the class, then reorganize students into their groups. After the groups have discussed and written answers to the first set of questions on Master 3.4a, reconvene the class to watch the second part of the video. Instruct students to return to their groups to answer the second set of questions on the handout. Follow this process until students have completed their study of Debi's story.

You may need to remind students of the information they learned about tuberculosis in Lesson 1.



As they use the results of their bacterial growth experiment to explain what happened to Debi French, students will experience how basic research leads to explanations for disease and for the success or failure of disease treatment. This understanding leads scientists to propose further research and policies directed at improving public health.

Steps 4 and 5 for classes using the print version of the lesson:



4. Tell students that they will learn about a young woman named Debi French and her battle with tuberculosis. They will use the results of their bacterial growth experiments to help explain what happened in her struggle with the disease.

Emphasize that the bacteria in their experiment (*P. fluorescens*) is not the kind that causes tuberculosis (*M. tuberculosis*). *P. fluorescens* does not cause disease in healthy people. Furthermore, the antibiotic kanamycin is not used clinically, so the resistant bacteria cultured in this exercise do not compromise medical treatments. Emphasize, however, that all bacterial cultures in your class are decontaminated before disposal and that aseptic conditions must be followed in all work with microorganisms.

5. Give each student one copy of Masters 3.3, *Debi's Story*, and 3.4, *Debi's Story: Explaining What Happened*. Indicate that students have 20 minutes to read about Debi and answer the questions on *Debi's Story*.

You may want to emphasize to students that this is a true story.

You may want to remind students of the information they learned about tuberculosis in Lesson 1.

6. Convene a whole-class discussion in which you ask several groups to share their responses to the questions on Master 3.4. Invite the other groups to add information and disagree with these responses. Then, ask students, "What explanation does the Debi French example suggest for the re-emergence of diseases like tuberculosis?"

Students should be able to provide answers such as the following:

Sentence 1

- **Debi contracted tuberculosis (TB) from** a student in one of her classes who had an active, misdiagnosed case of TB. Debi did not know this student.
- **The symptoms Debi had were** fatigue, weight loss, and a severe, persistent cough.

Sentence 2

- **The treatment to cure TB is** a combination of several antibiotics. Debi named standard drugs used for TB such as isoniazid and rifampin.
- **When Debi started the treatment,** she initially got better.

Sentence 3

- **Debi's health began improving when she started the drug therapy for TB because** the bacteria that caused her tuberculosis were killed (or their growth was inhibited) by the drugs she was taking.



The Debi French example reminds students of the major concept of the activity: One explanation for the re-emergence of infectious diseases is resistance of the causative agent to the treatment that once cured infections of that agent. The important public health issue is avoiding inappropriate use of antibiotics as a way to minimize, or at least delay, the evolution of resistant pathogens.

Sentence 4

- On Valentine’s Day 1994, Debi learned that her tuberculosis was active again.
- The drugs Debi took to cure her TB were not working because the bacteria that caused her TB had become resistant to the drugs.

Sentence 5

- Debi had a relapse (developed an active case of TB again), even though her health had improved and she was still taking the drugs to cure TB, because the initial treatment killed some of the disease-causing bacteria, but those that were resistant survived. They continued to multiply, passing their resistance on to their progeny. As a result, the disease in Debi’s lungs returned. But now, the disease-causing bacteria were all resistant to the drugs she was taking and the drugs were no longer able to cure her. Point out to students that this is an example of natural selection: The resistant bacteria survived and passed the genes for resistance on to their progeny, whereas the susceptible bacteria did not survive. Soon, all or most of the bacterial population, descendants of the resistant organisms, were resistant.

Sentence 6

- Debi was finally cured of TB by taking other drugs that were still able to kill the tuberculosis bacteria and by surgical removal of the upper third of one lung that had the greatest concentration of bacteria.
- Debi’s warning about infectious diseases like TB is not to be fooled by little bacteria. In her words, they are “stubborn” and develop ways to survive. A scientist would say that bacteria rapidly evolve resistance to the drugs we use to treat infections caused by those organisms.

7. Point out to students that while it was appropriate to treat Debi with the antibiotics that are usually effective in treating TB, it is not appropriate to use antibiotics to treat illnesses that are caused by viruses. Elicit an explanation of the dangers of this practice by asking a question such as, “Although an antibiotic doesn’t help you get over a viral infection, if you didn’t know any better, you might think it wouldn’t do any harm. But you know better. Explain what negative consequences can result from inappropriate use of antibiotics.”

Students should be able to explain that using antibiotics will select for bacteria that are resistant. Subsequent infections—either in the same person or in someone who is infected by the first person—will be caused by disease-causing bacteria that are resistant, and successful treatment will be much more difficult or even impossible. This line of logic requires extrapolation of the ideas students developed from their bacterial growth experiment and the Debi French story, so you may need to help them develop their explanation by giving them additional information and asking probing questions such as, “What if the antibiotic taken by a person who has a bacterial infection doesn’t kill all the disease-causing bacteria? What can you say about the

bacteria that survive?” and “Research experiments have shown that harmless bacteria that become resistant to antibiotics can transfer that resistance to other bacteria, including disease-causing bacteria. How does this help explain why doctors don’t want to prescribe antibiotics for viral infections?”

You may want to tell students that the evolution of antibiotic-resistant pathogens is a problem in treating more diseases than TB. For example, many strains of the organism that causes the sexually transmitted disease gonorrhea (*Neisseria gonorrhoeae*) and most strains of a common organism that causes many skin infections (*Staphylococcus aureus*) are now resistant to penicillin. Students consider a proposal to develop a new treatment for multiple-drug-resistant *Staphylococcus aureus* in Lesson 5, *Making Hard Decisions*.



This step provides an opportunity to evaluate students’ understanding of the evolution of antibiotic resistance and its relevance to personal and public health.

8. Give each group one copy of Master 3.5, *Antibiotic Concerns*, and assign one of the three statements to each group. Explain that each statement describes an example of an inappropriate or potentially inappropriate use of antibiotics. Instruct the groups to develop a brief public service announcement that would persuade the general public not to use antibiotics inappropriately. The announcement should be something that could be read on the radio, featured in a television commercial, or displayed on a public bulletin board. Collect the announcements and read several to the class; display all of them on a bulletin board in the classroom.

Laboratory Preparation for Lesson 3

1. *Three weeks before conducting the lesson.* Order the following materials from Carolina Biological Supply (<http://www.carolina.com>):
 - *Pseudomonas fluorescens* culture, item #15-5255
 - nutrient broth, item #78-5360
 - nutrient agar, item #78-5300
 - kanamycin, item #21-6881

Allow two weeks for delivery.

2. *One week before conducting the lesson.* Prepare the following additional materials:
 - petri dishes (at least 6 per group)
 - sterile, capped test tubes (about 4 per group)
 - sterile 1-mL pipets
 - pipet pumps or bulbs
 - glass rod spreaders
 - Bunsen burners
 - alcohol (for sterilizing the glass spreaders)
 - facilities for sterilizing and preparing growth media
 - disinfectant
 - grease pencils for labeling

3. Prepare a stock solution of 25 mg/mL kanamycin in water and filter-sterilize it into a sterile test tube.
4. Prepare nutrient broth medium and nutrient agar plates following the directions on the packages. For medium containing kanamycin, aseptically add 2 mL of the stock kanamycin solution per liter of medium after the medium has cooled (but before the agar solidifies, in the case of plates).
5. Dispense 5-mL aliquots of nutrient broth into sterile, capped test tubes. You will need 2 test tubes of nutrient broth and 1 test tube of nutrient broth containing kanamycin for each group. You will also need 3 nutrient agar plates and 3 nutrient agar plates containing kanamycin for each group. We recommend preparing extras to allow for contamination and errors.
6. Inoculate 1 nutrient broth tube with *P. fluorescens* for each group 2 days before Day 1 of the lesson (use a 0.1-mL inoculum). Incubate these cultures at 25°C.

If students are unfamiliar with aseptic technique, you will need to provide that instruction before they begin the experiment: Hands, equipment, and counter tops should be washed with a commercial disinfectant or with household bleach diluted 30-fold with water. You should also identify a place for students to discard their used cultures and explain that you will decontaminate all materials before disposal.



For classes with access to the Internet:

You may want to demonstrate these techniques by showing the *Day 1* segment of *Bacterial Growth Experiment on the Web* site. This segment shows students completing the first four steps of the experiment and observing aseptic techniques such as using sterile pipets, flaming the open mouth of a test tube before replacing the cap, and sterilizing and using a glass rod to spread a culture sample on a plate. The video also shows students observing safety practices such as tying back long hair, wearing lab coats and safety goggles, and washing their hands.

The *P. fluorescens* that is cultured in nutrient broth or on nutrient agar will grow up in 24 hours; however, the cultures in media containing kanamycin will take two or three days. We recommend that after 24 hours of incubation, you refrigerate students' cultures in media without kanamycin (broth culture A and Plates 1, 3, and 5). This will prevent overgrown cultures that may obscure the results.

Decontaminate all cultures when students have completed their work. Place used cultures in an autoclave at 1 atmosphere pressure for 15 minutes to kill bacteria. Place plastic petri dishes in heat-resistant plastic bags before autoclaving because the dishes will melt and leak. You can also use a kitchen pressure cooker to kill bacterial cultures.

Lesson 3 Organizer

What the Teacher Does	Procedure Reference
DAY 1 (5–7 days before Day 3 of the lesson)	DAY 1
Remind students of the theory of evolution. Explain that <i>theory</i> in science means a well-accepted explanation about some natural phenomenon, backed up with a great deal of scientific evidence.	Page 73 Step 1
Organize students into groups of three. Challenge groups to use what they understand about evolution by natural selection to write a hypothesis about what will happen in a population of bacteria that grows for several generations in the presence of an antibiotic.	Page 74 Step 2
Ask several groups to share their hypotheses in a class discussion. As a class, work together to refine the hypotheses into one similar to the following: <i>If a bacterial culture is grown in a medium containing an antibiotic, then after several generations, all the bacteria in the culture will be resistant to the antibiotic.</i>	Page 74 Step 3
<ul style="list-style-type: none"> • Tell students that they will conduct an experiment to test the hypothesis. Using aseptic technique, they will also consider what their results can tell them about controlling infectious diseases. (If you have chosen not to do the hands-on lab, please see page 74 for an alternative, Web-based approach.) • Give each student a copy of Master 3.1 and tell them to complete Steps 1 to 4 with their group members. 	Page 74 Step 4 
DAY 2 (2–3 days before Day 3 of the lesson)	DAY 2
Direct groups to complete Steps 5–8 on Master 3.1b .	See master 
DAY 3	DAY 3
Tell students that they will now analyze their bacterial growth experiment and use the results to explain what happened to a student who had tuberculosis.	Page 74 Step 1
<ul style="list-style-type: none"> • Have students return to their groups, and tell them to collect their bacterial growth plates. • Give each student a copy of Master 3.2. Tell groups to draw (or describe) their results on the flow chart on Master 3.1 first and then refer to the results as they discuss and write answers to the questions on Master 3.2. As groups work, circulate among them and help students reach the appropriate understandings. 	Page 75 Step 2 

What the Teacher Does	Procedure Reference
Hold a brief class discussion to clarify any answers to questions on Master 3.2 and to allow students to ask questions about the experimental results.	Page 77 Step 3
<p>For classes with Internet access, Steps 4 and 5 (preferred)</p> <ul style="list-style-type: none"> • Tell students to watch a short video of a young woman discussing her battle with tuberculosis. They will then use what they have learned in their experiment to help explain what happened in this person’s struggle with the disease. • Give each student a copy of Master 3.4. Allow approximately 20 minutes for students to watch the video and answer the questions on the master. 	Page 77 Steps 4 and 5  
<p>For classes without Internet access, Steps 4 and 5</p> <ul style="list-style-type: none"> • Tell students they will learn about a young woman and her battle with tuberculosis. They will then use what they have learned in their experiment to help explain what happened in this person’s struggle with the disease. • Give each student one copy each of Masters 3.3 and 3.4. Allow about 20 minutes for students to read Master 3.3 and answer the questions on Master 3.4. 	Page 78 Print Steps 4 and 5  
Convene a class discussion and ask several groups to share their responses to the questions on Master 3.4 . Conclude the discussion by asking, “What explanation does the Debi French example suggest for the re-emergence of diseases like tuberculosis?”	Page 78 Step 6
Point out that it is not appropriate to use antibiotics to treat illnesses caused by viruses. Assess students’ understanding with the following situation: “Although an antibiotic doesn’t help you get over a viral infection, if you didn’t know any better, you might think it wouldn’t do any harm. But you know better. Explain what negative consequences can result from the inappropriate use of antibiotics.”	Page 79 Step 7
Give each group a copy of Master 3.5 . Assign one of the three inappropriate (or potentially inappropriate) statements to each group. Ask groups to develop a brief public service announcement that would persuade the general public not to use antibiotics inappropriately.	Page 80 Step 8 

Note: Shaded text highlights the steps for classes with access to the Internet.



= For classes without access to the Internet.

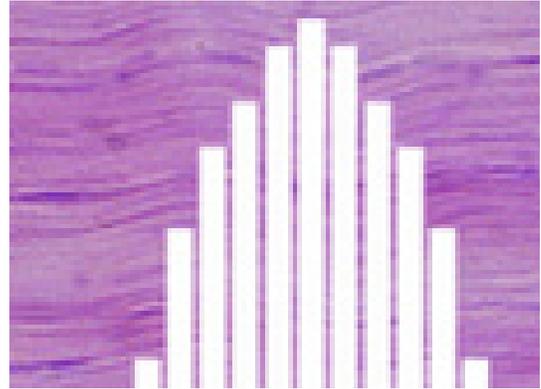


= Involves copying a master.



= Involves using the Internet.

Protecting the Herd



Overview

Students use in-class and Web-based simulations of the spread of an infectious disease through a population to discover the phenomenon of herd immunity.

Major Concepts

The re-emergence of some diseases can be explained by the failure to immunize enough individuals, which results in a greater proportion of susceptible individuals in a population and an increased reservoir of the infectious agent. Increases in the number of individuals with compromised immune systems (due to the stress of famine, war, crowding, or disease) also explain increases in the incidence of emerging and re-emerging infectious diseases.

Objectives

After completing this lesson, students will

- be able to explain how immunizing a significant proportion of a population against a disease prevents epidemics of that disease (herd immunity),
- be able to list factors that affect the proportion of a population that must be immunized to prevent epidemics, and
- understand how large-scale vaccination programs help control infectious diseases.

Prerequisite Knowledge

Students should be familiar with how immunization protects individuals from infectious diseases.

Basic Science–Public Health Connection

This lesson introduces students to modeling as a scientific exercise. Students learn how models based on observations of disease transmission can be used to predict the likelihood of epidemics and to help public health officers recommend policies to protect the public from infectious diseases.

At a Glance

Introduction

Global vaccination strategies are a cost-effective means of controlling many infectious diseases. Because immunized people do not develop diseases that must be treated with antimicrobial drugs, opportunities for pathogens to evolve and disseminate drug resistance genes are reduced. Thus, mass immunization reduces the need to develop newer and more expensive drugs.

As long as a disease remains endemic anywhere, vaccination programs must be maintained everywhere. This is because an infected person can travel anywhere in the world within 24 hours. Once global vaccination programs eliminate the infectious agent (as in the case of the smallpox virus), vaccination is no longer necessary, and the expense of those programs is also eliminated. It is estimated that the United States has saved \$17 billion so far as a result of the eradication of smallpox (which cost, according to the World Health Organization, \$313 million across a 10-year period).

Lapses in vaccination programs explain the re-emergence of some infectious diseases. For example, the diphtheria outbreak in Russia in the early 1990s may have been due to lapses in vaccination programs associated with the breakup of the Soviet Union. Inadequate vaccines and failure to obtain required “booster shots” also explain some disease re-emergence. The dramatic increase in measles cases in the United States during 1989–1991 was likely caused by failure to give a second dose of the vaccine to school-age children. The American Academy of Pediatrics now recommends that all children receive a second dose of the measles vaccine at either ages 4–6 or 11–12 years.

Seasonal vaccination for influenza is one of the most underused preventive measures in the United States. Morbidity and mortality might be mitigated if there were better compliance with vaccination recommendations.

This lesson and Lesson 3, *Superbugs: An Evolving Concern*, both provide explanations for the re-emergence of some infectious diseases. Lesson 3 explained that some re-emerging diseases are due to the evolution of antibiotic resistance among pathogens. Lesson 4, *Protecting the Herd*, introduces students to the idea that the re-emergence of other infectious diseases can be explained by a failure to immunize a sufficient proportion of the population. On the first day of the lesson, students learn that epidemics can be prevented by immunizing part of the population, leading to herd immunity. The concept of herd immunity is elaborated in the optional, second day of the lesson. Here, students learn that the threshold level of immunity required to establish herd immunity (and thus prevent epidemics) varies depending on the transmissibility of the disease, the length of the infectious period, the population density, and other factors.

For Day 1

In Advance

Photocopies and Transparencies	Equipment and Materials
<ul style="list-style-type: none">• 1 copy per student of Masters 4.1, 4.2,• 2 copies per student of Master 4.3• 2 transparencies of Master 4.3	<ul style="list-style-type: none">• 1 overhead projector• red, pink, and black cards (1 of each per student)• folded pieces of paper labeled “immune” and “susceptible” (make enough of each for half the students)

(Optional) For Day 2

Photocopies and Transparencies	Equipment and Materials
<ul style="list-style-type: none">• 1 copy per student of Master 4.4• 1 transparency of Masters 4.5 and 4.6	<ul style="list-style-type: none">• 1 overhead projector• blank transparencies• (Optional) Computers with access to the Internet

Note to teachers: If you do not have enough computers with Internet access, you will not be able to conduct the optional Day 2 of this lesson.

DAY 1

Procedure

1. Introduce the lesson by distributing one copy of Master 4.1, *Measles Outbreak at Western High*, to each student and asking the students to read it.

The scenario described on *Measles Outbreak* is fictitious, but it's based on an outbreak of measles that occurred in Washington State in 1996.

An alternate way to introduce the lesson is to assign students to make a list of the childhood diseases that they, their parents (or someone from their parents' generation), and their grandparents (or someone from their grandparents' generation) had. Explain that “childhood diseases” means diseases that people usually have just once and do not get again (for example, chicken pox). Explain that you do not mean diseases like the flu, strep throat, and colds. On the day you wish to begin the lesson, ask students to name some of these diseases, then ask them to count the *number of different diseases* each generation in their family had. Total these numbers across all of the students in the class and ask students to suggest why (in general) their parents and grandparents had more diseases than they did. Students likely will suggest (correctly) that vaccination against many diseases is now available.



This is an opportunity to point out that research in microbiology and related disciplines in the past 50 years has led to the development of many vaccines in addition to the measles vaccine. Children of the 1990s who receive recommended vaccinations are protected from many infectious diseases that plagued children in the past, including diphtheria, whooping cough, measles, hepatitis B, and chicken pox.

2. **After students have read Master 4.1, ask them to speculate about what might have happened to cause a sudden outbreak of a disease such as measles that normally, today, is relatively rare in the United States.**

Students will likely know that most children in the United States today are vaccinated against measles. They may speculate that the students at Western High were not vaccinated, or that the vaccine did not work in their cases, or even that the pathogen causing this form of measles was somehow able to evade the immune defenses that had been triggered by the vaccinations these children received.

3. **Distribute one copy of Master 4.2, *A Little Sleuthing*, to each student, and ask the students to read the story and think about the question that ends it.**
4. **Point out that despite the success of the measles vaccine, there continue to be small outbreaks of measles in the United States. Explain that the key to understanding why this is true and to answering the question that ends the story about Western High lies in understanding how disease spreads in a population.**
5. **Explain to students that to help them understand how disease spreads in a population, they will participate in a simulation of the spread of a fictitious disease you will call the “two-day disease.” Give two copies of Master 4.3, *Following an Epidemic*, to each student and display a transparency of this master. Then, direct students to perform two simulations of the spread of two-day disease, according to the instructions provided on pages 95–97, immediately after the lesson.**

An “epidemic” is typically defined as “more cases of a disease than is expected for that disease.” Although this is not a very specific definition, it does make clear that whether scientists call an outbreak of a disease an epidemic depends on the specific disease involved. Though there is no distinct line between an “outbreak” and an “epidemic,” epidemics are generally considered to be larger in scale and longer lasting than outbreaks. Today, five cases of measles within a population could be considered an epidemic because no cases are expected.

For this simulation, assume that an epidemic is in progress if 25 percent or more of the population is sick at one time.

Observations that students might make about the table and graph that result from the first simulation include

- an epidemic occurred because a large portion of the class was sick at the same time;
- at the beginning of the epidemic, only a few people were sick in the same day; in the middle of the epidemic, a lot of people were sick at the same time; and at the end, only a few people were sick;

- by the end of the simulation, everyone was immune; and
- once it started, the disease spread rapidly.

Observations that students might make about the table and graph that result from the second simulation include

- only a few people were sick on any one day;
- no epidemic occurred;
- at the end of the simulation, some people were still susceptible; and
- some people in the population never got sick.

Tip from the field test: Do a practice run of several days of the simulation before you do the runs in which you collect data. This will allow you to address any confusion students have about the simulation and will make subsequent runs go much faster. If you have time, you may want to repeat the simulation, especially the second one, in which half the class is immune. In order for students to observe herd immunity, some susceptible students in the population should not get sick. Depending on the arrangement of immune and susceptible students in the class (which is random), this may not happen the first time you run this simulation.

6. Debrief the activity by asking, “Why did an epidemic occur in the first population but not in the second?” and “Why didn’t all the susceptible people in the second population get sick?” Introduce the term “herd immunity” and describe it as a phenomenon that occurs when most of the people in a population are immune to an infectious disease. Susceptible people in the population are protected from that disease because the infectious agent cannot be transmitted effectively.

Allow students to discuss their responses to the two questions before you introduce the term herd immunity. Students will likely make comments such as, “Everyone sitting near John was immune, so the disease just died out.” At that point, you can respond by saying, “Yes, what you have just explained is what epidemiologists call *herd immunity*.” Then you can provide a more complete definition.

7. Ask students to explain, based on their experience in the disease-transmission simulation, what would happen if measles vaccinations dropped to a low level in a population.

Students should be able to explain that there would be many susceptible people in the population, so the disease would be transmitted from one to another without dying out. A measles outbreak or epidemic would occur. If students do not mention “re-emergence,” emphasize this point by saying, “Yes, measles would re-emerge in the population.”



This step takes students to the major concept of the activity: The re-emergence of some diseases can be explained by immunity levels that are below the level required for herd immunity.



Collect and review students' paragraphs to assess their understanding of the major concept of the activity. Address common misunderstandings in the next class session and read two or three of the best paragraphs to the class.

8. Remind students about the measles-outbreak story. Ask them to write a final paragraph to the story in which they use the term *herd immunity* to answer the following questions:

- Why didn't the unvaccinated or inadequately vaccinated students and teacher at Western High get measles when they were children rather than as teenagers or adults?

Students should be able to explain that the unvaccinated or inadequately vaccinated students at Western High were protected by herd immunity when they were younger: Because most of the people around them were immune, the infectious agent could not be transmitted from those people.

- Why is vaccination not only a personal health issue, but also a public health issue?

Vaccination is a public health issue because maintaining high levels of immunity in a population prevents epidemics and protects the small percentage of susceptible people from the disease.

DAY 2 (Optional) For classes with access to the Internet



1. Open the activity by reminding students about two-day disease and the simulation they completed. Then, ask them what characteristics may vary between two-day disease and other diseases. Point out that differences in these characteristics affect the likelihood that an epidemic of a particular disease will occur and the percentage of the population that must be immune to that disease to achieve herd immunity.

Expect students to suggest that people who are sick may contact more than one person per day, may be sick (and infectious) for more than two days, may die from the disease, and may not get sick from just one contact. Students may also point out that the disease may require "intimate" rather than casual contact, or it may not require person-to-person contact.

2. Ask students to predict what the results of the simulation would be if they varied each of four characteristics of the disease: virulence (the likelihood of dying from the disease), duration of infection, rate of transmission (how contagious the disease is), and level of immunity in the population. Insist that students provide some rationale for their predictions. Write their predictions on the board or a blank transparency.

To help students think about this, you may wish to ask questions such as, "Do you think there would have been an epidemic of two-day disease if people sometimes died from the disease? If so, do you think it would have been a more or less severe epidemic?"

Virulence, duration of infection, rate of transmission, and level of immunity are the four parameters that the computer simulation will allow students to vary. Students may make predictions such as, “The more virulent a disease is, the greater the likelihood of an epidemic,” or “The higher the immunity level of a population, the less likely it is that an epidemic will occur.”

3. Tell students they will use a computer simulation to investigate the likelihood of an epidemic when they vary one of the four characteristics they just discussed. Give one copy of Master 4.4, *Disease-Transmission-Simulation Record*, to each student and ask students to work in their groups. Assign each group one of the four characteristics to investigate and direct students to circle this characteristic on the master.

Tell students that because the computer simulation uses a larger population size, an epidemic is defined as an outbreak of disease in which 10 percent or more of the population is sick at one time.

4. Tell students to go to this part of the Web site and click on “Protecting the Herd”: <http://science.education.nih.gov/supplements/diseases/activities/>. Explain briefly how to use the simulation, then direct students to use it to test their assigned characteristic. Explain that groups should test four different levels of their assigned characteristic and that they have 15 minutes to complete this work before reporting their findings to the class.

You may wish to explain the following features of the simulation:

- Users can set each disease characteristic at a variety of levels (as indicated on the screen).
- Users can have the simulation run automatically for 30 days or step through those days one by one, depending on the button they click.
- To repeat a run or to change the settings and do another run, users must click the Reset button.
- Once a run begins, users cannot change the settings unless they click the Reset button.

You may want to suggest that the groups that were assigned the virulence characteristic select four levels from the low end of the available range (less than 0.1 or 0.2) to test. Because of the levels students will be using for duration of infection and rate of transmission, any disease that has moderate to high virulence rapidly dies out in a population. Students will have more interesting results if they use the lower levels for virulence.

A range from 0.001 to 0.1 encompasses estimated rates of transmission for many infectious diseases. The algorithm for this simulation assumes that each infected person makes 100 contacts per day. Thus, the range of settings available to students is 0.1 (0.001×100) to 10 (0.1×100). The simulation would have to be adjusted for populations that are more or less dense than the one assumed by the simulation.

5. Reconvene the class and ask questions such as, “Did your predictions match what you discovered using the simulation?” or “Were you surprised by the results of the simulation?” Ask one of the groups that investigated the effect of varying virulence level to read its summary statement to the class. Invite other groups that investigated that characteristic to add more information to the statement or to disagree with it. Repeat this process for the other three characteristics the groups investigated.

Students should have discovered the following, according to the computer simulation:

Virulence. A disease that is not very virulent remains at a low level in the population, whereas diseases that are quite virulent rapidly die out. Real disease examples that show this are colds and Ebola hemorrhagic fever. Colds are not very virulent, and infected individuals remain contagious for several days. Thus, colds tend to remain at a fairly constant low level in the population. Ebola fever is very virulent (50 to 90 percent mortality) and death occurs shortly after infection, lessening the opportunities for an infected individual to spread the virus beyond his or her immediate surroundings. Therefore, at least until recent improvements in travel in areas where Ebola has occurred, it tended to occur in isolated outbreaks that died out fairly quickly.

Duration of infection. As the duration of infection increases, infected individuals have more opportunities to transmit the infection to others. In turn, each secondarily infected individual has more opportunity to infect still others. Therefore, because larger numbers of people become infected within a short period of time, epidemics become apparent sooner after introduction of infected individuals into the population, reach a higher peak incidence, and last longer. Real disease examples showing this are influenza and chicken pox.

Rate of transmission. According to the computer simulation, a disease dies out at low levels of transmission, whereas it stabilizes and becomes endemic at high levels. Real disease examples of this include malaria and many diarrheal diseases. Public health measures and access to medical care result in dramatically decreased transmission of these diseases in the United States, but they remain endemic in developing countries where such public health measures and medical care are not readily available.

Initial percent immune. With virulence, duration of infection, and rate of transmission set at the values for two-day disease, the computer simulation predicts that an epidemic will not occur when the proportion of immune people in the population is greater than 15 percent.

6. Explain to students that computer simulations such as the one they have explored are useful tools for epidemiologists, who use them to make predictions about the likelihood that an epidemic will occur in a particular population or to estimate the level of vaccination coverage they must achieve to prevent epidemics in the population.
7. Challenge groups to use the simulation to estimate the level of immunization required to prevent epidemics of three real diseases: smallpox, polio, and measles. Assign each group one of the diseases and display the transparency of Master 4.5, *Characteristics of Smallpox, Polio, and Measles*, which provides the settings they need for the simulation. Tell groups they have 10 minutes to complete their work.

Smallpox was declared eradicated from the world in 1980. Because epidemiologists knew it would not be possible to vaccinate everyone in the world, they used mathematical models of the spread of disease to estimate the level of vaccination coverage they needed to achieve and maintain to establish herd immunity in a population. (The computer simulation in this activity is based on a similar mathematical model.) Epidemiologists knew smallpox would eventually be eliminated because there would not be enough susceptible people to transmit the smallpox virus. Polio and measles are among the next targets for global eradication.

8. Poll groups for their results and add them to the appropriate column of Master 4.5. Explain that epidemiologists using more sophisticated simulations make similar predictions: 70 to 80 percent for smallpox; 82 to 87 percent for polio; and 90 to 95 percent for measles.

On the basis of the computer simulation, students should suggest the following percentages be vaccinated to avoid an epidemic:

- smallpox—no epidemic if 78 percent or more of the population is immune;
- polio—no epidemic if 86 percent or more of the population is immune;
- measles—no epidemic if 90 percent or more of the population is immune.

The critical proportions of the population to be immunized for eradication, above, are reported by Anderson and May (1992). You may want to write those percentages beside the students' findings.

9. Explain to students that the predictions made by models are sometimes inaccurate: A predicted epidemic may or may not occur in a real population. These comparisons between actual disease epidemics and epidemics predicted by models reveal the limitations of a model. For example, additional factors, not accounted for by a model, may have an impact on the spread of a disease.
10. As an example of the limitations of their model of the spread of a disease, display a transparency of Master 4.6, *Cases of Smallpox in Niger and Bangladesh*. Tell students to make an observation about how accurate their prediction for smallpox was for each of the two countries.

Students should observe that, even though both countries had about the same level of vaccination coverage (79 percent for Niger and 80 percent for Bangladesh), outbreaks of smallpox apparently occurred in Bangladesh (0.23 cases per square kilometer) but not in Niger (0.00002 cases per square kilometer). The students' model predicted that if 76 percent of the population is immune, such outbreaks would not occur.

11. Ask students to suggest factors their model did not take into account that may explain discrepancies between their prediction and the actual result in Bangladesh. Then, add the following information to the transparency: In 1969, Niger had 310 people per square kilometer, while in 1973, Bangladesh had 50,000 people per square kilometer.

Students may note that crowded conditions will affect the spread of a disease because a sick person would be able to contact and transmit the disease to more people. This "population density" factor appears to be the explanation for the occurrence of outbreaks of smallpox in Bangladesh even though recommended levels of vaccination had been achieved. (The impact of different population densities is not accounted for in the computer simulation in this activity, which assumes the same population density for all populations.)

Other factors not accounted for in the simulation that also may affect the likelihood of epidemics include the general health of the population, the nutritional status of the population, and the level of sanitation in the population. Point out that the immune system is stressed when it is combating a disease, so people who are already sick are more susceptible to additional diseases. Similarly, good nutrition is essential for a healthy immune system, so people who are malnourished are likely targets for pathogens. Unsanitary conditions provide greater opportunities for transmission of infectious agents. All these factors will increase the proportion of the population that must be immune to achieve herd immunity.



This step gives students an opportunity to revisit the idea of herd immunity and to reflect on their expanded understanding of the concept.

12. Ask students to think about the ways they used the computer simulation in this lesson and what the results of their simulations revealed about the spread of diseases. Then, ask them to write down one thing they learned from the activity. Ask several students to share what they learned and clarify anything that students have misunderstood.

The major point of this activity is that the characteristics of diseases vary and these characteristics have an impact on the likelihood of epidemics. Similarly, these characteristics have an impact on the percentage of people in a population who must be vaccinated to achieve herd immunity.

The World Health Organization's Web site includes information on infectious diseases targeted for eradication. Ask students to review the site and report 1) the vaccination coverage goal for a particular disease, 2) the challenges that face healthcare workers for meeting that goal, and 3) the strategies epidemiologists are using to meet their goals.

The address for the site is <http://www.who.org/aboutwho/en/disease-er.htm>.

Potential Extensions

The disease-transmission simulation simulates the spread of two-day disease in a population. Explain to students that during the first simulation, all the students will be susceptible to two-day disease. When 25 percent or more of the class is sick, the class is experiencing an epidemic.

Give each student one red card, one pink card, and one black card. Explain that on the first day they become sick, they will hold up a red card. On the second day of their illness, they will hold up a pink card, which signifies that they are recovering but still infectious. On the third day, they will hold up a black card to show that they have recovered and are immune. They will hold the black cards and remain immune until the simulation ends.

Tip from the field test: Have the students stack the cards with black on the bottom, pink in the middle, and red on top.

Simulating the Transmission of Two-Day Disease

Simulation 1 0% immune, 100% susceptible

1. Write "Simulation #1: 0% immune, 100% susceptible" at the top of one of the transparencies of **Master 4.3, *Following an Epidemic***. Tell students to do the same on one of their copies of Master 4.3.

2. Identify one student sitting in the center of the class to be the individual who introduces the disease to the population. Tell that student to pick up his or her red card. This is **Day 1**. On the transparency, tally the number of currently sick people and the number currently immune. Tell students to record those results on their copies as well.
3. Tell the sick student to tap one person *he or she can reach from a seated position*, then announce the end of **Day 1**.
4. Announce the beginning of **Day 2** and remind the original sick student that he or she is still sick but recovering and should be holding the pink card. Remind the tagged student that he or she is now sick and should be holding the red card. Complete the **Day 2** row of the table, asking students to do the same.
5. Tell the sick students to tag other students *they can reach from their seated position*. Announce the end of **Day 2**.
6. Announce the beginning of **Day 3**. The original sick student should now put down the pink card and pick up the black card to indicate that he or she is immune. The student tagged first should put down the red card and pick up the pink card. The newly tagged students should pick up their red cards. Complete the **Day 3** row of the table.
7. Tell the sick students to tag other students they can reach from a seated position. Announce the end of **Day 3**.
8. Repeat Steps 6 and 7 until all students have had the illness or until transmission of the disease stops because there are no susceptible students near sick students.
9. Ask students to raise their hands if they were sick at some point during the simulation. Count the number of hands and record this number at the bottom of the transparency.
10. Plot the data from the table on the graph and draw the curve on the graph. Tell students to do the same and then ask them to make three or four observations about the table and graph the class has created.

Simulation 2

50% immune, 50% susceptible

1. Write “Simulation 2: 50% immune, 50% susceptible” at the top of the other transparency of **Master 4.3**. Tell students to do the same on their other copy.
2. Tell students to restack their cards, with black on the bottom, pink in the middle, and red on top.

3. Explain that they will complete the simulation again, but this time half of the students in the class will be immune to the disease. Note that, as is often the case in real life, students will not know who is immune and who is susceptible. Give half the students, chosen at random, a folded card that says “immune,” and give the other half a folded card that says “susceptible.” **They should read their card, but they should not share this information with anyone.**
4. Explain that if they received a card that says “immune,” they are not to pick up their black cards until they are tapped by a sick student. Write the number of immune cards you distributed in the “Day 1, Number of People Immune” cell on the transparency and tell students to do the same on their second copy of the table. This is the initial number of immune people.
5. Identify one student sitting in the center of the class to be the individual who introduces the disease to the population. Tell that student to pick up his or her red card. This is **Day 1**. On the transparency, tally the number of currently sick people and the number currently immune. (For the latter, add the number of people who were sick and have recovered to the number who were already immune.) Do *not* ask students to indicate by a show of hands how many people are immune, because this may influence the choices students make as they transmit the disease. Tell students to record the number of sick and the number immune on their copies as well.
6. Continue the simulation as before, but this time, when an immune student is tapped, he or she should immediately hold up the black card and the card that says immune. He or she is not infectious and so will not tap another student. (Do **not** add this person to the number who are currently immune, because he or she was already included in the initial count of immune individuals.)
7. Continue until either all students are immune or have had the illness, or until transmission of the disease stops because there are no susceptible students near sick students.
8. Ask students to raise their hands if they were sick at some point during the simulation. Count the number of hands and record this number at the bottom of the transparency.
9. Plot the data from the table to the graph and draw the curve on the graph. Tell students to do the same and then ask them to make three or four observations about the table and graph the class has created.

Lesson 4 Organizer

What the Teacher Does	Procedure Reference
DAY 1	DAY 1
Give each student a copy of Master 4.1 and ask students to read it.	Page 87 Step 1 
Ask students to speculate about the cause of a sudden outbreak of a disease such as measles that is normally relatively rare in the United States.	Page 88 Step 2
Give each student a copy of Master 4.2 and ask students to read the story and think about the question at the end.	Page 88 Step 3 
Point out that even with a successful vaccine, there continue to be small outbreaks of measles in the United States. Tell students that to understand why this is true—and why unvaccinated or inadequately vaccinated people get measles as teenagers or adults—they need to understand how disease spreads in a population.	Page 88 Step 4
Explain that students will participate in a simulation that will help them understand how disease spreads in a population. The fictitious disease is called “two-day disease.” Give each student two copies of Master 4.3 and display this master. Explain that students will use these handouts to record the simulation data.	Page 88 Step 5  
Conduct the simulation: Follow <i>Simulating the Transmission of Two-Day Disease</i> instructions.	Page 95–97
Ask students to discuss the following questions: <ul style="list-style-type: none"> • Why did an epidemic occur in the first population but not in the second? • Why didn’t all of the susceptible people in the second population get sick? Introduce the term <i>herd immunity</i> : a phenomenon that occurs when most of the people in a population are immune to an infectious disease. Susceptible people are protected from the disease because the infectious agent cannot be transmitted effectively.	Page 89 Step 6
Ask students to explain, based on what they learned from the simulations, what would happen if measles vaccinations dropped to a low level in a population.	Page 89 Step 7
Remind students of the measles-outbreak story they read earlier. Ask them to write a final paragraph for the story using the herd-immunity concept to answer the following questions: <ul style="list-style-type: none"> • Why didn’t the unvaccinated or inadequately vaccinated students and teacher at Western High get measles when they were children rather than as teenagers or adults? • Why is vaccination not only a personal health issue, but also a public health issue? 	Page 90 Step 8

What the Teacher Does	Procedure Reference
<p>DAY 2 (Optional) Note: Only for classes with access to the Internet.</p>	<p>Day 2 </p>
<p>Remind students of the two-day-disease simulation they did. Ask what characteristics may vary between two-day disease and other diseases. Point out that differences in these characteristics affect</p> <ul style="list-style-type: none"> • the likelihood that an epidemic will occur and • the percentage of the population that must be immune to achieve herd immunity. 	<p>Page 90 Step 1</p>
<p>Ask students to predict the results of the simulation if they varied each of the four characteristics of the disease:</p> <ul style="list-style-type: none"> • virulence (the likelihood of dying from the disease) • duration of infection • rate of transmission (how contagious the disease is) • level of immunity in the population. <p>Insist that students provide rationale for their predictions. Display predictions.</p>	<p>Page 90 Step 2</p>
<p>Tell students they will use a computer simulation to investigate the effects of varying one of the four characteristics. Give each student one copy of Master 4.4 and ask students to work in their groups. Assign each group one of the four characteristics to investigate.</p>	<p>Page 91 Step 3 </p>
<p>Briefly explain how to access and use the simulation. Tell groups they will have 15 minutes to investigate their assigned characteristic and test four different levels of their characteristic. Tell them they will report their findings to the class.</p>	<p>Page 91 Step 4 </p>
<p>Reconvene the class and debrief the simulations using questions such as,</p> <ul style="list-style-type: none"> • Did your predictions match what you discovered using the simulation? • Were you surprised by the results of the simulation? <p>For each characteristic, ask groups to read their summary statements to the class. Ask other groups that investigated the same characteristic to add more information or to disagree with a statement.</p>	<p>Page 92 Step 5</p>
<p>Explain that computer simulations similar to the one they explored are useful tools for epidemiologists, who use them to make predictions about the likelihood of an epidemic or to estimate the level of vaccination coverage necessary to prevent epidemics.</p>	<p>Page 93 Step 6</p>

What the Teacher Does	Procedure Reference
Challenge groups to use the simulation to estimate the level of immunization required to prevent epidemics of three real diseases: smallpox, polio, and measles. Assign each group one of the diseases and display Master 4.5 , which provides the settings needed for the simulation. Allow 10 minutes for groups to work.	Page 93 Step 7  
Poll groups for their results and add them to the appropriate column on Master 4.5 . Explain that epidemiologists using more sophisticated simulations make similar predictions to what they obtained in their simulations: <ul style="list-style-type: none"> • Smallpox: 70 to 80 percent • Polio: 82 to 87 percent • Measles: 90 to 95 percent 	Page 93 Step 8
Explain that predictions made by models are sometimes inaccurate. Comparisons between actual disease epidemics and epidemics predicted by models reveal the limitations of the model. Additional factors not accounted for by the model may have an impact on the spread of the disease.	Page 94 Step 9
Display Master 4.6 . Ask students to make an observation about how accurate their prediction for smallpox was for each of the two countries.	Page 94 Step 10 
Ask students to suggest factors that the model did not take into account that may explain discrepancies between their predictions and the actual result in Bangladesh. Add the following information to the transparency: <p style="padding-left: 40px;">In 1969, Niger had 310 people per square kilometer, while in 1973, Bangladesh had 50,000 people per square kilometer.</p>	Page 94 Step 11
Encourage students to think about how they used the computer simulation in this lesson and what their results revealed about the spread of diseases. Ask students to record one thing they learned from the activity. Ask students to share their ideas and thoughts with the class and clarify misunderstandings.	Page 95 Step 12

Note: Shaded text highlights the steps for classes with access to the Internet.

 = Involves copying a master.

 = Involves making a transparency.

 = Involves using the Internet.

Making Hard Decisions



Overview

Students explore several resources to evaluate proposals to combat AIDS, VRSA, and measles and recommend one proposal to support.

At a Glance

Major Concepts

Infectious diseases have a devastating impact nationally and globally, but a variety of strategies can alleviate suffering due to these diseases. Because resources are limited, allocating funds among projects that address different diseases raises complex ethical questions. Understanding the relevant biological principles can help in making these difficult decisions.

Objectives

After completing this lesson, students will

- understand that proposals to combat infectious diseases can be evaluated using several criteria,
- be able to provide a rationale for accepting or rejecting proposals based on the magnitude of the situation and their likely effectiveness,
- understand that different people will define and weigh criteria differently as they evaluate questions about allocating funds for specific purposes, and
- understand that it is possible for people to hold quite different positions on a controversial topic and still participate in a reasoned discussion about it.

Prerequisite Knowledge

Students should be familiar with problems in controlling infectious diseases, such as the evolution of drug resistance and the challenge of administering vaccines to a significant proportion of the population.

Basic Science–Public Health Connection

Basic research has led to effective treatments and preventive measures to control infectious diseases. In this lesson, students see that implementing these measures is challenging, both financially and logistically, and requires making difficult decisions. Implementation also brings us full circle: The problems we discover as we attempt to control infectious diseases are new problems for research to address.

Introduction

The continuing—and growing—problem of infectious diseases in the world requires funding for studying the factors involved in infectious diseases and their spread, alleviating suffering, and preventing disease where possible. Much of the money spent in the United States to fight infectious diseases is Federal money, allocated through well-established and closely monitored agencies and programs. Some of the money, however, is private money, made available through the beneficence of private foundations and individual donors.

Whether the money is public or private, someone, somewhere, has to decide how to allocate it: to whom it will be given and why, and how it will be spent and where and when. These decisions are not easy. Frequently, they are made by carefully considering many competing requests for funds, and the decisions reflect the degree to which, in the minds of reviewers, the requests meet the funding criteria established for use of the money.

In this lesson, students consider three proposals for spending \$5 million that a private foundation has made available to combat infectious diseases. Each proposal addresses a different infectious disease (AIDS; measles; and vancomycin-resistant *Staphylococcus aureus*, or VRSA) and proposes different actions. Students use three reference databases to learn about each disease and evaluate the proposals on the basis of two criteria: magnitude (how important it is that the situation described in the proposal be addressed now) and effectiveness (how likely it is that the proposed project will address the situation successfully). Finally, students recommend which proposal to fund, provide reasons for their recommendations, and discuss differences in their evaluations as a way to understand how complex such decisions can be.

In Advance

Photocopies and Transparencies	Equipment and Materials
<ul style="list-style-type: none">• 1 copy per student for the print-based version only of Masters 5.1, 5.2, 5.3, 5.4• 1 copy per student of Masters 5.5 and 5.6• 1 transparency of Master 5.7	<ul style="list-style-type: none">• 1 overhead projector• (Optional) Computers with access to the Internet

-
1. Introduce the lesson by saying something like, “We’ve been studying infectious diseases and the reasons why ‘new’ diseases are emerging and ‘old’ ones are re-emerging. What are some of those reasons? What steps can we take to avoid disease emergence and re-emergence? How can research contribute to better ways to control infectious diseases?”

Reasons for disease emergence and re-emergence developed in the previous lessons include environmental changes, indiscriminate use of antibiotics, and failure to vaccinate populations. Steps that can be taken to avoid disease emergence and re-emergence include carefully considering the impact of development in wilderness areas and being alert to the possibility of pathogens having access to a new and/or larger host population, avoiding unnecessary uses of antibiotics, and increasing efforts to enforce vaccination. Research can help us develop better ways to recognize and understand new pathogens, create new or improved antimicrobial drugs to prevent or treat infection, develop new vaccines to protect individuals and the population, and discover new ways to prevent transmission of infection.

2. Continue the discussion by saying something like, “Fighting infectious diseases requires money as well as knowledge. There is a limit, though, to the money available for this. How do people decide where to invest money in fighting infectious diseases?” Entertain some answers, then explain that in this activity, students will consider proposals to fight three different diseases, investigate each of these diseases, and recommend one proposal to fund. Indicate that their recommendations will be based on two criteria, magnitude and effectiveness, which will be described in the activity. Their recommendations must also include reasons for funding one proposal but not the other two.

In the first scenario (see Step 3), the representative of the funding agency explains that students’ recommendations are to be based on the criteria of magnitude and effectiveness, and gives examples of the questions that students must answer to determine the magnitude of each situation and how effective the proposed plan is likely to be. Those and additional questions related to magnitude and effectiveness also appear on Master 5.5, *Proposal Criteria Matrix*.

You may want to indicate to students that there are valid reasons for recommending each proposal. Explain that this activity is like “real life” in that we frequently have to make difficult choices among several “good” options (or among several “bad” options).

Magnitude of the problem and effectiveness of the proposed approach are two criteria that are typically applied in making decisions about a plan to address a societal problem. With regard to infectious disease, magnitude refers to the current burden of illness, as well as the potential for this burden to increase in the future. Effectiveness refers to how well the proposal will alleviate the serious consequences of the disease.

Procedure



This is an opportunity for students to review what they learned in the previous activities and for you to assess their understanding informally. For a more formal assessment of student understanding, ask students to write individual responses to the questions.



Basic research has contributed to the public health management of all three of these diseases. Research on the measles virus in the 1950s and 1960s led to the development of a vaccine to prevent the disease. Research into HIV replication revealed vulnerable points in its infectious cycle, leading to the proteases now used to increase both the quality and the length of life for those who are HIV-positive. Research demonstrating that antimicrobial-resistance genes can be passed from one bacterial species to another alerted health officials to the need for increased surveillance for resistant pathogens and reinforced the need to use antimicrobials prudently and to conduct research to develop new, more effective drugs.

A third criterion—means—is often used to make decisions about plans to address societal problems. Means refers to how well we can accomplish the actions described in the plan. For example, proposing that we spend money to distribute a “cure” for AIDS is not realistic because no cure is available at this time. In this activity, students consider means as part of their evaluation of the second criterion, effectiveness. That is, if a group judges a proposed project to have high “effectiveness,” the group believes there are means available to accomplish it.

Most funding agencies have an established review process and evaluation criteria for proposals submitted to them. NIH uses a peer-review system, that is, external scientists familiar with the health issues, techniques, and research models in the proposals review and make recommendations about the scientific merit of the proposals. NIH specifies five major criteria for evaluation of proposals: significance (similar to the criterion of magnitude in the activity), approach (similar to effectiveness), innovation, experience of the principal investigator(s), and institutional support for the project.

Step 3 for classes with access to the Internet



3. Organize students into their groups and direct them to watch the video segments “Foundation Officer”, “Proposal 1”, “Proposal 2”, and “Proposal 3” on the Web site (<http://science.education.nih.gov/diseases/activities/lesson5>). Then, have them begin their research using the databases on the Web site. Tell the groups that they have 30 minutes to complete their work.

Step 3 for classes without access to the Internet



3. Organize students into their groups. Give each student one copy of Master 5.1, *The Proposals*. Give each group one copy each of Masters 5.2, 5.3, and 5.4, *Reference Databases*. Direct them to read Master 5.1 and then proceed directly into their research using the information provided in the reference databases. Tell the groups that they have 30 minutes to complete their work.
4. Distribute Master 5.5, *Proposal Criteria Matrix*, and Master 5.6, *Proposal Summary Matrix*, as students begin their work. Tell them that at the end of the 30 minutes, each group should be prepared to announce its recommendation and explain its rationale to the class.

While the student groups are conducting their research, move among them to make sure they understand each situation and the questions they are to answer. For example, ask them what each group of applicants proposes to do (AIDS applicants: produce and distribute drugs to HIV-positive individuals; measles applicants: produce and distribute vaccine to susceptible people around the world; VRSA applicants: develop new drug therapies against *Staphylococcus aureus*).

5. Ask each group to identify a spokesperson to tell the class which proposal the group recommends and the reason it selected that proposal. As the groups report their decisions, tally the number recommending each proposal.
6. Invite students to look at the results of the tally and ask them if they can explain the differences, considering that each group worked with the same information.

Students may respond with comments such as, “We thought that, even if the plan had problems, AIDS is so terrible that we should support any plan that could possibly help,” or “We thought that the measles plan had a pretty sure chance of working, whereas the others weren’t as likely to be effective.” Encourage this kind of discussion and point out that some groups gave more weight to the magnitude criterion and others gave more weight to the effectiveness criterion.

If all groups recommended the same proposal, tell them that other evaluators may well have recommended different proposals. Give them some possible rationales for those recommendations and ask them what explanation they can give for the different choices.

7. Display a transparency made from Master 5.7, *Reflection Questions*, and ask each group to work together to list as many responses to each question as they can. Conclude the lesson by asking each group to give one of its answers and list it on the transparency.

Question 1. How did understanding the biology of infectious diseases help you make your decision?

Students may indicate that understanding how natural selection leads to the evolution of antibiotic-resistant bacteria helped them evaluate the likelihood of the emergence of VRSA, or that understanding herd immunity helped them assess the effectiveness of a vaccination program to eliminate measles.

Question 2. What else did you consider in making your decisions?

Students may say that they felt it was important to consider the number of people affected by the disease, or the impact the disease would have on the families of the victims (for example, “AIDS orphans”) or on the countries where the victims live (for example, the loss of productivity due to illness and death of AIDS victims in their prime working years).



Step 7 addresses the activity’s major concept. Students should understand that making policy decisions about spending money to combat infectious diseases is complex and there is typically no one “right” decision. Students also should recognize that understanding the biology underlying such diseases can help inform the decisions that ultimately are made.

Lesson 5 Organizer

What the Teacher Does	Procedure Reference
<p>Tell students, “We’ve been studying infectious diseases and the reasons why ‘new’ diseases are emerging and ‘old’ ones are re-emerging.” Ask the class</p> <ul style="list-style-type: none"> • What are some of those reasons? • What steps can we take to avoid disease emergence and re-emergence? • How can research contribute to better ways to control infectious diseases? 	<p>Page 103 Step 1</p>
<p>Say something like this: “Fighting infectious diseases requires money as well as knowledge. There is a limit, though, to the money available for this. How do people decide where to invest money in fighting infectious diseases?”</p>	<p>Page 103 Step 2</p>
<p>Explain that students will now</p> <ul style="list-style-type: none"> • consider proposals to fight three different diseases, • investigate the three diseases, and • recommend one proposal to fund. <p>Tell them to base their choice on two criteria—magnitude and effectiveness—and to include reasons for their choice (compared with the other two proposals).</p>	<p>Page 103 Step 2</p>
<p>For classes with Internet access (preferred) Step 3 Organize students into groups and have them watch these videos on the Web site: <i>Foundation Officer, Proposal 1, Proposal 2, and Proposal 3</i>. After that, have them use the databases on the Web site to do their research.</p>	<p>Page 104 Web Step 3</p> 
<p>For classes without Internet access, Step 3 Organize students into groups. Give each student a copy of Master 5.1 and each group one copy each of Masters 5.2, 5.3, and 5.4, Reference Databases. Ask them to read Master 5.1 and then start their research using the reference databases.</p>	<p>Page 104 Print Step 3</p>  
<p>Give each student one copy each of Masters 5.5 and 5.6. Tell them to be prepared to share their group’s recommendation and rationale with the class.</p>	<p>Page 104 Step 4</p> 

What the Teacher Does	Procedure Reference
Ask groups to pick a spokesperson to tell the class which proposal they are recommending and why. Tally the number of groups recommending each proposal.	Page 105 Step 5
Ask the class if they can explain why groups may have reached different decisions about the proposals even though they were all using the same information.	Page 105 Step 6
Display Master 5.7 and ask students to work with their groups to list as many responses as they can. Conclude the lesson by asking each group to give one of their answers. Write responses on the transparency.	Page 105 Step 7 

Note: Shaded text highlights the steps for classes with access to the Internet.



= For classes without access to the Internet.



= Involves copying a master.



= Involves making a transparency.



= Involves using the Internet.

Masters

Lesson 1, *Deadly Disease among Us*

Master 1.1, <i>Causes of Death Quiz</i>	transparency
Master 1.2, <i>Disease Cards</i>	classroom set
Master 1.3, <i>Disease Classifications</i>	transparency

Lesson 2, *Disease Detectives*

Master 2.1, <i>Three Mysterious Diseases</i>	student copies
Master 2.2, <i>Documents from Physician’s Investigation File</i>	classroom sets
Master 2.3, <i>Documents from Laboratory Scientist’s Investigation File</i>	classroom sets
Master 2.4, <i>Documents from Field Researcher’s Investigation File</i>	classroom sets
Master 2.5, <i>Notes from the Physician’s Investigation</i>	group copies
Master 2.6, <i>Notes from the Laboratory Scientist’s Investigation</i>	group copies
Master 2.7, <i>Notes from the Field Researcher’s Investigation</i>	group copies
Master 2.8, <i>Mystery Disease 1 Final Report</i>	group copies
Master 2.9, <i>Mystery Disease 2 Final Report</i>	group copies
Master 2.10, <i>Mystery Disease 3 Final Report</i>	group copies
Master 2.11, <i>Mystery Diseases Summary Table</i>	student copies and transparency

Lesson 3, *Superbugs: An Evolving Concern*

Master 3.1, <i>Bacterial Growth Experiment</i>	student copies
Master 3.2, <i>Discussion Questions for the Bacterial Growth Experiment</i>	student copies
Master 3.3, <i>Debi’s Story</i>	student copies (print version only)
Master 3.4, <i>Debi’s Story: Explaining What Happened</i>	student copies
Master 3.5, <i>Antibiotic Concerns</i>	group copies

Lesson 4, *Protecting the Herd*

Master 4.1, <i>Measles Outbreak at Western High</i>	student copies
Master 4.2, <i>A Little Sleuthing</i>	student copies
Master 4.3, <i>Following an Epidemic</i>	student copies and transparencies
Master 4.4, <i>Disease-Transmission-Simulation Record</i>	student copies (optional)
Master 4.5, <i>Characteristics of Smallpox, Polio, and Measles</i>	transparency (optional)
Master 4.6, <i>Cases of Smallpox in Niger and Bangladesh</i>	transparency (optional)

Lesson 5, *Making Hard Decisions*

Master 5.1, <i>The Proposals</i>	student copies (print version only)
Master 5.2, <i>Reference Database—AIDS</i>	student copies (print version only)
Master 5.3, <i>Reference Database—Measles</i>	student copies (print version only)
Master 5.4, <i>Reference Database—VRSA</i>	student copies (print version only)
Master 5.5, <i>Proposal Criteria Matrix</i>	student copies
Master 5.6, <i>Proposal Summary Matrix</i>	student copies
Master 5.7, <i>Reflection Questions</i>	transparency

Causes of Death Quiz

1. Which of the following diseases has been recognized since antiquity?
 - a. AIDS
 - b. Ebola hemorrhagic fever
 - c. guinea worm disease
 - d. Legionnaire's disease
2. In the 1700s and 1800s, a terrible, wasting disease killed thousands of European and American city dwellers. What disease was this?
 - a. AIDS
 - b. lung cancer
 - c. polio
 - d. tuberculosis
3. What infectious disease causing severe fever and chills plagued settlers in the Southern and Midwestern United States during the 1800s and early 1900s?
 - a. Legionnaire's disease
 - b. Lyme disease
 - c. malaria
 - d. schistosomiasis
4. Most deaths among U.S. servicemen in 1918 were due to what cause?
 - a. automobile accidents
 - b. flu
 - c. injuries sustained on the battlefields of World War I
 - d. plague
5. In 1994, a terrible disease nearly killed an 18-year-old high school student in California. Which of the following diseases was it?
 - a. AIDS
 - b. breast cancer
 - c. cystic fibrosis
 - d. tuberculosis
6. According to the World Health Organization, which of the following diseases caused the most deaths in 2008?
 - a. AIDS
 - b. diabetes
 - c. heart disease
 - d. pneumonia

Disease Cards

Acquired Immunodeficiency Syndrome (AIDS)

Infectious Agent:	virus (human immunodeficiency virus, or HIV)
Evidence of the Disease:	pneumonia, certain types of cancer, and other illnesses typical of people with failing immune systems
Treatment:	no cure exists, but a combination of antiviral drugs can prolong a reasonable quality of life for years
Transmission:	intimate contact: vaginal, anal, and oral sexual contact; blood-to-blood contact through shared needles, needle-stick accidents, transfusions, and transplants; and mother-to-newborn infection
Preventive Measures:	implement educational programs to promote “safer” sex and prevent drug abuse; screen blood sources for HIV; follow hospital procedures to prevent accidental spread of HIV
History:	first recognized in 1983; currently a global epidemic

Cholera

Infectious Agent:	bacteria (<i>Vibrio cholerae</i>)
Evidence of the Disease:	diarrhea, dehydration
Treatment:	fluids and antibiotics
Transmission:	ingestion of bacteria in contaminated food and water
Preventive Measures:	purify water; treat sewage; cook and promptly refrigerate food
History:	present from antiquity; increasing number of worldwide cases in recent years

Creutzfeldt-Jakob Disease (CJD)

Infectious Agent:	prion (scrapie PrP)
Evidence of the Disease:	deteriorating mental capacity, loss of coordination
Treatment:	none available at this time
Transmission:	infectious cases: intimate contact with infected tissues (most cases are due to an unknown cause; a few are inherited)
Preventive Measures:	none known at this time
History:	first described in 1982

Ebola Hemorrhagic Fever

Infectious Agent:	Ebola virus
Evidence of the Disease:	headache; fever; vomiting; diarrhea; bleeding from the nose, mouth, eyes, and other orifices
Treatment:	no cure exists; treatment is to relieve symptoms
Transmission:	intimate contact with infectious agent in blood
Preventive Measures:	follow appropriate disease-control procedures in hospitals; avoid burial customs that allow contact with tissues of deceased victims; initial victim in an outbreak likely was infected with the virus from an animal that carries the virus with no ill effects; that animal "reservoir" is unknown at this time
History:	first recognized in 1976; more than 28 outbreaks since then

Guinea Worm Disease (Dracunculiasis)

Infectious Agent:	helminth (the roundworm <i>Dracunculus medinensis</i>)
Evidence of the Disease:	inflammation, severe joint pain, severe itching under the skin, skin ulcers
Treatment:	antihelminthic drugs may hasten expulsion of worm
Transmission:	ingestion of water contaminated by the copepod (the intermediate host) that carries the larvae
Preventive Measures:	purify water
History:	present from antiquity; decreased dramatically in the last half of the 20th century

Influenza

Infectious Agent:	influenza virus
Evidence of the Disease:	headache, fever, chills, muscle aches; possibly sore throat, cough, chest pain
Treatment:	relieve symptoms
Transmission:	casual contact with the infectious agent in secretions or on droplets from those who are infected
Preventive Measures:	use vaccines against current strains; wash hands frequently
History:	present from antiquity; epidemics occur at regular intervals

Legionnaire's Disease

Infectious Agent:	bacteria (<i>Legionella pneumophila</i>)
Evidence of the Disease:	fever, cough, chest and abdominal pain, diarrhea
Treatment:	antibiotics
Transmission:	inhalation of bacteria on airborne particles, especially from water tanks
Preventive Measures:	disinfect cooling-tower water
History:	first recognized in 1977; occasional outbreaks since then

Lyme Disease

Infectious Agent:	bacteria (<i>Borrelia burgdorferi</i>)
Evidence of the Disease:	arthritis often an expanding, ringlike rash; may also present as arthritis, fever, fatigue, headache, and/or neurological symptoms
Treatment:	antibiotics
Transmission:	bites from infected ticks
Preventive Measures:	wear socks, long pants, and long-sleeved shirts in tick-infested areas and check carefully for ticks after leaving the area; a vaccine for individuals at high risk of contracting the disease
History:	first recognized as an infectious disease in 1975; infectious agent identified in 1982

Malaria

Infectious Agent:	protozoa (various <i>Plasmodium species</i>)
Evidence of the Disease:	cyclic fever and chills, anemia
Treatment:	antiprotozoan drugs
Transmission:	bites from infected mosquitoes
Preventive Measures:	follow procedures to reduce mosquitoes such as eliminating standing water and spraying with insecticides; follow procedures to limit contact between humans and mosquitoes such as installing screens and bed nets and using insect repellent
History:	present from antiquity; has increased in recent years

Streptococcal Pharyngitis ("Strep Throat")

Infectious Agent:	bacteria (<i>Streptococcus pyogenes</i>)
Evidence of the Disease:	painful, red, and inflamed throat; tonsils may swell and become coated with white patches
Treatment:	antibiotics
Transmission:	casual contact with infectious agent in secretions or on droplets
Preventive Measures:	wash hands frequently; disinfect contaminated materials
History:	present from antiquity

Plague

Infectious Agent:	bacteria (<i>Yersinia pestis</i>)
Evidence of the Disease:	bubonic form: swollen lymph nodes, fever, blocked circulation pneumonic form: pneumonia, blood infection
Treatment:	antibiotics
Transmission:	usually bites from infected fleas carried by wild rodents; also inhalation of airborne bacteria from individual with pneumonic plague
Preventive Measures:	eliminate rodents near human habitation; use insect repellants to avoid flea bites; use insecticides to treat domestic animals likely to come in contact with infected rodents
History:	present from antiquity; responsible for several global epidemics including the Black Death in 14th-century Europe

Pneumonia

Infectious Agent:	several types of bacteria, viruses, and fungi
Evidence of the Disease:	fever, cough, chest pain
Treatment:	antimicrobials for bacterial and fungal pneumonias; treatment to relieve symptoms for viral pneumonias
Transmission:	casual contact with infectious agent in secretions or on droplets from infected individuals
Preventive Measures:	use vaccines available to prevent some forms of pneumonia; improve social conditions such as crowded living quarters
History:	present from antiquity; remains the leading cause of death from infectious disease among elderly people

Polio

Infectious Agent:	polio virus
Evidence of the Disease:	fever, fatigue, headache, nausea, muscle pain; in severe cases, paralysis
Treatment:	generally none; respiratory assistance in acute paralytic cases
Transmission:	ingestion of virus in contaminated food and water
Preventive Measures:	vaccinate against current strains
History:	present from antiquity; continues to be a problem in some developing countries, although it has been eliminated in most countries

Schistosomiasis

Infectious Agent:	helminth (several species of the flatworm <i>Schistosoma</i>)
Evidence of the Disease:	may include a variety of symptoms such as fever, diarrhea, anemia, and liver failure
Treatment:	antihelminthic drugs may be effective if used early enough; cure not usually possible once the parasites are established
Transmission:	<i>Schistosoma</i> larvae enter human skin from snail-infested water (snails are intermediate hosts)
Preventive Measures:	reduce snail habitats (still pools of water); wear rubber boots in infested waters; treat sewage (to prevent eggs from reaching water sources)
History:	present from antiquity; increasing incidence in recent years

Tuberculosis

Infectious Agent:	bacteria (<i>Mycobacterium tuberculosis</i>)
Evidence of the Disease:	persistent cough, fever, fatigue, weight loss
Treatment:	antibiotics
Transmission:	inhalation of bacteria on airborne particles
Preventive Measures:	improve social conditions such as crowded living quarters; vaccine available, although its effectiveness varies among different populations
History:	possibly present from antiquity, peaked in early 19th century, and has declined until a significant increase in late 1980s and early 1990s

Disease Classifications

Criterion: Infectious Agent

Category (fill in for each row)	Disease and symptoms

Criterion: Mechanism of Transmission

Category (fill in for each row)	Disease

Criterion: History of Occurrence

Category (fill in for each row)	Disease

Three Mysterious Diseases

Characters:

Public Health Official, Farmer, Homemaker, Family Doctor

Segment 1: The Assignment

Public health office

PUBLIC HEALTH OFFICIAL: I am swamped with mysterious disease cases. Any time a cluster of people with an unidentifiable disease shows up in an area hospital, I get the call. It's my job to follow up, identify the disease, and marshal resources to prevent a possible epidemic. I mobilize my staff and send them out to interview the patients, their families, and their coworkers, check out the area where the disease first appeared, and so on. I get copies of the lab tests and find out what treatments have been tried and whether they worked. This information is plugged into the national database, which can sort through the information and find parallel cases—which might tell me what the disease is, where it's coming from, why it's happening, and what we can do about it. If I work fast enough, we can nip a problem in the bud, before it becomes an epidemic. Here are three strange cases. Can you sort through the information and figure out what is going on?

Segment 2: Mystery Disease 1

Front porch of farmhouse

FARMER: Bill and I, we've had a lot of years together. But that's what a brother's for, I guess, to share the years, long and short, good and bad. We had rain all last winter, a perfect spring, and one of our best wheat crops yet. Yeah, a good, long year. Once the harvesting was done, Bill was so happy he got it into his head that the barn needed a whole new roof. He was in a workin' mood, I guess, and that roof was going bad. We went at it hard. Bill never stopped. He was workin' four, five hours past when I'd go home to the wife and kids. When we got done, Bill went to bed with chills and a fever. Overwork, I figured. Then he had trouble breathing, so we took him right to the hospital. Two days later, he was dead. And he was only 46 years old.

Segment 3: Mystery Disease 2

Kitchen of suburban home

HOMEMAKER: I love my home. I see deer and pheasant out the window. . . . It makes me feel like I live in the woods. Two centuries ago, this was all woods, then it was mostly cleared for farming. Then, about 10 years ago, I think, they turned this whole area into a housing development. Fortunately, they left a lot of the woods, and a lot of the farmland has started returning to forest again. Everybody loved it here until our kids started having problems. My son Michael started complaining that his knees hurt. I thought it was just growing pains, but it didn't get better, so we took him to the doctor. After extensive testing, they finally said it was rheumatoid arthritis. But then I found out other children, like Mary Martinez and Zack Jones, were diagnosed with the same thing. The pediatricians told us juvenile arthritis is not contagious—but three kids in the same area suddenly getting the exact same thing? Can that just be coincidence?

Segment 4: Mystery Disease 3

Doctor's office in hospital

FAMILY DOCTOR: Jennifer went to Sierra Leone as a medical volunteer. The hospital she was working in over there was dealing with some strange epidemic, so they put her right to work. The patients she was working with were very sick. But they just airlifted her back to the States because she is desperately ill now, too. She arrived here in the hospital last night in terrible pain with a raging fever. Her throat is so raw she can't swallow, so we're administering nourishment and medications intravenously. I think she may be bleeding internally. Her parents are in the waiting room hoping I've got some answers.

Documents from Physician's Investigation File

Physician's Notes and Database Searches

Master 2.2a

10-17

Assisted in treatment of farmer with acute respiratory distress syndrome (ARDS) last week—he died two days ago. We were unable to determine the cause, so death was listed as due to “ARDS of unknown cause.” The case was particularly disturbing because the man was relatively young (46 yrs.) & had been in good health prior to this illness. Yesterday, I talked with a colleague in New Mexico who mentioned a similar case involving a teen-ager; he died at her hospital last August. I became concerned that we might be witnessing the beginning of an epidemic & took the following actions:

- Initiated a computer search of diseases with ARDS-type symptoms common in southwest U.S.*
- Initiated computer search of chemicals that cause ARDS-type symptoms*
- Called records offices in hospitals in New Mexico, Arizona, & Colorado to get info. on all deaths in those hospitals that were attributed to ARDS of unknown cause in last 6-month period*

[10-27: results of the above actions are collected in this file]

10-23

Received specimens from the 5 victims & sent them by courier to the national lab for analysis.

*Call Mary—
555-0112
No. AZ—Records*

10-18

Began calling hospitals in NM, AZ and CO—requested info. on deaths due to “ARDS of unknown cause”

Results—

<i>Victim</i>	<i>Symptoms</i>	<i>Died</i>	<i>Hospital</i>	<i>Notes</i>
<i>Male, 46 yrs.</i>	<i>Fever, respiratory distress</i>	<i>10-15</i>	<i>Western CO Health Center</i>	<i>(case I assisted with) farmer; re-roofed barn just prior to illness</i>
<i>Male, 17 yrs. (talked with Sue)</i>	<i>Fever, respiratory failure</i>	<i>8-26</i>	<i>Gallup Memorial Hospital</i>	<i>(Sue's case) track star; spent 3 days backpacking prior to symptoms</i>
<i>Male, 19 yrs. (talked with Brett in Records office)</i>	<i>Fever, headache, resp. distress</i>	<i>4-30</i>	<i>Central NM Medical Center</i>	<i>Long-distance runner; lived in trailer in rural area*</i>
<i>Female, 22 yrs. (talked with Dr. Simons, attending physician)</i>	<i>Fever, cough, resp. failure</i>	<i>5-6</i>	<i>Indian Health Service Clinic</i>	<i>Lived in trailer in rural area*</i>
<i>Female, 39 yrs. (talked with Mary in Records)</i>	<i>Fever, headache, resp. distress</i>	<i>5-14</i>	<i>Northern AZ Health Center</i>	<i>Prior to symptoms, victim spent several days cleaning out garden shed</i>

**These were brother and sister; sister had returned to college after visit home and prior to symptoms appearing*

Results of Internet Search

Searched on: acute respiratory distress syndrome (ARDS)

Screen: Southwest United States

Number of matches: Four (see below)

Bacterial Pneumonia

Incidence:	throughout the world; in temperate zones, highest incidence in winter and spring; often accompanies epidemics of influenza
Infectious Agent:	90 percent of U.S. cases due to 1 of more than 80 strains of <i>Streptococcus pneumoniae</i> ; other bacteria that cause pneumonia include <i>Hemophilus influenzae</i> (usually in children), <i>Klebsiella pneumoniae</i> (typically among alcoholics, diabetics, or those with cardiopulmonary disease), <i>Pseudomonas aeruginosa</i> (typically among those with cystic fibrosis)
Symptoms:	sudden onset of chills, fever, cough, chest pain
Diagnosis:	isolation of bacteria from blood or lower respiratory tract secretions
Transmission:	droplet spread or oral contact
Fatality Rate:	20 to 40 percent if untreated; death more common among infants, elderly people, and those with other illnesses
Reservoir:	humans
Treatment:	penicillin G, erythromycin

Influenza

Incidence:	annually throughout the world, usually during colder months
Infectious Agent:	viral—myxoviruses
Symptoms:	sudden onset of fever, muscle aches, sometimes sore throat; slow recovery with overexertion leading to relapse
Diagnosis:	molecular methods for direct identification of virus in nasal and throat cells; antibody response to the virus in patient's blood
Transmission:	contact with droplets from respiratory secretions of infected individual, followed by transfer to mouth
Fatality Rate:	varies depending on viral strain; usually more serious among elderly people
Reservoir:	humans; possibly other warm-blooded animals
Treatment:	treat symptoms

Master 2.2d

Plague

Incidence:	10 to 15 cases per year in the United States, usually in the Southwest; 1,000 to 3,000 cases worldwide
Infectious Agent:	bacteria— <i>Yersinia pestis</i>
Symptoms:	bubonic form: painful, swollen lymph nodes; fever; circulation blocked in toes and fingers; may progress to the pneumonic form pneumonic form: pneumonia, followed by blood poisoning
Diagnosis:	microscopic observation of <i>Y. pestis</i> in material taken from affected lymph nodes or sputum
Transmission:	bubonic form: bites from infected fleas pneumonic form: progression from bubonic plague or inhalation of droplets from another person with pneumonic plague
Fatality Rate:	bubonic form: 50 percent if untreated pneumonic form: near 100 percent if untreated
Reservoir:	rodents and their fleas. In Southwest United States, prairie dogs and ground squirrels are permanent reservoirs. Cats and dogs that host infected fleas may also bring plague bacteria in contact with humans.
Treatment:	streptomycin, tetracycline

Viral Pneumonia

Incidence:	throughout the world; in temperate zones, occurs most often during fall and winter
Infectious Agent:	a variety of viruses, including adenoviruses and parainfluenza viruses
Symptoms:	gradual onset, less pronounced fever than with bacterial pneumonia
Diagnosis:	identification of viral antigens in respiratory secretions; antibody response to virus in patient's blood
Transmission:	droplet spread or oral contact
Fatality Rate:	low
Reservoir:	humans
Treatment:	treat symptoms

Welcome to Chemical Databases

To initiate your search,

1. Select database desired:

Database:	Toxic Chemicals	▼
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2. Identify additional characteristics:

Symptoms:	Acute Respiratory Distress Syndrome	▼
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3. Click here:

Begin Search

Number of matches: Two (see below)

Phosgene	
Reports indicate that symptoms of acute respiratory distress syndrome (ARDS) may occur 24 hours or more after exposure to the chemical.	
Use(s):	Used by Germany during World War I
Current Status:	Banned in the United States

Phosphene	
Causes acute respiratory distress syndrome (ARDS) more rapidly than related compound, phosgene.	
Use(s):	Used to kill prairie dogs
Current Status:	Legal in the United States for prairie dog eradication

Documents from Laboratory Scientist's Investigation File

Results of Laboratory Analyses from National Laboratory

Master 2.3a

INTEROFFICE

MEMO

Date: 24 October
To: Lori
From: Yolanda
Subject: Samples

Lori,

Contained in this packet are tissue samples from five patients from the Southwest United States who died of ARDS of unknown cause. Test the samples for the presence of bacteria and viruses that cause diseases with ARDS-type symptoms and are common in the Southwest: bacterial and viral pneumonias, influenza, plague.

Thanks,

Yolanda

MEMORANDUM

DATE: October 25

TO: Y. Johnson

FROM: L. Kauffman

RE: Results of tests on tissue samples from patients who died of ARDS

Yolanda, here are results of the tests on the tissue samples from the five victims of “ARDS—Unknown Cause” that you requested. As directed, I tested samples for the presence of bacteria and viruses that cause diseases with ARDS-type symptoms and are common in the Southwest United States.

Lori

Results of Tissue Samples

Disease	Infectious Agent	Test Result
bacterial pneumonia	<i>Streptococcus pneumoniae</i>	all samples negative
influenza	myxovirus	sample from Victim 4 positive; all other samples negative
plague	<i>Yersinia pestis</i>	all samples negative
viral pneumonia	adenoviruses, parainfluenza viruses, and others	all samples negative

LAB NOTES – Additional tests requested on samples from patients who died of ARDS of unknown cause

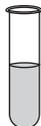
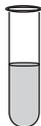
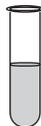
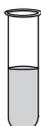
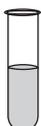
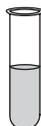
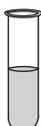
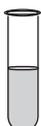
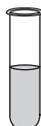
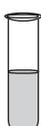
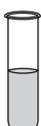
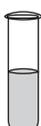
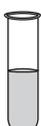
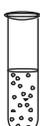
SCIENTIST – L. Kauffman

DATE: 10-27

PURPOSE: Received autopsy samples (blood) from 5 victims of acute respiratory distress syndrome (ARDS) of unknown cause to test against antibodies for viruses we have in stock.

- PROCEDURE:**
- (1) Placed each victim's blood into 5 test tubes labeled: "Arenaviruses," "Filoviruses," "Hantaviruses," "Myxoviruses," and "Retroviruses."**
 - (2) Added antibodies against each of the five types above to the appropriate tubes.
 - (3) Examined for clumping (indicates reaction of virus in patient's blood with antibodies added).

RESULTS:

Blood from:	Antibodies added:**				
	A	B	C	D	E
Victim 1 Male, 46 yrs.					
Victim 2 Male, 17 yrs.					
Victim 3 Male, 19 yrs.					
Victim 4 Female, 22 yrs.					
Victim 5 Female, 39 yrs.					

 = no reaction;
  = clumping

- ** A = arenaviruses
 B = filoviruses
 C = hantaviruses
 D = myxoviruses
 E = retroviruses

* The 5 classes of viruses; known to cause the following diseases:

Virus Type	Disease(s)
Arenaviruses	Bolivian & Argentine hemorrhagic fever; Lassa fever
Filoviruses	Ebola & Marburg fever
Hantaviruses	hemorrhagic fever with kidney involvement
Myxoviruses	influenza
Retroviruses	AIDS; adult T-cell leukemia

Date: October 30
To: Mario
From: Yolanda
Subject: Testing specimens from trapped animals

Mario,

Lori found that blood samples from patients from Colorado, Arizona, and New Mexico who died of "ARDS of unknown cause" strongly reacted with antibodies against hantaviruses. Field investigators in those states trapped a variety of animals in the areas where the victims resided; tissue samples from those trapped animals are in this packet. Please test them for the presence of hantaviruses and get the results to me as soon as possible. Thanks!

11-2

Yolanda—Here are the results:

<i>Animal</i>	<i>% with Positive Hantavirus Test</i>
<i>Chipmunks</i>	<i>3%</i>
<i>Deer mice</i>	<i>33%</i>
<i>Prairie dogs</i>	<i>0.5%</i>
<i>Raccoons</i>	<i>0%</i>
<i>Rats</i>	<i>2%</i>
<i>Skunks</i>	<i>1%</i>

Documents from Field Researcher's Investigation File

Epidemiology Reports and Other Notes

Master 2.4a

Phone Call

Southwest Regional Public Health Office

For: D. Martinez Date: 10-20 Time: 10:00 a.m.
From: Western CO Health Center Phone: 555-0156

Message:

Phone call noting a number of deaths due to acute respiratory distress syndrome (ARDS) of unknown cause in Colorado, Arizona, and New Mexico. Dave wondered whether these deaths might be related and expressed concern about a possible epidemic.

Action:

Date: 10-20

1. Alerted L. Morton (CO), A. Garcia (AZ), and J. McDonald (NM) to the cases of ARDS of unknown cause in their regions. Requested field surveys of deceased victims' homes and workplaces and interviews with surviving family members and friends about events surrounding the deaths. Asked them to complete investigations as soon as possible and return reports to me. Also asked them to trap animals in area of disease cluster and forward tissue samples to the national laboratory for analysis.
2. Contacted weather bureau and wildlife association for information on unusual climate and environmental events in the past year.

Results:

Results of these actions follow in this file.

- Phoned
- Returned your call
- Please call
- Will call again
- Came to see you
- Wants to see you

Interview Transcript

Investigator: A. Garcia

Victim's Sex and Age: Female, 39 years

Interview with: Husband

Date of Interview: October 28

AG: Thank you for agreeing to talk with me. I know this is very difficult for you, so I'll make this as brief as possible.

Husband: If anything I can tell you will help prevent this tragedy from happening to anyone else. . . .

AG: First, when did your wife first become ill?

Husband: Oh, I guess it was May 9th, 10th . . . Jan said she thought she was getting the flu. She took aspirin and went to bed, but the next day she didn't feel any better. And the day after that . . . well, I knew that it was more than just the flu. She kept coughing and coughing and said she couldn't breathe. She said she'd make a doctor's appointment, but I said, no, we're going to the emergency room now. And they admitted her to the hospital right away, but nothing they did helped. Jan just kept getting worse, and two days after she got to the hospital . . . we lost her.

AG: Was your wife doing anything unusual or out of the ordinary for her the day she got sick?

Husband: No, just the usual stuff. You know, getting the kids off to school, she had a part-time job at the local newspaper in the mornings, then home. She made dinner, kept the house and yard up . . . she took such good care of us . . . I don't know what we'll do without her.

AG: Did she work with any unusual chemicals at her job? Or anything at home?

Husband: No, not at her job—she mostly used the phone, you know, calling clients who advertise in the paper. Not at home either, except your basic cleaning stuff . . . Well, maybe in the garden shed . . . hmmm. I'd have to check. Jan's passion was the garden, you know. And she had been spending lots of time out there last May cleaning it out and getting ready to do some planting. Would that be "unusual activity"?

AG: Maybe. So you don't know what kinds of garden sprays or other chemicals she might have had out there?

Husband: No, we can go look. I haven't had the heart to go into her special place since she passed on. . . I guess I felt kind of guilty because she'd been after me for a couple weeks to get out to the shed and set up some mousetraps. She'd seen several mice while she was working and, even though I told her mice are supposed to be out by the garden, she didn't like them at all. Maybe she went out and got some mouse poison. Do you think that could have made her sick?

AG: It's possible, but I doubt it. I don't want to take any more of your time. Thank you so much for talking with me; you've given me some really useful information. Maybe we could take a look at the garden shed on my way out?

Investigation of Victim's House

Victim's sex and age: Female, 39 yrs.

1. Description of dwelling

Victim lived in suburban, ranch-style home with 3 bedrooms, kitchen, dining room, living room, & 2 bathrooms. Full, finished basement included a family room, guest room, & half-bath. Screened-in porch off the dining room looked out over yard, which included a garden shed.

2. Condition of dwelling

Home showed evidence of good care, recently painted, beautifully decorated. (Victim's family—husband & two children—still live in the home.) Lawn & gardens well-landscaped. Interior of garden shed equally tidy with garden tools hanging on peg boards, seed & soil containers lidded & labeled on wooden work bench or on dirt floor of shed, etc. Mouse poison had been put out beneath work bench.

3. Unusual chemicals or equipment found

Typical household chemicals in the home; the garden shed included, in addition to the mouse poison, fertilizer & insecticide sprays. All were relatively new and capped and stored appropriately.

4. Other comments

None

Date of investigation: 10-28

Signature of investigator: A. Garcia

Interview Transcript**Investigator:** L. Morton**Victim's Sex and Age:** Male, 46 years**Interview with:** Sister-in-law**Date of Interview:** October 21

- LM: Thank you for taking this time to talk with me. I'll try to be brief, but any information you can give me about your brother-in-law's activities before he became ill could help us determine what caused his death and how to prevent more deaths like his from occurring.
- Sister-in-law: Of course ... my husband just couldn't do this; his brother's death was just so sudden
- LM: I understand. Tell me, when did your brother-in-law first complain of not feeling well?
- Sister-in-law: I remember exactly. Bill was never sick, you see—at least, nothing more than a cold ... that's part of why this is all so shocking. He and John—that's my husband—had finished the harvest early, on October 8. I was so pleased; it had been such a good year. But I've been married to a farmer long enough to know that their work is never done! Bill and John decided since the weather was still good and they had time before the snows, they'd just go ahead and reroof the old barn. They started right in, putting in long, hard days just like during harvesting. Bill usually had dinner with us since he's not married, and I know he just went back out to work on the barn after dinner, even though I insisted John stay home and spend some time with us. Well, two days after they started on the roof, Bill complained to John that he was exhausted and not feeling well. What else would you expect after all that work! But when I checked on him the next day, he really looked bad, had a fever, and was having trouble breathing. We got him to the hospital that day, and ... well, you know the rest.
- LM: Did your brother-in-law live with you and your family?
- Sister-in-law: Oh, no. He lived in the little house ... you see, this is a family farm; the boys inherited it from their folks. My husband grew up in this house and, after we married, we lived in the little house for a while until my in-laws retired and moved to Arizona. By then we'd had our first baby, so we moved in here and Bill moved to the little house.
- LM: I see. Would it be possible for me to see your brother-in-law's home? Maybe something would give me a clue about what caused his death.
- Sister-in-law: Oh, of course, we have a key. We've only gone in long enough to get a funeral suit ... (sob) ... we haven't been up to going in to pack up Bill's stuff, so everything should be pretty much as it was. Would you like to see the barn they were working on too?
- LM: Yes, that would be helpful. Do you have livestock in the barn?
- Sister-in-law: No, it's a hay barn, mostly. A little bit of equipment. We used to have a cat out there—really helps with the rodent population!—but the poor old thing died last spring and we haven't gotten another one yet.
- LM: Thank you for your time. We'll just take a look at the barn and your brother-in-law's home and then I'll be out of your way.

Investigation of Victim's House

Victim's sex and age: Male, 46 years

1. Description of dwelling

Victim lived alone in a small farmhouse 2 miles from his brother & family who
live in the larger house on the family farm. The 2-story farmhouse had a kitchen,
living room, & 1 bedroom & bath downstairs; upstairs were 2 additional bedrooms.
House also had a small root cellar.

2. Condition of dwelling

Neither upstairs room appeared to have been used recently; one was used as a
storage room, the other was a study. Living room was tidy, with newspapers
scattered on ottoman. Kitchen was clean with little food in refrigerator: milk,
apples, oranges & package of cheese. Mouse & rat poisons found in lower cupboards.
Bed was unmade, but the bedroom was otherwise neat. Root cellar seemed unused,
although mouse & rat poison had also been put out there.

3. Unusual chemicals or equipment found

Typical household chemicals found (detergent, cleanser, window cleaner, bleach),
in addition to the mouse & rat poison.

4. Other comments

Also examined the barn the victim had re-roofed prior to death—a wood
construction originally built about 50 years ago. Used mostly for storing hay, also
housed tools & some smaller pieces of farm equipment. Found a dish—apparently
used for water for cats.

Date of investigation: 10-21

Signature of investigator: L. Marton

Investigation of Victim's House

Victim's sex and age: Male, 19 years: female, 24 years

1. Description of dwelling
The first victim lived with his mother in a rural area, about 3 miles from the nearest town. The second victim, a college student & sister of first victim, visited the home prior to becoming ill. Trailer was small, including a kitchenette, small living/dining area, two bedrooms, and one bathroom.

2. Condition of dwelling
Trailer was somewhat cluttered with victim's clothes and books; dirty dishes were in sink and carton of milk and open loaf of bread were left on table. Mother had moved to her sister's home following her son's death. I presume trailer had been vacant since then. Mouse feces gave evidence of rodent infestation.

3. Unusual chemicals or equipment found
None. Only typical household chemicals were found (dishwashing detergent, floor wax, scouring powder, etc.) No unusual equipment or supplies found. Five mouse traps were found on the premises; one had caught a mouse.

4. Other comments
Victim's mother & aunt refused interviews. Learned from aunt's neighbors that, even prior to moving in, the victim's mother spent most nights at her sister's home in town where she was nearer to her job.

Date of investigation: 10-25

Signature of investigator: J. McDonald

10-21 - Jim at Weather Bureau

Record high snowfalls in mountains of CO & AZ this year—good water levels in reservoirs—led to good harvests

10-25

3:30 Meet Sally

10-24 - Talked with Gretchen at Wildlife Assoc.

Noted high pinon nut harvest this year—food source for small mammals Gave me name of director of long-term ecological research survey team:

Mike Lee 555-0135—call him

10-25 - Mike Lee

Said most interesting finding of past year was size of deer mouse population—10 times higher than any previous year of records

Notes from the Physician's Investigation

Physicians are typically the individuals who first encounter and report a mysterious disease. They may collect information on the symptoms exhibited by victims and use that information to suggest possible causes.

Work with your fellow experts to review the documents in the Physician's File and complete this form. When your group meets again, you will pool your information to create a final report.

Disease Symptoms

Suspected Cause

Evidence:

Other Notes about the Disease

Notes from the Laboratory Scientist's Investigation

Laboratory scientists isolate and examine bacteria, viruses, and other infectious agents from samples of the victims' tissues and characterize those agents. They also test for antibodies against likely infectious agents in the victims' blood. They may also check possible vectors (nonhuman carriers for antibodies) and conduct tests to see what drugs will kill or limit the growth of the agent.

Work with your fellow experts to review the documents in the Laboratory Scientist's File and complete this form. When your group meets again, you will pool your information to create a final report.

Disease Symptoms

Suspected Cause

Evidence:

Suspected Route of Transmission of Infectious Agent

Evidence:

Other Notes about the Disease

Notes from the Field Researcher's Investigation

Field researchers interview victims or victims' family members and visit victims' homes, workplaces, or other places where they spent time to identify commonalities among victims that may give clues about the disease. They also collect information about unique environmental events that coincided with outbreaks of the disease.

Work with your fellow experts to review the documents in the Field Researcher's File and complete this form. When your group meets again, you will pool your information to create a final report.

Disease Symptoms

Suspected Route of Transmission of Infectious Agent

Evidence:

Relevant Environmental Factors

Other Notes about the Disease

Mystery Disease 1 Final Report

Name: _____

Pool the information from all members of your group to complete each item below.

Disease Symptoms

Suspected Cause

Evidence:

Suspected Route of Transmission of Infectious Agent

Evidence:

Relevant Environmental Factors

Recommendations for Prevention of Disease

Classify This Disease As

emerging re-emerging endemic

Evidence:

Mystery Disease 2 Final Report

Disease Symptoms

Initial symptoms are fever, fatigue, headache, and swollen lymph nodes, typically following the appearance of a distinctive, expanding, ringlike rash. Within four weeks to a year or more, swelling or pain in the large joints occurs, resulting in chronic arthritis.

Suspected Cause

A spirochete type of bacteria

Evidence: People diagnosed with this disease have antibodies against the spirochete, whereas people without the disease do not.

Suspected Route of Transmission of Infectious Agent

Spirochete bacteria infect humans through bites from infected deer ticks.

Evidence: Many people diagnosed with the disease recall a distinct rash radiating from the site of a tick bite; spirochetes were found in 61 percent of *Ixodes dammini* ticks (deer ticks), the type of tick suspected of biting victims of the disease.

Relevant Environmental Factors

Most cases occurred among suburban dwellers living in recently established residential areas near woods. Peak incidence of new cases of the disease occurs in summer and early fall; some research studies predict peak years for the disease will be two years following heavy acorn production.

Recommendations for Prevention of Disease

Wear socks, long pants, and long-sleeved shirts in wooded areas and check carefully for ticks after leaving the woods; if rash described above appears, see a physician for diagnosis and antibiotic treatment (if diagnosis is positive).

Classify This Disease As

emerging re-emerging endemic

Evidence: The characteristics of the spirochete isolated from deer ticks did not match any known spirochetes.

Mystery Disease 3 Final Report

Disease Symptoms

Persistent fever, headache, fatigue, sore throat, vomiting and diarrhea, chest and abdominal pain; in some cases, bleeding from body orifices occurs.

Suspected Cause

A virus in the arenavirus family

Evidence: Specimens from victims failed to react with antibodies against more than 250 different viruses; one weak reaction was found against antibodies produced in response to a virus in the arenavirus family.

Suspected Route of Transmission of Infectious Agent

(1) Through close contact with hospitalized victims of the disease. (2) Through contact with urine and feces of the *Mastomys natalensis* rat.

Evidence: (1) clusters of disease cases that occurred in hospitals could be traced to an initial, hospitalized victim; (2) the virus found in victims of the disease was found in *M. natalensis* and no other animals tested.

Relevant Environmental Factors

The main competitor of *M. natalensis* is the more aggressive rat *Rattus rattus*. Where *R. rattus* is eliminated by antirodent control measures such as poisoning, *M. natalensis* may move into an inhabited area.

Recommendations for Prevention of Disease

Avoid contact with *M. natalensis* rats and their urine and droppings.

Classify This Disease As

emerging re-emerging endemic

Evidence: Tests of antibodies from victims against more than 250 known viruses showed only one weak reaction, indicating the disease was caused by an unknown virus.

Mystery Diseases Summary Table

Name: _____

Mystery Disease	Infectious Agent Transmitted by	Emerging, Re-emerging, or Endemic?	Relevant Environmental Factors
1			
2			
3			

1. An important reason for the emergence of new diseases is . . .
2. This means that to reduce the chances of new epidemics among people, we should . . .

Bacterial Growth Experiment

Pseudomonas fluorescens, the bacterium used in the laboratory exercise you will begin soon, does not cause disease in healthy people. However, people who have weakened immune systems should not have contact with most microorganisms or with people who handle those organisms. Your immune system may be weakened if you are undergoing antibiotic therapy, if you are taking immunosuppressive drugs or drugs for cancer treatment, or if you have AIDS or are HIV-positive. If you have a weakened immune system for these or any other reasons, let your teacher know and he or she will provide you with an alternative experience that is safer for you.

Follow the directions below to test the hypothesis using the bacterial species *Pseudomonas fluorescens* and the antibiotic kanamycin. The flow chart on **Master 3.1c** provides an overview of the experiment.

Hypothesis (insert here): _____

DAY 1

1. Collect the following materials from your teacher:

- 1 test tube culture of *P. fluorescens* (the parental culture)
- 1 test tube containing nutrient broth
- 1 test tube containing nutrient broth with kanamycin
- 1 nutrient agar plate
- 1 nutrient agar plate with kanamycin

You will need the following materials at your laboratory station: 4 sterile 1-milliliter pipets, pipet pump or bulb, container with disinfectant for disposing of used pipets, Bunsen burner, grease pencil for labeling, and beaker of alcohol with a bent glass rod spreader.

2. For your safety and the success of your experiment, you must use aseptic techniques when handling bacterial cultures. You must also discard used cultures safely. Your teacher will explain and demonstrate aseptic techniques and indicate where you should discard your used cultures (with caps and lids in place). Your teacher will decontaminate all of the cultures before disposal.

Swirl the *P. fluorescens* culture gently to distribute the bacterial cells evenly. Then, follow your teacher's instructions for maintaining sterile conditions while transferring 0.1 milliliter from the culture into the test tube of nutrient broth and into the test tube of nutrient broth with kanamycin. Label the first test tube "A," the second test tube "B."

3. Swirl the *P. fluorescens* culture again and follow your teacher's instructions to deposit 0.1 milliliter from the culture on each of the nutrient agar plates. Use a sterile, bent glass rod to spread the culture evenly over the surface of the plates. Label the nutrient agar plate "1" and the nutrient agar plate with kanamycin "2."
4. After the culture has soaked into the plates (about 5 to 10 minutes), invert the plates and incubate them and the two broth cultures at 25°C (77°F) for two to three days.

Master 3.1a

DAY 2 (2–3 days later)

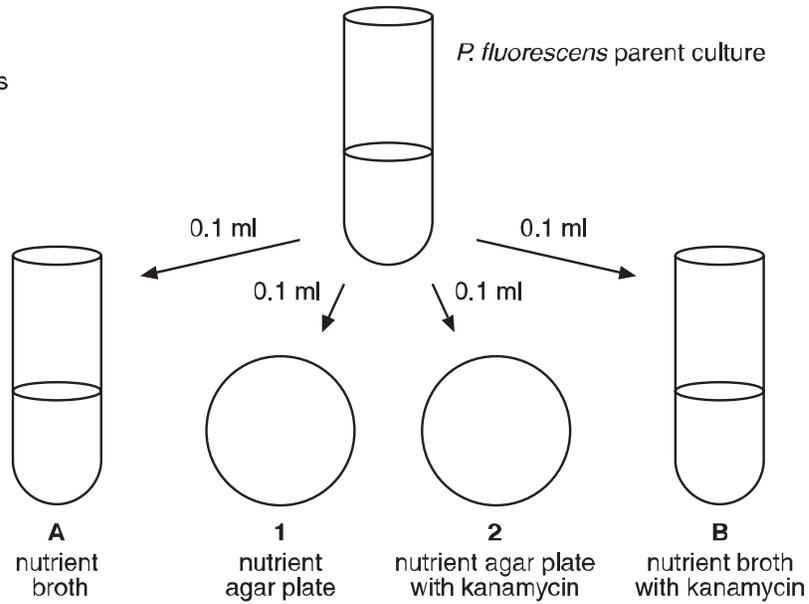
5. Retrieve the broth cultures (A and B) from the first session and collect 2 new nutrient agar plates and 2 nutrient agar plates with kanamycin. Check that you have 4 sterile 1-milliliter pipets, pipet pump or bulb, pipet disposal container, Bunsen burner, and alcohol with a bent glass rod spreader.
6. Swirl culture A gently and follow the procedure in Step 3 to prepare two plates, one nutrient agar plate and one nutrient agar plate with kanamycin. Label the first plate “3” and the second plate “4.”
7. Swirl culture B gently and repeat Step 6 using samples from this culture. Label the nutrient agar plate “5” and the nutrient agar plate with kanamycin “6.”
8. After the culture has soaked into the plates, invert them and incubate them at 25°C for two or three days. Dispose of the A and B cultures as your teacher directs.

DAY 3 (2–3 days later)

9. Collect all six plates and draw the amount of bacterial growth on each plate on the flow chart.

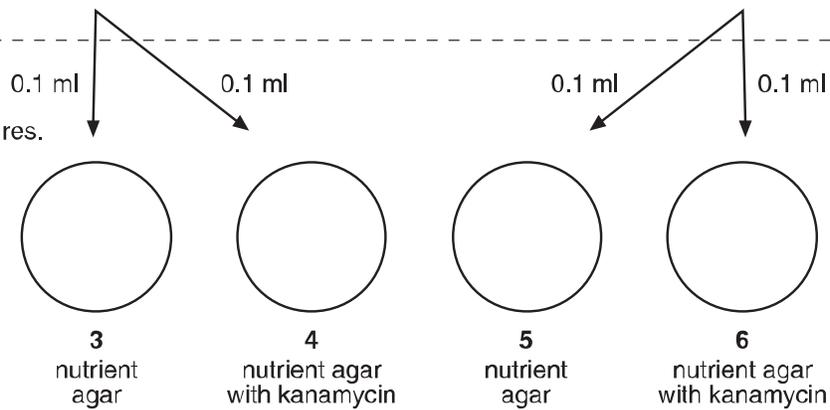
Day 1

Steps 1 to 4:
Prepare 2 broth cultures
and 2 plate cultures.



Day 2

Steps 5 to 8:
Prepare 4 plate cultures.



Day 3

Step 9: Collect plates and record results above by drawing the amount of bacterial grown on each plate.

Master 3.1c

Discussion Questions for the Bacterial Growth Experiment

Name: _____

Refer to the results from your bacterial growth experiment as you answer the following questions.

1. Compare the bacterial growth on the two plates from the parental culture (Plates 1 and 2). Which has more growth? Explain why. How do you explain the presence of bacteria on the plate containing kanamycin?
2. Compare the growth on Plates 3 and 4, which you prepared from culture A (without kanamycin). How does the growth on the plates with and without kanamycin appear? What does this tell you about the bacteria grown in culture A?
3. Compare the growth on Plates 5 and 6, which you prepared from culture B (with kanamycin). How does the growth on the plates with and without kanamycin appear? What does this tell you about the bacteria grown in culture B?
4. Compare the growth of cultures A and B on Plates 4 and 6 (with kanamycin). Explain how culture B could have so many more resistant bacteria than culture A, even though they both came from the same parental culture.
5. How do you explain the presence of some resistant bacteria in the parental culture and culture A?

Debi's Story

Read the following transcript of an interview conducted in 1999 with Debi French.

The Diagnosis

My name is Debi French, and I'm 23. The winter of 1993, when I had chronic bronchitis, as I had most of my life, I was not getting any better from the medical therapy. So I went to the doctor and said, "Fix me. There's something wrong."

He did chest X-rays, and that's when we found out I had tuberculosis.

I was coughing. I was extremely exhausted; I fell asleep in almost every class I had every day. I lost nearly 50 pounds. Those were the main symptoms—excessive coughing to the point where, the day I went to the doctor's office, I coughed till I puked.

We did the chest X-rays, and the doctor reviewed them and then had another doctor give a second opinion. Then he came in and told me and my mom. ... And the first thing he said was, "Well, you don't have to go to school." And the first words out of my mouth were, "But I have a parade on Saturday I have to march in."

To say the least, I was not thrilled. My mom was relieved because in her mind, it was something curable.

At the time, the only thing I knew about tuberculosis was that people had died from it. And far be it from me to allow myself to die from a little bacteria.

It's not every day that your typical middle-class white girl, living in suburbia, gets a disease like this. Somebody in one of my classes had an active case and continued to go to school, where it spread like wildfire. By the time the testing was complete, they revealed that there were 12 active cases of tuberculosis and 350 positive skin tests showing exposure. So in a small school of about 1,200 people, that's nearly a quarter of the population.

The Initial Treatment

At first, I was on four different medications, including the antibiotics isoniazid and rifampin. After six weeks or so, it seemed like they had done their job. My sputum tests came back negative, so I wasn't active any more. But I would still have to continue drug therapy for about a year.

It worked for a while. ...

The Treatment Fails

During my senior year—February 14, 1994—I'll never forget—my doctor called me and said that the tests that they had been doing to see if I could get off my medication came back positive. I had an active case all over again.

I spent two weeks in UCLA Medical Center, which included my 18th birthday. After that, my parents decided that because I wasn't getting any better, there was no reason to put me and them and the rest of the family through the torture of my having to stay in the hospital, when, aside from the fact I had a communicable disease, I was normal.

So they let me go home, and I was home for about six weeks. Still, I wasn't getting any better, even on new medications. After six weeks, the health department basically told my mom that if they didn't take me to this hospital in Colorado, I was going to die.

A Happy Ending

So I went to Colorado. We had to get a private plane to take us, because when you're contagious, you can't just hop on a commercial airline. The day we were supposed to leave, the plane company—the pilot—called and canceled. He backed out. He was afraid for his health, which is understandable, but, nonetheless, it hurt.

Two days later, we got another plane (another pilot) and took off for Denver. It was a nice change of pace. The staff at the hospital knew what was going on and knew how to help me and help my family get better. It was incredible—they saved my life. Between them and my attitude—that's why I'm still here. I ended up losing a third of my right lung—the upper third. I have a lovely scar across my back, and I left the hospital with a tube in my chest.

I could have come out of this and still had my right lung, but the largest collection of bacteria was in my right upper lung. It was [a mass] about the size of a golf ball. And they decided that for the best chance of eradicating it completely from my body, it was just safer and easier to take it out. Otherwise, I could still be on medication and that stuff is nasty—really nasty. You really don't want it. Trust me.

Don't be fooled that things like this are of the past, because they have a way of resurging. Bacteria are stubborn.

Debi's Story: Explaining What Happened

Name: _____

Follow the steps below to explain what happened to Debi French.

1. If you have Internet access, go to the lesson's Web site, click on Lesson 3, Debi's story, *The Diagnosis*, and view Debi's description of her initial diagnosis (<http://science.education.nih.gov/supplements/diseases/activities/>). If you don't have Internet access, read "The Diagnosis" on **Master 3.3a, Debi's Story**.

Summarize what you learned by completing the following sentences:

Debi contracted tuberculosis (TB) from

The symptoms Debi had were

2. If you have Internet access, click on *The Initial Treatment* to hear Debi describe the treatment prescribed by her doctor and its outcome. If you don't have Internet access, read "The Initial Treatment" on **Master 3.3a**. Summarize what you learned by completing the following sentences:

The treatment to cure TB is

When Debi started the treatment,

3. Review the results and conclusions you drew from Plates 1–4 of your bacterial growth experiment. Put together those conclusions with the observations from the first two parts of *Debi's Story* and complete the following sentence:

Debi's health began improving when she started the drug therapy for TB because

Master 3.4a

4. If you have Internet access, click on *The Treatment Fails* to learn what happened to Debi next. If you don't have Internet access, read "The Treatment Fails" on **Master 3.3b, *Debi's Story***. Summarize what you learned by completing the following sentences:

On Valentine's Day 1994, Debi learned

The drugs Debi took to cure her TB were not working because

5. Review the results and conclusions from Plates 5 and 6 of your bacterial growth experiment. Put together those results and Debi's experience to complete the following sentence:

Debi had a relapse (developed an active case of TB again), even though her health had improved and she was still taking the drugs to cure TB, because

6. If you have Internet access, click on *A Happy Ending* to learn what finally happened to Debi. If you don't have Internet access, read "A Happy Ending" on **Master 3.3b**. Summarize what you learned by completing the following sentences:

Debi was finally cured of TB by

Debi's warning about infectious diseases like TB is

Master 3.4b

Antibiotic Concerns

Each of these statements describes a potentially inappropriate use of antibiotics. How would you persuade people to eliminate unnecessary use of antibiotics in these cases?

Statement 1

In response to pressure from patients to “give me something,” some doctors prescribe antibiotics before they know whether a patient’s illness is caused by a virus or bacteria.

Statement 2

Antibiotics are widely used in livestock feed to improve the growth of animals.

Statement 3

A popular marketing strategy for some products intended for healthy people (for example, hand soaps and children’s toys) is to include antibacterial drugs in the products.

Measles Outbreak at Western High

Read the following story about some students at Western High.

It began with Naoko Yomata. She and her family had just moved when she started the second half of her junior year at Western High in a small town in Washington State. One week into the semester, she had a sore throat, felt exhausted, and developed a fever of 102°F. Soon, she had a red rash all over her body—measles.

Ten days later, Caleb Miller and Jessica Johnson came down with measles. These students were in Naoko's biology class, and Jessica was her lab partner. The following week, a sophomore, Michael Chen, had measles and so did the students' biology teacher, Ms. Baker.

The local public health officer was alarmed. Western High hadn't had a case of measles in 10 years, and now there were five cases in less than a month.

A Little Sleuthing

Read the rest of the story about the measles outbreak at Western High and think about the question that ends it.

A little sleuthing revealed the following:

Naoko had just arrived in the United States from her home country, Japan, where she apparently contracted measles. She had not been vaccinated as a child. Caleb was also susceptible to measles because his parents had objected to vaccinations. Jessica and Michael were vaccinated when they were 15 and 18 months old, respectively, but they had missed the required “booster shot” during elementary school.

Ms. Baker was vaccinated in 1966 when she was 5 years old. Later studies showed that the initial “killed measles” vaccine was not very effective compared with the currently used “live measles” vaccine, first available in 1968. Ms. Baker was unaware that her vaccination was not effective or that she needed a booster shot.

The results of the public health officer’s detective work explained why Naoko, Caleb, Jessica, Michael, and Ms. Baker got the measles.

In the 1950s and 1960s (before the measles vaccine was developed), most people got this disease as preschool children or as elementary school students. This raises another question: Why didn’t the unvaccinated or inadequately vaccinated students and teacher at Western High get measles when they were children, rather than now, as teenagers or adults?

Following an Epidemic

Name: _____

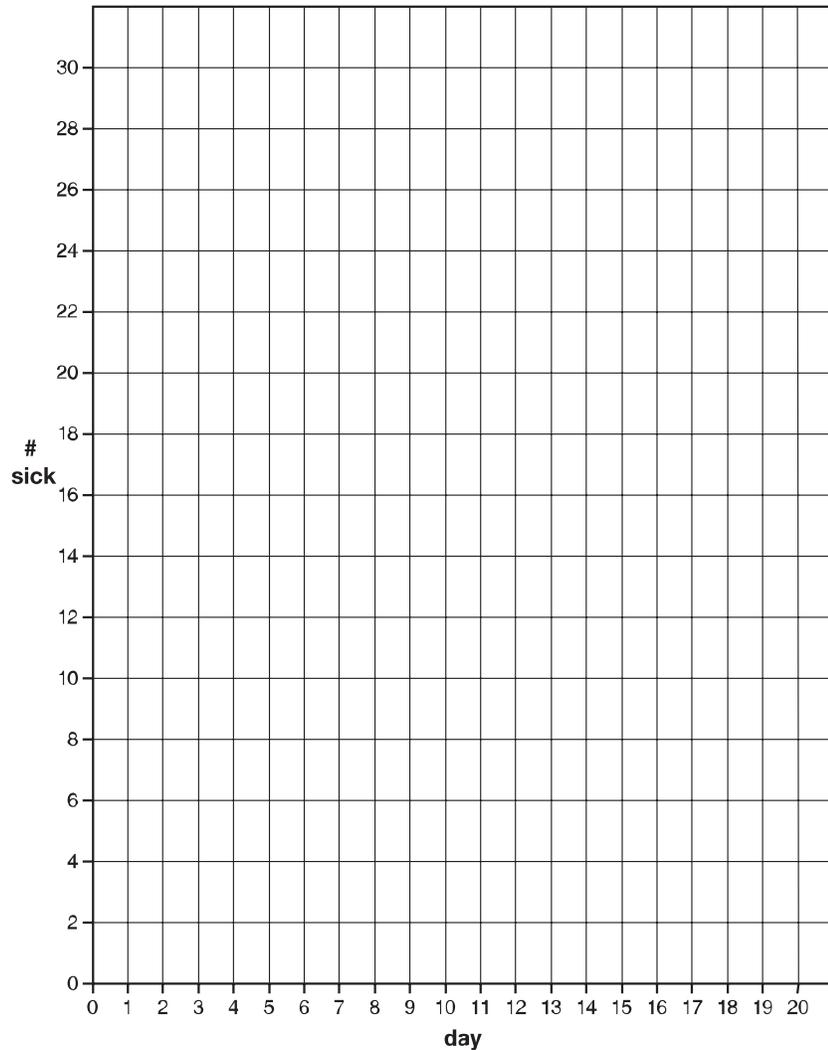
This worksheet will help you track the results of the disease-transmission simulation. Follow your teacher's instructions for completing the following tables and graphs.

Observations

Review your data on the table and graph, then make three or four observations about the transmission of two-day disease. For example, did an epidemic occur in both simulations? How long did it last? Did everyone get sick at some point?

Time Course of an Epidemic

Day	Number of People Sick	Number of People Immune
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		
11		
12		
13		
14		
15		
16		
17		
18		
19		
20		



Total number of students who got sick: _____

Disease-Transmission-Simulation Record

Name: _____

Use the computer simulation of disease transmission to investigate the effect of changing a disease characteristic on the occurrence of an epidemic.

- Run the computer simulation of disease transmission first with the disease characteristics values set for two-day disease: initial percent immune = 0; virulence = 0; duration of infection = 2; rate of transmission = 1. Record the results below.

Did an epidemic occur? (circle one) Yes No

Maximum number of sick _____

Maximum percentage sick _____

Maximum occurred on day _____

- Circle the disease characteristic you were assigned to investigate:

virulence duration of infection rate of transmission immunity level

- Test four settings for that characteristic across the range that the simulation allows. Keep the settings for the other disease characteristics the same as for two-day disease. Record the results below.

<p>Simulation 1</p> <p>Characteristic tested set at _____</p> <p>Did an epidemic occur? Yes No</p> <p>Maximum number sick _____</p> <p>Maximum percentage sick _____</p> <p>Maximum occurred on day _____</p>	<p>Simulation 2</p> <p>Characteristic tested set at _____</p> <p>Did an epidemic occur? Yes No</p> <p>Maximum number sick _____</p> <p>Maximum percentage sick _____</p> <p>Maximum occurred on day _____</p>
<p>Simulation 3</p> <p>Characteristic tested set at _____</p> <p>Did an epidemic occur? Yes No</p> <p>Maximum number sick _____</p> <p>Maximum percentage sick _____</p> <p>Maximum occurred on day _____</p>	<p>Simulation 4</p> <p>Characteristic tested set at _____</p> <p>Did an epidemic occur? Yes No</p> <p>Maximum number sick _____</p> <p>Maximum percentage sick _____</p> <p>Maximum occurred on day _____</p>

Summary

Write a one- to two-sentence summary that describes how the likelihood of an epidemic changes as your disease characteristic changes.

Characteristics of Smallpox, Polio, and Measles

Disease	Virulence	Duration of Infection	Rate of Transmission	Immunization Level for Herd Immunity
smallpox	high (0.25)	14 days	high (2.5)	
polio	low (0.01)	18 days	average (1)	
measles	low (0.01)	8 days	very high (10)	

Cases of Smallpox in Niger and Bangladesh

Country	Year	Population	Percent of People Vaccinated	Number of Smallpox Cases	Cases of Smallpox per Square Kilometer
Bangladesh	1973	72 million	80	33,000	0.23
Niger	1969	3.9 million	79	25	0.00002

Source: Anderson, R.M., and May, R.M. 1992. *Infectious Diseases of Humans*. New York: Oxford University Press, page 89.

The Proposals

Characters

- Foundation Officer
- AIDS Treatment Administrator
- Public Health Physician
- Hospital Administrator

Segment 1: Introducing the Proposals

Foundation Office

FOUNDATION OFFICER: Our organization funds research projects focused on relieving human suffering from disease. This year we have \$5 million to award for a single project. I've narrowed the field down to three strong proposals for work on three very different diseases. Believe me, these are tough decisions. We'd like you to consider two major criteria in making your recommendation. First, evaluate the magnitude of the situation. For example, how many people are affected by the disease? How serious are the consequences of the disease for the individual and for society?

Second, we need to know how effective the proposed plan will be for fighting or preventing the disease. Will we be able to get the treatments to people affected by the disease? If the plan is to develop a new treatment or prevention strategy, how likely is it to be successful? Rate these proposals using these two criteria and then give me a final recommendation.

Segment 2: Proposal 1

AIDS Clinic

AIDS TREATMENT ADMINISTRATOR: AIDS is now a worldwide epidemic that affects every sector of society. The most effective way to deal with AIDS is with powerful drugs. We attack the disease with drugs like AZT. It stops the virus from replicating and keeps the amount of virus in the blood low. By doing that and treating the symptoms at the same time, the patient will survive 5, 10 years, even more. Hopefully, then, maybe the body takes over and holds off the disease on its own. It isn't a cure. But living with the disease is better than dying with it. The problem is that these drugs are expensive. Our proposal is simple. Give us the money and we will give years of life to our patients.

Segment 3: Proposal 2

Physician's Office

PUBLIC HEALTH PHYSICIAN: Any disease like measles that affects millions of individuals is a significant public health problem. It may not seem like a big deal to people in the United States, where it is a somewhat uncommon childhood disease. Most children who get it develop an itchy red rash and miss a week of school. Then, they are immune. But measles is a major killer in developing countries where there are not enough vaccination programs and medical care and general nutrition are poor. We have an excellent vaccine that could eliminate the virus just as we have eliminated smallpox. We would use the grant money to prepare and distribute measles vaccine globally as part of a coordinated effort to wipe out the measles virus.

Segment 4: Proposal 3

Hospital Administrator's Office

HOSPITAL ADMINISTRATOR: Patients come to our hospital for routine surgery and then, five days later, they have a life-threatening infection of *Staphylococcus aureus*. But that's not new. *Staph* is everywhere, especially in hospitals where infants, surgical patients, and others in poor health provide an environment with plenty of easy prey for the bacteria. What's changed is that the antibiotics that once cured a *Staph* infection are not effective anymore. We're lucky, because we have vancomycin, which kills the most resistant strains of *Staph aureus*. But recently, we've discovered isolated cases of vancomycin-resistant *Staph aureus* (or VRSA). We must work quickly to develop new drug therapies before these resistant strains become widespread. Our proposal is to develop and test drug therapies that can stop *Staph aureus* before we have an epidemic.

Reference Database—AIDS

For up-to-date statistics on HIV/AIDS, visit the Web sites for the Centers for Disease Control and Prevention and the World Health Organization: <http://www.cdc.gov> and <http://www.who.int>.

AIDS—Cause

AIDS is caused by the human immunodeficiency virus (HIV). HIV attacks particular cells of the victim's immune system. As a result, the person's immune defenses are weakened tremendously, and the victim is unable to fight off infections. Even worse, the victim is left vulnerable to many serious diseases, such as tuberculosis, pneumonia, fungal infections, and cancer. Death usually occurs as a result of one of these diseases.

AIDS—Cost

The economic cost of the AIDS epidemic is staggering. First, there is the cost of caring for one patient with AIDS. The most common treatment in the United States is a “cocktail,” or mixture, of drugs that can cost up to \$23,000 per patient per year. These drugs slow the progress of the disease but do not eliminate HIV from the patient's body. Research also shows that these drugs must be taken regularly from the time of diagnosis for the rest of the patient's life: As soon as the drugs are stopped, the virus bounces back, as dangerous and life threatening as ever. A further drawback is that the virus in a patient may become resistant to these drugs.

In the United States alone, the cost of providing these drugs to AIDS patients is in the millions of dollars and is rising each year. Unfortunately, developing nations cannot afford to treat their HIV-infected citizens with these drugs. African nations have an average of \$10 per year per person for medical care, yet Africa is the part of the world that is hardest hit with the disease.

The epidemic has other costs, too. In some countries, such as Uganda, Zambia, and Zimbabwe, three-fourths of the hospital beds are filled with children who are HIV-positive. Millions of adults have died, and many of them have left orphaned children. Many others have left surviving spouses who also are ill, need treatment, and cannot work. Families cannot find money to pay for funerals, and employers must find and train new employees. This problem is eating away at these countries' economies.

As one scholar described the problem, “The epidemic's direct and indirect consequences are wiping out the gains that many of these countries have made in the past 30 years.”

AIDS—Death Rate

The total number of worldwide deaths from AIDS in 1998 was about 2.5 million (2 million adults and 510,000 children under the age of 15). In 2011, it was 1.7 million (1.5 million adults and 230,000 children under the age of 15).

In 1998, the total number of worldwide deaths since the beginning of the epidemic was about 13.9 million (10.7 million adults and 3.2 million children under the age of 15). By 2010, that number had reached 30 million, and there are roughly 7,000 new HIV infections in the world every day.

AIDS—Definition

AIDS, acquired immune deficiency syndrome, is a disease in which the immune system no longer functions effectively. It is caused by the human immunodeficiency virus (HIV). People with AIDS are vulnerable to a variety of other diseases (opportunistic infections) that only rarely occur in people with healthy immune systems.

Master 5.2a

AIDS—Diagnosis

If a person is infected with HIV, his or her body will make antibodies, special proteins produced by the immune system that recognize and can attach to HIV. To test for HIV infection, doctors look for these antibodies in the person's blood. If antibodies against HIV are present, they are evidence that the person is infected with HIV. If antibodies against HIV are not present, the person either is not infected or was infected recently enough that his or her body has not yet made these antibodies in detectable quantities. Only another test at a later date can distinguish between these possibilities.

Infection with HIV is not the same as having AIDS. When a physician suspects that a person may have AIDS, he or she may order another laboratory test of the person's blood. The diagnosis of AIDS is confirmed if the person's CD4 T-cell concentration is lower than 200 cells per cubic millimeter of blood (normal levels are at least 800 cells per cubic millimeter of blood) or if the person develops one or more of the opportunistic infections associated with AIDS.

AIDS—Incidence (Predictions)

Globally, great strides have been made in terms of scientifically proven HIV-prevention modalities, such as medically supervised, voluntary adult male circumcision; preventing mother-to-child HIV transmission and using HIV drugs as prevention; and increasing access to HIV treatment for those who need it. As a result, the scientific community is much more hopeful that an end to the HIV/AIDS pandemic is possible. To achieve this, however, will require significant scale-up of these proven HIV-prevention measures as well as a commitment by countries, governments, and communities to strengthen their healthcare systems and build the capacity to provide HIV treatment and prevention. Further, continued basic and clinical research is needed to find additional HIV treatment and prevention interventions as well as a preventive vaccine and, ultimately, a cure.

AIDS—Incidence (United States)

In the United States, roughly 1.1 million people were living with HIV infection as of 2009. Each year, about 50,000 more people are infected. In 1998, AIDS was the leading cause of death for men between the ages of 25 and 44 and the fourth-highest cause of death for women in this age category. By 2008, AIDS ranked sixth as a cause of death for men and women in this age group.

The largest number of new HIV infections in the United States currently occurs among men who have sex with men of all races and ethnicities, followed by African-American heterosexual women. Injection-drug users and transgender people also represent populations at highest risk for HIV infection.

AIDS—Incidence (Worldwide)

Since the early 1980s, more than 60 million people worldwide have contracted the human immunodeficiency virus (HIV), and more than 25 million have died of HIV-related causes. In 2011, more than 34 million people were living with HIV, and there were 2.5 million new infections and 1.7 million deaths.

Worldwide, the highest incidence of HIV infection is in sub-Saharan Africa. Two-thirds of all HIV-positive people and 90 percent of all infected children live in this area. In some African countries, one in four adults is HIV-positive.

The second highest incidence of HIV infection is in Southeast Asia. Here, the epidemic is worst in India and Thailand.

AIDS—Modes of Infection

You can get HIV (the virus that causes AIDS) from anyone who is infected with the virus, even if they do not look sick, do not know they're sick, and do not yet test positive for the virus (that is, are not yet HIV-positive).

Most people get HIV by

- having unprotected sex with a person who is infected,
- sharing a needle (shooting drugs) with a person who is infected, or
- being born from or drinking the breast milk of a woman who is infected.

There are no known cases of someone getting HIV through contact with an infected person's tears or saliva, but it is possible to catch HIV through oral sex, especially if you have open sores in your mouth or bleeding gums.

In the past, some people were infected with HIV from getting a blood transfusion from an infected person. Today, the blood supply is carefully tested, and the risk of infection from a blood transfusion in the United States is very low.

AIDS—Name

The name "AIDS" means "acquired immune deficiency syndrome."

The word "acquired" means that a person can catch AIDS; it is an infectious disease.

The words "immune deficiency" mean that the disease causes a weakness in a person's immune system. The immune system is the part of the body that fights disease.

The word "syndrome" is a medical term for a group of health problems that all are associated with a particular disease. People with AIDS display many health problems, such as weight loss, problems with infections, brain tumors, and other health problems.

AIDS—Treatment (General Information)

There is still no cure for AIDS. Drugs are available that can slow down the damage to a person's immune system and the multiplication of the virus. Some scientists think that the new, strong, anti-HIV drugs that are currently available might eliminate all the HIV from a person's body if the drugs are taken for several years. Research is under way to determine whether this is the case.

Drugs are available that can prevent some of the opportunistic infections that people with AIDS are susceptible to. There is little that a person can do to prevent some of the other infections.

AIDS—Treatment (Drug Therapies, General Information)

The best and most widely used treatment for AIDS today is designed to slow down a person's progression from being HIV-positive to having AIDS. This treatment involves taking a "cocktail," or mixture, of several drugs that suppress the multiplication of the human immunodeficiency virus (HIV), which slows down the damage to a person's immune system.

The use of these drugs has led to a 44 percent decline in AIDS deaths in the United States, as well as to a significant drop in the number of cases of opportunistic infections among AIDS patients. These drugs do not, however, cure AIDS, because they do not completely eliminate HIV from a person's body.

Master 5.2c

Following this treatment plan correctly is a challenge for patients. The cost of these drugs is about \$15,000 per year per patient. Side effects include nausea, diarrhea, rashes, headaches, and elevated triglyceride and cholesterol levels in the blood. Patients must take several pills every day, some of which must be taken on an empty stomach, some with food, and some with or without other pills. If patients miss doses, they risk not completely suppressing the multiplication of the virus and also risk the appearance of strains of HIV that are resistant to the drugs.

AIDS—Treatment (Drug Therapies, Viral Resistance)

When drugs against HIV do not work, it is often because the virus has become resistant to one of the drugs being used. This resistance is the result of mutations that occur in the viral genes.

Unfortunately, use of anti-HIV drugs can actually promote the reproduction of resistant virus particles. Untreated, HIV makes approximately 10 billion new virus particles every day in an infected person. But HIV does not copy its genetic material very accurately. Because of its sloppy replication, each one of these new virus particles may be different from the parent virus in one or more genes. And because so many virus particles are produced each day, it is very likely that at least one virus is produced each day that is resistant or partially resistant to one of the antiviral drugs the person is taking. This virus particle now has an advantage over other virus particles that are not resistant to the drug, and it may reproduce faster than nonresistant strains. Thus, taking anti-HIV drugs can actually promote the reproduction and accumulation of viruses that are not inhibited by the drugs the patient is taking.

Because resistance can occur so easily and because no single drug on the market can inhibit HIV reproduction completely on its own, physicians now treat patients with mixtures (cocktails) of drugs. Physicians must also stay on the lookout for signs of viral resistance emerging in a patient, and if resistance appears to be emerging, must consider new combinations of drugs that will be effective for that patient.

HIV—Course of Infection

Many people do not know when they are first infected by HIV because they have no symptoms. Other people don't know because although they get a fever, a headache, and sore muscles and joints for one or two weeks, they think it is just the flu.

The virus multiplies inside the victim's body for a few weeks (or even a few months) before his or her immune system responds. During this period of time, the person is infected with HIV and can infect others, but he or she won't test positive for HIV.

When a person's immune system begins to respond to the virus by making antibodies, the person will test positive for HIV.

Some people with HIV stay healthy for many years after infection. During this time, however, the virus is damaging the person's immune system. Healthcare professionals can measure this damage by counting the number of CD4 T-cells a person has. These cells, also called T-helper cells, are part of a person's immune system. Healthy people have between 500 and 1,500 CD4 T-cells in each cubic millimeter of blood, but people with HIV disease have many fewer. As a person's CD4 T cell count goes down, he or she may start having signs of HIV disease (for example, fevers, night sweats, diarrhea, weight loss, or swollen lymph nodes).

HIV disease is diagnosed as AIDS when the person's CD4 T-cell count drops below 200 CD4 T-cells per cubic millimeter of blood or when the person gets one of the opportunistic infections identified by the Centers for Disease Control and Prevention as characteristic of AIDS.

Master 5.2d

AIDS progresses at different rates in different people. Some people die within five years of being infected with HIV, whereas other people live for many years, even after they develop AIDS. In the early years of the epidemic 30 years ago in the United States, people with HIV could expect to die from AIDS within about 10 years after becoming infected. With the treatment nowadays, though, people who are HIV-positive can expect to live for decades and to die from other causes.

HIV—Definition

HIV stands for “human immunodeficiency virus.” HIV is the virus that causes AIDS.

HIV—Definition of HIV-Positive (or HIV Disease)

When a person is infected with HIV, his or her body responds by making antibodies against the virus. (Antibodies are special proteins that fight disease.) Blood tests for AIDS look for antibodies in the blood against HIV. People who have antibodies against HIV in their blood are said to be “HIV-positive.” They also might be said to have “HIV disease.”

Being HIV-positive (or having HIV disease) is not the same as having AIDS. Many people are HIV-positive, meaning that they have been infected with HIV, but they are not yet sick. As HIV remains in the body, it slowly wears down the immune system.

HIV—Rate of Mutational Change

Untreated, HIV reproduces very rapidly inside a person’s body, making approximately 10 billion new virus particles every day. But HIV does not copy its genetic material very accurately. In fact, because of its sloppy replication, each one of these new virus particles may be different from the parent virus in one or more genes. Thus, HIV shows a very rapid rate of mutational change.

The result of this high rate of mutational change is that there are many different HIV strains, not only in the world, but even within one person’s body. This presents a problem for developers of new drugs to combat HIV (some of these different strains may be resistant to the drug) and for developers of vaccines against HIV (the vaccine may be effective against one strain of HIV but not another).

Sources for the data include the UNAIDS and the CDC Wonder Web sites (<http://www.unaids.org/en/> and <http://wonder.cdc.gov/>).

Master 5.2e

Reference Database—Measles

For up-to-date statistics on measles, visit the Web sites for the Centers for Disease Control and Prevention and the World Health Organization: <http://www.cdc.gov> and <http://www.who.int>.

Measles—Definition

Measles (also called rubeola) is a severe and highly contagious viral infection of the respiratory tract, although its most prominent symptom is a skin rash.

The measles virus spreads by direct contact with an infected person. Usually, the virus spreads via droplets of fluid from the person's respiratory tract. These droplets contain millions of virus particles that can infect another person, entering through the respiratory tract. Here, the virus incubates for one to two weeks before symptoms appear: fever, discomfort, sore throat, coughing, and finally a painful and itchy rash. After a few more weeks, the infection usually subsides. In a few cases, infection leads to pneumonia, brain damage, ear and sinus infections, convulsions, and sometimes death.

In developed countries, measles is usually not a fatal disease. In many developing countries, however, measles has a much higher mortality rate, accounting for 10 percent of all deaths in children under five years old.

Measles—Diagnosis

People who have measles show a variety of symptoms, ranging from mild fever to severe skin rashes, to life-threatening seizures and infections. Doctors diagnose measles by the presence of Koplik's spots—tiny, white specks, surrounded by a red halo, that appear on the inside of the cheek, near the molars. Doctors can also use blood tests to check for antibodies against the measles virus.

Measles—Epidemics

Measles epidemics occur when the measles virus spreads rapidly through a susceptible population. Epidemics pose the greatest threat to unvaccinated people or people who have had only one dose of the vaccine and failed to develop antibodies against the virus.

Populations with high vaccination rates are less susceptible to epidemics. However, such populations can experience measles outbreaks in which three or more linked cases of the disease occur. Outbreaks are shorter in duration and more limited in transmission than epidemics.

The higher the percentage of unvaccinated people, the more susceptible a population is to an epidemic. The "epidemic threshold" is the point at which the percentage of unvaccinated people is high enough to risk an epidemic.

Measles—Immunity

There are three kinds of immunity to measles: passive immunity, natural immunity, and immunity derived from vaccination. Infants born to mothers who have either had measles or been vaccinated are protected by maternal antibodies; that is, they have passive immunity. This protection lasts six months, on average, and then the child becomes susceptible to measles. A person is naturally immune if he or she has had contact with the measles virus and has developed antibodies against it. People born before 1957 are considered naturally immune because of the high probability that they were exposed to the virus during childhood. People born after 1957 are considered immune if they have been fully vaccinated, have had a confirmed case of measles, or have had blood tests that confirm previous exposure to the virus.

Full vaccination requires two doses of vaccine: one between the ages of 12 and 18 months, and the other between the ages of 4 and 6 years or 11 and 12 years. (The second dose helps catch the small number of people who do not become immunized by the first dose.)

Measles—Incidence (Historic)

During this century, there has been a dramatic decrease in measles epidemics. Before the development of the measles vaccine, 5.7 million people died each year from measles. (Some historians have suggested that measles might have contributed to the decline of the Roman Empire.)

In 1920, the United States had 469,924 measles cases and 7,575 deaths due to measles. From 1958 to 1962, the United States had an average of 503,282 cases and 432 deaths each year. (Measles reporting began in 1912; before that, no statistics are available.) In large cities, epidemics often occurred every two to five years.

When the measles vaccine came on the market in 1963, measles began a steady decline worldwide. By 1995, measles deaths had fallen 95 percent worldwide and 99 percent in Latin America. In the United States, the incidence of measles hit an all-time low in 1998, with 89 cases and no deaths reported. In 2008, there were 140 cases.

There have been several epidemics in the United States since 1963: from 1970 to 1972, 1976 to 1978, and 1989 to 1991. The epidemic of 1989–1991 claimed 120 deaths out of a total of 55,000 cases reported. More than half of the deaths occurred in young children.

Measles—Incidence (United States)

In 1997, the Centers for Disease Control and Prevention (CDC) reported a total of 138 cases of measles in the United States. In 2008, there were 140 cases. Most of these outbreaks probably began when an infected person from another country (specifically Germany, Italy, Switzerland, Brazil, and Japan) entered the United States. The virus subsequently spread through the population, with the longest chain of transmission lasting five weeks. Children were most affected by these outbreaks: 29 percent of cases were children 1–4 years; 28 percent were children 5–19; 26 percent were adults 20–39. In addition, unvaccinated people accounted for 77 percent of cases; people who received only one dose of vaccine accounted for 18 percent of cases; and people who received the full two doses of vaccine accounted for 5 percent of cases. (These statistics demonstrate that a small percentage of people fail to develop immunity after one or even two doses of vaccine.)

In 1998, the United States had only 89 cases of measles and no deaths from the disease. Measles cases clustered in a few states. Arizona, California, Florida, Massachusetts, Minnesota, New York, Pennsylvania, South Dakota, and Texas reported 64 percent of measles cases in 1997. Most of these cases were from foreign visitors who brought the virus with them or from U.S. citizens who contracted the virus while traveling abroad. These patterns suggest that there is no established measles virus circulating in the United States. By 2008, the number of cases per year had increased again, to 140.

Measles—Incidence (Western Hemisphere)

The Western Hemisphere (countries in the Americas and the Caribbean) has the lowest incidence of measles worldwide, with only 2,109 cases reported in 1996 and 204 in 2008. However, low rates of vaccination among some populations resulted in several outbreaks: in 1997 in Brazil (51,000 cases); in 1998 in Argentina (3,000 cases and 11 deaths); and in 1998 in Bolivia (111 cases). Children under four years old were most commonly affected by these outbreaks. An outbreak at a Canadian university also suggested that low immunization rates among students had left an opening for the measles virus. In all cases, gene sequencing indicated that the virus had come from a foreign source.

Master 5.3b

Measles—Incidence (Worldwide)

According to the World Health Organization (WHO), there were 31 million cases of measles in 1997, resulting in almost 1 million deaths. In 2008, reported cases totaled 281,972, and there were 164,000 deaths. (These figures are estimates because only a fraction of measles cases worldwide are actually reported.) The majority of these cases occurred in Africa, followed by Asia, India, and the Middle East. In fact, in 1997 roughly 99 percent of all measles deaths occurred in developing countries; in 2007, it was 95 percent.

In 2001, the Measles Initiative was launched. It is a partnership among public health organizations committed to reducing measles deaths globally. By 2008, the number of deaths from measles had dropped to 164,000, or 450 per day. This is a 90 percent reduction since 2000. The majority of deaths occur among undernourished young children. In developing countries, measles accounts for 10 percent of all deaths in children under age 5.

Measles—Transmission (General)

Some reports claim measles is the most contagious of all infectious diseases. The measles virus spreads easily by direct contact. Usually, this happens when infected people exhale minute droplets containing the virus particles; these droplets come in contact with other people and cause infection. In addition, people who have had the disease sometimes have low levels of virus for many decades afterwards. These viruses also can infect other people.

Scientists use gene-sequence data to determine origin and transmission patterns of the measles virus. If the virus is established and circulating among members of a population, it is said to be *endemic* or *indigenous*. Currently, the virus is endemic in many African, Asian, and European countries. The Western Hemisphere has no endemic measles virus, and the only outbreaks occur when visitors and foreign travelers carry the virus from other countries.

Measles—Transmission (Reservoirs of Infection)

Although the measles virus has been eliminated from the Western Hemisphere, there are reservoirs of the measles virus in many countries around the world (for example, in Africa, Asia, and Europe). Because of widespread travel, it is impossible to isolate measles by country or hemisphere. As recent cases in the Western Hemisphere show, outbreaks can still occur despite the absence of any established virus in a population. (High levels of immunization prevented the virus from becoming re-established through an epidemic.) Until eradication efforts succeed globally, countries must maintain high rates of vaccination in order to protect their populations.

Fortunately, there is no reservoir of the measles virus in animals. Unlike some viruses, the measles virus is specific to humans and cannot survive or replicate in any other animal species. If the virus is eradicated in the human population, there are no animal reservoirs that could reintroduce the virus.

Measles—Treatment

Measles has a severe effect on the nutritional status of a child: well-nourished children who are otherwise healthy lose weight when they have the measles, while malnourished children become seriously ill. Treatment for measles consists of bed rest, medicines to control fever, and calamine lotion or other salves to relieve itching. Mortality rates are low in most developed countries where children have relatively good nutrition; however, complications occur rarely that require hospitalization: pneumonia, appendicitis, and severe infections of the brain or respiratory systems. In many developing countries where conditions of poor nutrition, poor sanitation, and lack of adequate health care are common, measles mortality rates are considerably higher, especially among children.

Measles—Vaccine (Definition)

Measles vaccine (also called the Measles Virus Vaccine Live) is an inactivated form of the measles virus. The measles vaccine came on the market in the United States in 1963. In the United States, children usually receive a combined measles, mumps, and rubella vaccine (MMR).

The measles vaccine causes the body to produce antibodies against the virus, providing lifelong protection from the active virus. To ensure immunization, a person usually receives two doses of the vaccine: One dose at roughly 1 year of age and a second dose between 4 and 6 years of age or between 11 and 12 years of age. One dose of vaccine is only 95 percent effective (95 percent of people develop antibodies and become immune, whereas 5 percent fail to develop antibodies). The second dose helps catch the small number of people who do not develop antibodies after the first dose.

Measles—Vaccine (Risks)

More than a decade of studies has shown little or no serious side effects associated with the measles vaccine. Those with a presumed higher risk of side effects include people with a history of allergic reactions to previous measles vaccine, the antibiotic neomycin, or other substances such as gelatin; pregnant women; infants younger than 6–12 months; people taking certain medications or receiving X-rays or cancer therapies; and people with immune deficiencies or severe illness with fever.

Measles—Vaccine (Side Effects)

The measles vaccine sometimes causes a range of mild side effects including low-grade fever, skin rash, itching, hives, swelling, reddening of skin, and weakness. Rarely, the vaccine causes seizures, double vision, headaches, vomiting, joint pain, or pain in the digestive system.

Eradication—Benefits

The ultimate benefit of eradication is the prevention of death. Eradication also saves money in the long run, as the case of smallpox demonstrates. When smallpox was eradicated in 1977, countries discontinued vaccination and prevention efforts. This meant an enormous savings in medical costs: By 1985, the United States was recovering the money it had invested in global eradication every 26 days. As with smallpox, money spent on measles eradication would eventually be recouped from savings in vaccination programs and medical treatment for measles patients.

Eradication—Challenges

Despite recent successes, several challenges remain in the fight for global eradication of measles. The magnitude of vaccination programs is staggering: Every day in the United States 11,000 children are born, each requiring 15–19 doses of different vaccines by the time they are 1½ years old. It is logistically impossible to ensure that 100 percent of these children are vaccinated. Instead, vaccination programs can only aim to eliminate the risk of a major epidemic; this goal can be achieved for measles with a 90 to 95 percent vaccination rate.

In developing countries, the eradication challenge is even greater because lack of funds results in minimal healthcare programs and inadequate surveillance. Because cost effectiveness is critical in these countries, vaccination programs must target the neediest populations. For example, in countries with a high incidence of measles and a low vaccination rate, school-age children are likely to have developed a natural immunity to the virus (due to previous contact with the virus). These countries should target vaccination programs at a narrow age range, focusing on young children (who are less likely to have had previous contact with the virus). In contrast, people living in the sparsely populated Sahel of West Africa have a lower incidence of measles and, therefore, many potentially susceptible adults. In this case, vaccination programs should best target a wider age range.

Master 5.3d

As campaigns succeed in eliminating measles from one country after another, experts predict that patterns of outbreaks and risks will shift. For example, older children and adults will be more likely to be susceptible; infants born to vaccinated mothers will be protected by maternal antibodies for a shorter period of time; people might become complacent about having their children vaccinated; and the number of susceptible people might increase, approaching the threshold level for epidemics. These changing patterns might require changes in vaccination strategies.

Eradication—Costs

Estimates of the cost of global measles eradication ran as high as \$4.5 billion by the year 2010, an amount that includes \$1.7 billion for vaccines in developing countries. In 1998 alone, the Centers for Disease Control and Prevention (CDC) budgeted \$8 million for international programs to eliminate measles.

The measles vaccine itself is relatively inexpensive. (For countries in the Pan American Health Organization, each dose costs just 10 cents.) Eradication, however, requires additional expense and effort. These include extensive surveillance systems, education and health campaigns, and systems to ensure quick response to contain outbreaks. These expenses weigh heavily on some developing countries, whose healthcare systems are already stretched to their limits.

Eradication—Definition

The goal of eradication efforts is to stop the global spread of the measles virus and thereby end the need for vaccination. Eradication is possible because there is a highly effective vaccine and the measles virus survives or replicates only in humans. This means that there is no hidden reservoir of the virus in animals that could lead to outbreaks in humans in the future.

To achieve global eradication, all countries must first eliminate any measles viruses that are established or circulating within the population. These elimination campaigns require ongoing surveillance and vaccination to prevent outbreaks from measles viruses imported from other countries.

Eradication—Feasibility

In 1996, the World Health Organization (WHO) confirmed that global eradication of measles is feasible between 2005 and 2010 using current vaccines. All countries were urged to: 1) use a two-dose strategy for immunization; 2) include rigorous diagnosis and surveillance; 3) view measles outbreaks as an opportunity to raise awareness and political support for eradication; and 4) work closely with other countries. Moreover, the WHO urges developing countries to link their measles and polio vaccination efforts to prevent conflicts over limited resources.

Eradication—Problems

Because of limited resources and logistical problems delivering the vaccine, measles remains a serious problem in some developing countries. Experts warn that vaccine shortages may prevent these countries from effectively controlling outbreaks. They also warn that measles vaccination programs compete with polio eradication efforts in some countries, making it difficult to make progress against either disease.

Some experts believe that the United States has become complacent in its attitude toward measles. They say that the United States views measles as a mild disease and focuses on the safety and effectiveness of vaccinations rather than on maintaining vaccination coverage so that global eradication can be achieved. These experts believe that by delaying eradication efforts, many of the hard won gains of the past decade will be wiped out.

Eradication—Campaigns (Western Hemisphere)

In 1994, countries in the Western Hemisphere set a goal of eliminating measles by the year 2000. Although it hasn't yet been eradicated, the number of cases has decreased significantly. From 1987 to 1994, numerous countries supplemented their routine vaccination programs with catch-up campaigns. All these countries now have laboratories that can report data to a regional surveillance network. As a result, in 1996 over half of the countries exceeded 90 percent vaccination coverage. That year saw a total of 2,109 cases of measles. This represents only 0.3 percent of the global total of measles cases. In addition, more than 60 percent of the countries in the Western Hemisphere reported no cases of measles. By 2008, there were only 204 cases.

Eradication—Campaigns (Worldwide)

Support for global measles eradication began to form in 1989, when the World Health Assembly set a goal for 1995 of decreasing measles deaths by 95 percent compared with measles deaths during the prevaccination period. In 1990, the World Summit for Children resolved to vaccinate 90 percent of children by the year 2000. Countries in the Western Hemisphere, Europe, and the Eastern Mediterranean formed organizations to pursue regional goals.

Current data suggest that vaccination programs have eliminated the measles virus from much of the Western Hemisphere, the United Kingdom, and the West Bank and Gaza. Countries in Europe, the South Pacific, the Middle East, and Southeast Asia have increasingly used catch-up vaccination programs to supplement their routine vaccinations. These campaigns reached an additional 32.8 million children. As of 1998, catch-up programs were continuing in Australia, the Philippines, Romania, and Tunisia.

Eradication—Surveillance

Surveillance is a critical component of measles eradication. Measles surveillance requires local, regional, and national efforts. Locally, doctors must work with microbiology labs to diagnose measles cases correctly. Regional and national laboratories then gather and analyze the data to determine the original source of the virus, how many other people might have come in contact with it, and how it might best be contained. Surveillance networks also monitor vaccination rates to determine the locations of populations especially at risk for measles epidemics. Without these data, measles elimination would not be possible because countries could not see how best to use scarce resources of money and technology. Although most developed nations have adequate surveillance networks, many developing countries have only one national laboratory dedicated to the problem of measles elimination.

Vaccination—Programs (At-Risk Populations)

In the United States, populations at risk for reduced levels of vaccination include people of low income, minority groups, large families, and young mothers. People at risk for contracting measles include those living in the inner city or an area of a previous measles outbreak, women of childbearing age, college students, foreign travelers, and healthcare workers.

People who receive only one dose of vaccine are also at higher risk for contracting measles. In 1999, an outbreak in Anchorage, Alaska, started when a 4-year-old child, visiting from Japan, developed a measles rash. A month later, students at a local high school started coming down with the disease. A total of 33 cases were reported, with no deaths. Despite a high immunization rate at the school, the outbreak occurred because half of the students had only had one dose of the vaccine. One dose is only 95 percent effective. This left a window of opportunity for the virus. Of the 33 cases, 29 were students who received at least one dose of vaccine. Afterward, school and health officials accelerated second-dose vaccinations in order to prevent future outbreaks.

Master 5.3f

Vaccination—Programs (Costs)

Costs of measles vaccination programs vary depending on the strategy and goals of the program. In 1998, the Australian government budgeted \$30 million for a vaccination program to immunize 95 percent of its children. The actual price for the measles vaccine varies. In the Americas, the vaccine is available at a cost of 10 cents per dose or 49 cents per dose if combined with the vaccines for mumps and rubella (German measles)—the MMR vaccine.

Cost estimates also must acknowledge that vaccination programs can lead to a decrease in medical costs for treating measles patients. According to one estimate, every \$1 spent on measles vaccine saves \$10.30 in medical costs and \$3.20 in indirect or social costs.

Vaccination—Programs (Definitions)

In addition to routine vaccinations, there are three different types of vaccination programs, each with a different strategy and goal. *Catch-up* programs are one-time campaigns that aim to vaccinate all children 9 months to 14 years, whether or not they have had measles or previous vaccinations. *Keep-up* programs are routine services that focus on vaccinating at least 90 percent of children at age 12 months in the years following the catch-up program. *Follow-up* programs take place at least once every four years and aim to vaccinate all children ages 1–4.

Vaccination—Programs (Challenges)

Public fears about possible adverse effects of the measles vaccine decrease vaccination rates. A study showed that in Wales, United Kingdom, vaccination rates fell roughly 14 percent (from 83 percent to 69 percent) after adverse publicity about the measles vaccine raised concern that the vaccine might cause chronic bowel disease or autism. However, intense scientific scrutiny has discredited any link. Experts warn that if such a decline in vaccination rates continues, it could undo recent progress that has almost eliminated measles in the United Kingdom.

Some researchers note that as the threat of measles declines, parents' concerns over safety take on greater importance. In Australia, of 1.1 million students offered immunization, only 86 percent received parental consent. In Chicago, the same populations that had suffered the highest incidence in a previous measles epidemic remained undervaccinated five years later. Even a free, mobile vaccination program had not increased vaccination rates to acceptable levels: More than 45,000 children in Chicago were still vulnerable to measles. Community outreach and education programs might improve this situation.

Vaccination—Rates (United States)

To prevent measles outbreaks, scientists estimate that 95 percent of the population must be immune. In the United States, vaccination rates are at record levels: Coverage exceeded 90 percent for children roughly 1½ to 3 years old and 95 percent for children ages 5 to 6 years. However, pockets of low immunization persist. In Chicago in 1994, coverage for children was 47 percent overall but only 29 percent for inner-city, African-American children. This occurred despite access to free vaccines and a measles outbreak in Chicago in 1989 that heightened awareness. By 2009, 87 percent of children had been vaccinated. Another study of young children in rural New York found that only 85 percent were vaccinated. And, according to the Centers for Disease Control and Prevention (CDC), just over one-half of all schoolchildren in the United States have had both doses of the vaccine. Note that one dose is only 95 percent effective. (Ninety-five percent of people with one dose will gain immunity; the other 5 percent will fail to develop antibodies and will be unprotected.) Even when both doses are given, some people fail to form antibodies, although the probability of this happening is extremely low. In 2008, 92 percent of children ages 19 to 36 months had had both doses.

Vaccination—Rates (Western Hemisphere)

In 1997, there was a resurgence of measles epidemics across the Americas, mainly in Brazil and Canada. In these countries, vaccination rates had fallen among some populations, making them more susceptible to epidemics. Gene-sequence data indicate that most of these outbreaks resulted from strains of measles virus imported from Europe and Asia that subsequently spread among unvaccinated or undervaccinated populations. This suggests that, despite the absence of established measles virus, populations can still be at risk for epidemics.

Vaccination—Rates (Worldwide)

Eradication is only feasible if all countries eliminate all the measles virus. Elimination requires that at least 90 percent and possibly as much as 95 percent of a population have immunity. At this time, all countries in the Western Hemisphere have achieved this goal, with vaccination rates over 90 percent. Worldwide, however, vaccination rates were only 83 percent in 2008. Rates are highest (93 percent) in the Americas and the Western Pacific. Rates are lowest (56 percent) in Africa; 10 African countries have rates of less than 50 percent. Moreover, 42 percent of the world's children live in areas with vaccination rates below 50 percent. More than two-thirds live in Africa or Southeast Asia.

In 1997, several vaccination campaigns targeted at-risk populations in an attempt to raise overall vaccination rates. These campaigns included five countries in Africa, four in Southeast Asia, and one in the South Pacific region. As a result, more than 5.8 million children were vaccinated.

Master 5.3h

Reference Database—VRSA

For up-to-date statistics on vancomycin-resistant *Staphylococcus aureus* (VRSA), visit the Web sites for the Centers for Disease Control and Prevention and the World Health Organization: <http://www.cdc.gov> and <http://www.who.int>.

***Staphylococcus aureus* (SA)—Antibiotic Resistance (General)**

Throughout history, SA has been a dangerous pathogen once it has successfully breached the normal defense system. The first effective antibiotic against SA, penicillin, became available in the 1940s. Soon after, SA evolved resistance to penicillin, and by the late 1950s, 50 percent of all SA were resistant. Today, fewer than 10 percent of SA infections can be cured with penicillin.

The next weapons against SA, methicillin and cephalosporins, became available in the 1960s and 1970s. By the late 1970s, some strains of SA had evolved resistance to these drugs. Today, as many as 50 percent of SA isolated from U.S. hospitals are resistant to methicillin.

The last effective defense against methicillin-resistant SA (called MRSA) is vancomycin. However, the increasing use of vancomycin has set the stage for the evolution of vancomycin-resistant SA (VRSA). Antibiotic use and resistance represent a vicious cycle: The more doctors use vancomycin, the more they create an environment that encourages the evolution of VRSA.

***Staphylococcus aureus* (SA)—Antibiotic Resistance (MRSA)**

MRSA, or methicillin-resistant *Staphylococcus aureus*, are strains of the bacterial pathogen *Staphylococcus aureus* (SA) that have evolved resistance to the antibiotic methicillin. These strains are also likely to be resistant to other antibiotics used to treat SA infections. MRSA strains first appeared in the late 1970s and currently 40 to 50 percent of SA isolated from U.S. hospitals are resistant to methicillin. These infections are treated with the powerful antibiotic vancomycin. Scientists hypothesize that the strains of SA most likely to evolve resistance to vancomycin are the MRSA.

***Staphylococcus aureus* (SA)—Antibiotic Resistance (VRSA)**

Scientists expect strains of the bacterium *Staphylococcus aureus* that are fully resistant to the antibiotic vancomycin to evolve soon. Vancomycin-resistant *Staphylococcus aureus* (VRSA) is the term used to describe these strains. The expected emergence of VRSA is alarming because vancomycin is the only antibiotic that is effective against MRSA, strains of SA that are resistant to the antibiotic methicillin (MRSA).

Although VRSA—strains of SA that are fully resistant to vancomycin—do not currently exist, medical workers have recently isolated strains of SA that are four times more resistant to vancomycin than SA strains found previously. Because infections due to these strains do not respond to the usual doses of vancomycin, many physicians and other experts incorrectly refer to them as VRSA. They should be described as SA strains with intermediate resistance to vancomycin. Infections due to these strains can be cured using higher doses of vancomycin.

***Staphylococcus aureus* (SA)—Definition**

Staphylococcus aureus (SA) is a bacterium commonly found on the skin and in the eyes, nose, and throat of animals and humans. SA is one of the most common causes of infections worldwide. Though not a problem for healthy adults, SA is potentially virulent and can cause serious infections of the skin, eyes, brain, blood, and respiratory and digestive tracts, as well as bone and connective tissue. Some SA infections, such as bacteremia, have death rates of 40 percent.

***Staphylococcus aureus* (SA)—Risk Factors**

Although the body's defenses must be weakened or breached before *Staphylococcus aureus* bacteria cause disease, many people are potential victims of SA infections. SA enters the body through wounds such as burns, deep cuts, and surgical incisions. People whose immune systems are weakened from bouts with other diseases—hospital patients with influenza, leukemia, skin disorders, or diabetes, or patients recovering from kidney transplants—are vulnerable. Patients receiving radiation or chemotherapy are also more susceptible to SA infection. In 1992, nearly 1 million of the 23 million U.S. citizens who had surgery developed infections, most of them due to SA. Likewise, SA poses a threat to newborns, whose immune systems are not yet fully functioning.

***Staphylococcus aureus* (SA)—Transmission**

Because *Staphylococcus aureus* (SA) bacteria can survive dry conditions, they remain alive for long periods of time on dust particles, clothing, furniture, or hospital equipment. SA is able to grow with or without oxygen. This allows the bacteria to survive the aerobic conditions of the skin or nasal passages, waiting for an opportunity to invade deeper tissues. Once inside, SA can produce powerful toxins that further destroy and disrupt the body's tissues. SA can also resist immune system cells that engulf and destroy invading bacteria, making it a formidable adversary for the immune system.

A high percentage of hospital workers are passive carriers for SA, harboring the bacteria on their skin and in their upper respiratory tracts without showing any symptoms. For this reason, SA often spreads from patient to patient via the hands of hospital workers. SA also spreads via dust, clothing, furniture, and medical equipment that has been in contact with infected patients.

Antibiotic Resistance—Cost

As more and more strains of disease-causing bacteria become resistant to commonly used antibiotics, physicians must switch to other, often more expensive, drugs. For example, switching from the penicillins to methicillin in the treatment of *Staphylococcus aureus* (SA) infections increased treatment costs about 10-fold.

It is difficult to assess the overall cost of antibiotic resistance. A report from the Government Accounting Office indicates that no federal agency adequately monitors antibiotic resistance or evaluates its social and financial costs. One estimate, however, places the annual cost of antibiotic resistance as high as \$34 billion per year.

Antibiotic Resistance—Definition

Antibiotic resistance describes the condition of bacteria whose growth and reproduction are unaffected by particular antibiotics. Bacteria have a variety of mechanisms for evading the toxic effects of antibiotics. In some cases, the bacterial cell membranes are altered so that an antibiotic cannot enter the cell. In other cases, resistant bacteria actively pump the antibiotic out of the cell as soon as it enters. Still other resistant bacteria make an enzyme that degrades an antibiotic as soon as it enters the cell. There are also other mechanisms for antibiotic resistance.

Mutations in genes that code for particular proteins may result in antibiotic resistance. For example, if an antibiotic uses a particular protein in the cell membrane to enter the cell, a change in that protein (due to a mutation in the gene that codes for it) may prevent the antibiotic from entering the cell. Many genes that result in antibiotic resistance are found on DNA molecules that are easily transferred from one bacterium to another.

Master 5.4b

Antibiotic Resistance—Evolution

Antibiotic resistance in bacteria evolves by mutations in the bacterium's genes, by rearrangement of the bacterium's genes, or by acquisition of genes that result in antibiotic resistance from other bacteria. Regardless of the way a bacterium becomes resistant to a particular antibiotic, once this has happened, a vicious cycle begins. The resistant bacterium will survive treatment while most of the susceptible bacteria in the population die. After antibiotic treatment is completed, the few surviving susceptible bacteria and the resistant bacterium will reproduce, and the resistant bacterium will pass the gene that provides antibiotic resistance on to its progeny. If the infection recurs, there will now be a larger number of antibiotic-resistant bacteria in the population. Antibiotic treatment will be less successful or may fail completely. Across time, almost all the bacteria of that type that people encounter will be resistant to the particular antibiotic, and new (and, in many cases, more expensive) antibiotics must be used to treat infections caused by that kind of bacterium.

Antibiotic Resistance—Prevention (Challenges)

Overuse of antibiotics has increased the numbers of antibiotic-resistant bacteria. The Centers for Disease Control and Prevention (CDC) estimates that half of the 100 million courses of antibiotics prescribed annually are unnecessary. This misuse means that bacteria will evolve resistance to common antibiotics sooner, and that doctors will have to use last-resort antibiotics such as vancomycin more and more. Therefore, to delay the development of antibiotic-resistant organisms, the CDC has developed a set of recommendations for appropriate use of antibiotics.

Nevertheless, following the CDC recommendations is challenging. One survey of pediatricians revealed that during a one-month period, 96 percent of pediatricians polled had been pressured by patients to prescribe antibiotics, even when they were not needed. Another study found that, despite education about appropriate uses of the antibiotic vancomycin, 40 to 60 percent of vancomycin treatments did not follow the CDC recommendations.

Another challenge for preventing antibiotic resistance is that restrictions on the use of one antibiotic often lead to increases in the use of others. In one hospital, restrictions on the use of the antibiotic cephalosporin not only decreased the incidence of cephalosporin-resistant bacteria but also increased the use of another antibiotic (imipenem). Thus, the number of bacteria resistant to that antibiotic increased.

Antibiotic Resistance—Prevention (Successful Programs)

Several initiatives are under way to promote more careful uses of antibiotics. One hospital in Arkansas created a program to wipe out enterococcal bacteria that are resistant to vancomycin (called vancomycin-resistant enterococci, or VRE) by using strict containment protocols as well as extensive education of staff. For example, some effective precautions can be as simple as hand washing. Though some staff complained that the program was overly complicated and labor intensive, rates of VRE infection declined, and the last case of VRE at that hospital was reported in May 1998.

Antibiotic Resistance—Research (Development Costs)

Pharmaceutical companies spend an average \$500 million and 12 to 15 years doing initial research to design a drug, developing large-scale production of it, conducting clinical trials of the drug's safety and effectiveness, and bringing the drug to market.

Master 5.4c

Vancomycin-Resistant SA (VRSA)—Definition

The term vancomycin-resistant *Staphylococcus aureus*, or VRSA, describes strains of *Staphylococcus aureus* (SA) bacteria that are resistant to doses of the antibiotic vancomycin at or above 32 micrograms per milliliter. Strains of SA that are killed by doses of vancomycin less than or equal to 4 micrograms per milliliter are considered susceptible to the antibiotic, whereas strains that require vancomycin doses of 8 to 16 micrograms per milliliter for killing are considered to have intermediate levels of resistance.

No strains of VRSA have yet appeared; however, since mid-1996, physicians in Japan, the United States, and Europe have described several cases of SA infections that required vancomycin doses of at least 8 micrograms per milliliter to cure the infection. Some medical workers have inaccurately called these strains of bacteria VRSA; however, they are actually SA with intermediate levels of vancomycin resistance.

Vancomycin-Resistant SA (VRSA)—Diagnosis

Emerging vancomycin-resistant *Staphylococcus aureus* (VRSA) bacterial infections would likely have similar symptoms to *Staphylococcus aureus* (SA) infections, except that the infection would persist after vancomycin drug therapy. Doctors test for vancomycin resistance by taking samples of bacteria from an SA infection, culturing or growing them, and measuring their growth in media containing various levels of vancomycin. SA that are killed by vancomycin at a concentration of 4 micrograms per milliliter are considered susceptible, those that require 8 to 16 micrograms per milliliter for killing are considered to have intermediate resistance, and those that are resistant to vancomycin concentrations at or above 32 micrograms per milliliter are considered fully resistant to the drug. To date, the most resistant SA strains show intermediate rather than full resistance to vancomycin.

Vancomycin-Resistant SA (VRSA)—Evolution

In bacteria, antibiotic resistance evolves by mutations in their genes, by rearrangement of their genes, or by acquiring genes that provide antibiotic resistance from other bacteria. The strains of *Staphylococcus aureus* (SA) bacteria that have intermediate resistance to vancomycin appear to be the result of mutations in their genes. However, scientists are concerned that SA also might acquire genes for full vancomycin resistance from other bacteria, specifically, vancomycin-resistant enterococci (VRE).

Enterococci are a group of bacteria closely related to *Staphylococcus* species, but they are less virulent than SA. When the first VRE strains appeared in 1986, they spread rapidly through hospitals. Currently about 25 percent of enterococci isolated in U.S. hospitals are VRE. Scientists are especially concerned about VRE because these bacteria could potentially transfer the genes that make them resistant to vancomycin to other species of bacteria. Because of their close relationship, it is highly likely that vancomycin-resistance genes will spread from VRE to SA. Laboratory experiments have already confirmed this possibility.

Vancomycin-Resistant SA (VRSA)—Incidence (Intermediate Resistance)

As of 1999, several cases of *Staphylococcus aureus* (SA) bacterial infections with intermediate resistance to the antibiotic vancomycin had been reported. The first case was reported in 1996 in Japan, when vancomycin failed to cure a 4-month-old boy who became infected with SA after heart surgery. Despite 29 days of vancomycin therapy, the infection persisted. Although doctors finally stopped the infection using a combination of different antibiotics, they understood that a barrier had been crossed. One researcher underscored the urgency of the situation: “*S. aureus*, a major cause of hospital-acquired infections, has thus moved one step closer to becoming an unstoppable killer.”

Since that time, three independent cases of SA with intermediate resistance to vancomycin have occurred in the United States: in Michigan, New York, and New Jersey. In these patients, doctors resorted to alternative antibiotics. Although they eliminated the infection in two of the patients, all the patients eventually died. (All these patients were quite ill, so the infection might not have been the critical factor in their deaths.) Individual cases of SA with intermediate resistance have also cropped up in France and Hong Kong.

Vancomycin-Resistant SA (VRSA)—Incidence (Predictions)

There have been only a handful of confirmed cases of *Staphylococcus aureus* (SA) with intermediate resistance to the antibiotic vancomycin. But researchers fear it is only a matter of time until strains of SA that are fully resistant to vancomycin (vancomycin-resistant SA, or VRSA) appear. VRSA will probably appear first in developed countries with the highest rates of vancomycin use, such as the United States.

Although there is no way to predict exactly when VRSA will appear or how rapidly it will spread, researchers can make reasonable estimates using a parallel case: the evolution of vancomycin-resistant enterococci (VRE). Enterococci are harmful bacteria closely related to staphylococci. Until the late 1980s, most enterococci were susceptible to vancomycin. The first case of VRE was reported in 1986 in Europe and the second, in 1988 in the United States. Then, between 1989 and 1993, the number of VRE cases in hospital patients increased 20-fold. In New York City in 1993, 97 percent of clinical labs had found at least one strain of VRE. By 1994, 61 percent of hospitals nationwide had reported cases of VRE, and by 2004, 64 percent had.

Vancomycin-Resistant SA (VRSA)—Prevention

In 1995, the Centers for Disease Control and Prevention (CDC) published recommendations for using the antibiotic vancomycin to prevent the rapid spread of vancomycin resistance among bacteria. It emphasized the importance of wise use of vancomycin, continuing education for healthcare providers on prevention and control, and active screening and microbiological testing for resistant strains. The CDC recommends that vancomycin use be restricted to

- Treatment of serious infections due to bacteria resistant to certain antibiotics such as methicillin.
- Treatment of serious infections due to bacteria in patients who have serious allergies to antibiotics such as methicillin.
- Treatment of antibiotic-associated colitis (an inflammation of the colon) that fails to respond to standard treatment or that is severe and potentially life threatening.
- Prevention of endocarditis (an infection of heart tissue) following certain procedures in patients at high risk for endocarditis.
- Preventative surgical procedures involving implants at hospitals that have a high rate of infection due to methicillin-resistant *Staphylococcus aureus* (MRSA). In this case, treatment should be discontinued after a maximum of two doses.

Vancomycin-Resistant SA (VRSA)—Research (Promising Therapies)

Research continues along several lines to develop new therapies to cure infections that are caused by emerging *Staphylococcus aureus* bacteria that are resistant to the antibiotic vancomycin (called VRSA). Some researchers hope to improve the effectiveness of vancomycin by modifying its structure. One promising experiment showed that a subpart of the vancomycin molecule killed bacteria 10 times better than the whole molecule. Other modifications to vancomycin may produce additional, effective antimicrobial drugs.

Another promising therapy uses synthetic peptides (short protein molecules) to block the release of toxins produced by *Staphylococcus aureus* (SA). One of the reasons that SA is so virulent is that it produces potent toxins. If the release of the toxins is prevented, much of the damage caused by SA is also prevented. The peptides bind to a receptor on the surface of the SA bacterium that controls the release of toxins. In preliminary tests, researchers have used synthetic peptides to reduce toxin release, curing mice infected with SA. Even though the peptides do not kill the bacteria, by preventing the damage caused by SA they could give patients' immune systems enough of an edge to knock out the infection. Research is needed to bring such a therapy to reality.

Other research studies may lead to the development of effective vaccines against SA or the toxins it produces. Scientists are currently testing yet another strategy. To slow the growth of virulent strains of SA, they infect patients with a non-disease-causing strain of SA. The hope is that the non-disease-causing strain will crowd out the virulent strain.

Vancomycin-Resistant SA (VRSA)—Risk Factors

People at the greatest risk from infections caused by emerging *Staphylococcus aureus* that are resistant to the antibiotic vancomycin (called VRSA) are the same as those at risk from the usual *Staphylococcus aureus* (SA) bacteria: people who have weak immune systems due to injury, illness, or age (either very young or very old). At particular risk will be hospital patients, because their health is already compromised and they are more likely to encounter VRSA in hospitals. Because of the increased risk, a VRSA epidemic might discourage people from having elective surgeries and make nonelective surgery more risky.

Vancomycin-Resistant SA (VRSA)—Vancomycin (Definition)

Vancomycin is a naturally occurring compound, derived from a fungus. It is also an antibiotic-of-last-resort: Vancomycin is the only drug effective against infections caused by strains of *Staphylococcus aureus* (SA) that are resistant to all the other drugs that previously cured SA infections.

Scientists do not know precisely how vancomycin kills bacteria. They hypothesize that it interferes with cell wall formation. A bacterium without an intact cell wall is likely to rupture during growth and cell division; thus, any drug that prevents or disturbs cell wall formation will kill the bacterium.

Master 5.4f

Proposal Criteria Matrix

Name: _____

View the video segments online or read the script segments on **Master 5.1**, and use the reference databases online or on **Masters 5.2, 5.3, and 5.4** to learn about the three infectious diseases addressed by the proposals. Make notes in the table below about the magnitude of each situation and the effectiveness of each plan. (Questions to ask yourself as you determine magnitude and effectiveness are on Master 5.5b.)

Proposal Criteria Matrix

Proposal	Criterion: What Is the Magnitude of the Situation?	Criterion: How Effective Is the Plan?
Proposal 1—AIDS Produce and distribute drugs to HIV-positive individuals.		
Proposal 2—Measles Produce and distribute vaccine to susceptible people.		
Proposal 3—VRSA Infections Develop new drug therapies against <i>Staphylococcus aureus</i> .		

To determine magnitude, ask yourself questions such as the following:

- How many people are affected by the disease? Who are they? Where are they?
- What are the consequences of having the disease, both for the affected individual and for society? How serious are the consequences?

To determine effectiveness, ask yourself questions such as the following:

- Is there a treatment for the disease? How effective is it? Are there any problems with the treatment?
- Are there preventive measures for the disease? How effective are they? Are there any problems with the preventive measures?
- Is there a way to get the treatment or preventive measures to those who are affected?
- What are the costs of the treatment or the preventive measures? What is the cost of delivering treatment or enforcing the preventive measures?
- If there is no treatment or prevention, is there a plan for developing an effective treatment or prevention that is likely to be successful?

Proposal Summary Matrix

Name: _____

Review the notes you made on the *Proposal Criteria Matrix (Master 5.5)*. Place checkmarks in the matrix below to indicate the magnitude and level of effectiveness of each of the three proposals. Use the following scale:

- ✓ = low magnitude/effectiveness
- ✓✓ = intermediate magnitude/effectiveness
- ✓✓✓ = high magnitude/effectiveness

Below the matrix, write the name of the proposal you recommend for funding and the reason for recommending that proposal instead of the others.

Proposal Summary Matrix

Proposal	Criterion: What Is the Magnitude of the Situation?	Criterion: How Effective Is the Plan?
Proposal 1—AIDS		
Proposal 2—Measles		
Proposal 3—VRSA Infections		

Proposal recommended for funding:

Reasons for recommendation:

