Emerging and Re-emerging Infectious Diseases

under a contract from the
National Institutes of Health

National Institute of Allergy
and Infectious Diseases

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This material is based on work supported by the National Institutes of Health under Contract No: 263-97-C-0073. Any opinions, findings, conclusions, or recommendations expressed in this publication are those of the authors and do not necessarily reflect the views of the funding agency.

NIH Publication No. 99-4645

ISBN: 1-929614-02-0

Contents

Foreword

This curriculum supplement brings into the classroom new information about some of the exciting medical discoveries being made at the National Institutes of Health (NIH) and their effects on public health. This set is being distributed to teachers around the country free of charge by the NIH to improve science literacy and to foster student interest in science. These tools may be copied for classroom use, but may not be sold.

This set was developed at the request of NIH Director Harold Varmus, M.D., as part of a major new initiative to create a curriculum supplement series (for grades kindergarten through 12) that complies with the *National Science Education Standards*.[1] This set is part of a continuing series being developed by the NIH Office of Science Education (OSE) in cooperation with NIH institutes with wide-ranging medical and scientific expertise. Three new supplements are planned per year.

The curriculum supplements use up-to-date, accurate scientific data and case studies (not contrived). The supplements contain extensive background information for teachers and

- -use creative, inquiry-based activities to promote active learning and stimulate student interest in medical topics;
- deepen students' understanding of the importance of basic research to advances in medicine and health;
- offer students an opportunity to apply creative and critical thinking;
- - foster student analysis of the direct and indirect effects of scientific discoveries on their individual lives and on public health; and
- - encourage students to take more responsibility for their own health.

Each supplement contains several activities that may be used in sequence or as individual activities designed to fit into 45 minutes of classroom time. The printed materials may be used in isolation or in conjunction with the CD-ROMs, which offer scenarios, simulations, animations, and videos.

The first three supplements in the series (listed below) are designed for use in senior high school science classrooms:

- - *Emerging and Re-emerging Infectious Diseases* (with expertise from the National Institute of Allergy and Infectious Diseases)
- - *Cell Biology and Cancer* (with expertise from the National Cancer Institute)
- - *Human Genetic Variation* (with expertise from the National Human Genome Research Institute)

We appreciate the invaluable contributions of the talented staff at Biological Sciences Curriculum Study (BSCS) and Videodiscovery, Inc., who developed these materials. We are also grateful to the scientific advisers at the NIH institutes who worked long and hard on this project. Finally, we thank the teachers and students across the country who participated in focus groups and field tests to help ensure that these materials are both engaging and effective.

We are eager to know about your particular experience with the supplements. Your comments help this program to evolve and grow. For continuing updates on the curriculum supplement series or to make comments, please visit http://science-education.nih.gov/supplements. You may also send your suggestions to

Curriculum Supplement Series
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National Institutes of Health
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I hope you find our series a valuable addition to your classroom and wish you a productive school year.

Bruce A. Fuchs, Ph.D.
Director
Office of Science Education
National Institutes of Health

1 The National Academy of Sciences released the *National Science Education Standards* in December 1995 to outline what all citizens should understand about science by the time they graduate from high school. The *Standards* encourage teachers to select major science concepts or themes that empower students to use information to solve problems rather than to stress memorization of large volumes of unconnected bits of information.

About the National Institutes of Health ⟆

The National Institutes of Health (NIH)—the world's top medical research center—is charged with addressing the health concerns of the nation. The NIH is the largest U.S. governmental sponsor of health studies conducted nationwide.

Simply described, the NIH's goal is to acquire new knowledge to help prevent, detect, diagnose, and treat disease and disability, from the rarest genetic disorder to the common cold. The NIH works toward that goal by conducting research in its own laboratories in Bethesda, Maryland; supporting the research of nonfederal scientists throughout the country and abroad; helping to train research investigators; and fostering communication of medical information to the public.

The NIH Supports Research A principal concern of the NIH is to invest wisely the tax dollars entrusted to it for the support and conduct of medical research. Approximately 82 percent of the investment is made through grants and contracts supporting research and training in more than 2,000 universities, medical schools, hospitals, and research institutions throughout the United States and abroad.

Approximately 10 percent of the budget goes to more than 2,000 projects conducted mainly in NIH laboratories. About 80 percent covers support costs of research conducted both within and outside the NIH.

NIH Research Grants To apply for a research grant, an individual scientist must submit an idea in a written application. Each application undergoes a peer review process. A panel of scientific experts, who are active researchers in the medical sciences, first evaluates the scientific merit of the application. Then, a national advisory council or board, comprised of eminent scientists as well as public members who are interested in health issues or the medical sciences, determines the project's overall merit and priority. Because funds are limited, the process is very competitive.

The Nobelists The rosters of those who have conducted research, or who have received NIH support over the years, include some of the world's most illustrious scientists and physicians. Among them are 97 scientists who have won Nobel Prizes for achievements as diverse as deciphering the genetic code and learning what causes hepatitis.

Five Nobelists made their prize-winning discoveries in NIH laboratories: Doctors Christian B. Anfinsen, Julius Axelrod, D. Carleton Gajdusek, Marshall W. Nirenberg, and Martin Rodbell.

Impact of the NIH on the Nation's Health The research programs of the NIH have been remarkably successful during the past 50 years. NIH-funded scientists have made substantial progress in understanding the basic mechanisms of disease and have vastly improved the preventive, diagnostic, and therapeutic options available.

During the last few decades, NIH research played a major role in making possible achievements like these:

- Mortality from heart disease, the number one killer in the United States, dropped by 36 percent between 1977 and 1999.
- Improved treatments and detection methods increased the relative five-year survival rate for people with cancer to 60 percent.
- Those suffering from depression now look forward to returning to work and leisure activities, thanks to treatments that give them an 80 percent chance to resume a full life in a matter of weeks.
- Vaccines protect against infectious diseases that once killed and disabled millions of children and adults.
- In 1990, NIH researchers performed the first trial of gene therapy in humans. Scientists are increasingly able to locate, identify, and describe the functions of many of the genes in the human genome. The ultimate goal is to develop screening tools and gene therapies for the general population for cancer and many other diseases.

Educational and Training Opportunities at the NIH The NIH offers a myriad of opportunities including summer research positions for students. For details, visit http://science-education.nih.gov/students.

For more information about the NIH, visit http://www.nih.gov.

The NIH Office of Science Education

The NIH Office of Science Education (OSE) is bringing exciting new resources free of charge to science teachers of grades kindergarten through 12. OSE learning tools support teachers in training the next generation of scientists and scientifically literate citizens. These materials cover information not available in standard textbooks and allow students to explore biological concepts using real world examples. In addition to the curriculum supplement, OSE provides a host of valuable resources accessible through the OSE Web site (http://science-education.nih.gov), such as:

- **Snapshots of Science and Medicine**.[2] This online magazine—plus interactive learning tools—is designed for ease of use in high school science classrooms. Three issues, available for free, are published during the school year. Each focuses on a new area of research and includes four professionally written articles on findings, historical background, related ethical questions, and profiles of people working in the field. Also included are a teaching guide, classroom activities, handouts, and more. (http://science-education.nih.gov/snapshots)
- **Women Are Scientists Video and Poster Series**.[3] This series provides teachers and guidance counselors with free tools to encourage young women to pursue careers in the medical field. The informative, full-color video and poster sets focus on some of the careers in which women are currently underrepresented. The first set, titled "Women are Surgeons," has been completed. The second, "Women are Pathologists," will be finished in 2000, and the third, "Women are Researchers," in 2001. (http://science-education.nih.gov/women)
- **Internship Programs**. Visit the OSE Web site to obtain information on a variety of NIH programs open to teachers and students. (http://science-education.nih.gov/students)
- **National Science Teacher Conferences**. Thousands of copies of NIH materials are distributed to teachers for free at the OSE exhibit booth at conferences of the National Science Teachers Association and the National Association of Biology Teachers. OSE also offers teacher-training workshops at many conferences. (http://science education.nih.gov/exhibits)

In the development of learning tools, OSE supports science education reform as outlined in the *National Science Education Standards* and related guidelines.

We welcome your comments about existing resources and suggestions about how we may best meet your needs. Feel free to send your comments to us at http://science-education.nih.gov/feedback.

2, 3 These projects are collaborative efforts between OSE and NIH Office of Research on Women's Health.

About the National Institute of Allergy and Infectious Diseases

The National Institute of Allergy and Infectious Diseases (NIAID) had its origins in the earliest days of the Public Health Service. In 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 present name to reflect the inclusion of allergy and immunology research. Today, NIAID provides the major support for scientists conducting research aimed at developing better ways to diagnose, treat, and prevent the many infectious, immunologic, and allergic diseases that afflict people worldwide.

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 have 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 has evolved to defend 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). More than 13 million Americans each year acquire infectious diseases other than AIDS through sexual contact. Such STDs 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 last century. 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 a number of 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 its Web site: http://www.niaid.nih.gov.

Introduction to 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 (an idea that continues today in descriptions of AIDS as God's punishment of homosexuals and drug abusers). Nevertheless, as early as 1530 Gerolomo 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. Koch devised a set of steps, now called Koch's postulates, to prove that a particular bacteria 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.

Figure 1 Discovery of Bacterial Causes of Several Diseases

Disease	Year Discovered	Scientist
anthrax	1876	Koch
gonorrhea	1879	Neisser
tuberculosis	1882	Koch
plague	1894	Kitasato, Yersin
whooping cough	1906	Bordet, Gengoe

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 visualized.

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. Recent evidence indicating that some neurological disorders are due to infection by unusual proteins, named prions, suggests that other types of pathogens may also exist.

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 to 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, however, 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 bacteria) 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 the mold *Penicillium* 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 antibiotics 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 replication. In contrast, the newer protease inhibitors used to treat AIDS interfere with the process of virus packaging. Antifungal, antiprotozoan, and antihelminthic drugs also have been discovered; these drugs frequently have serious side effects and must be administered carefully.

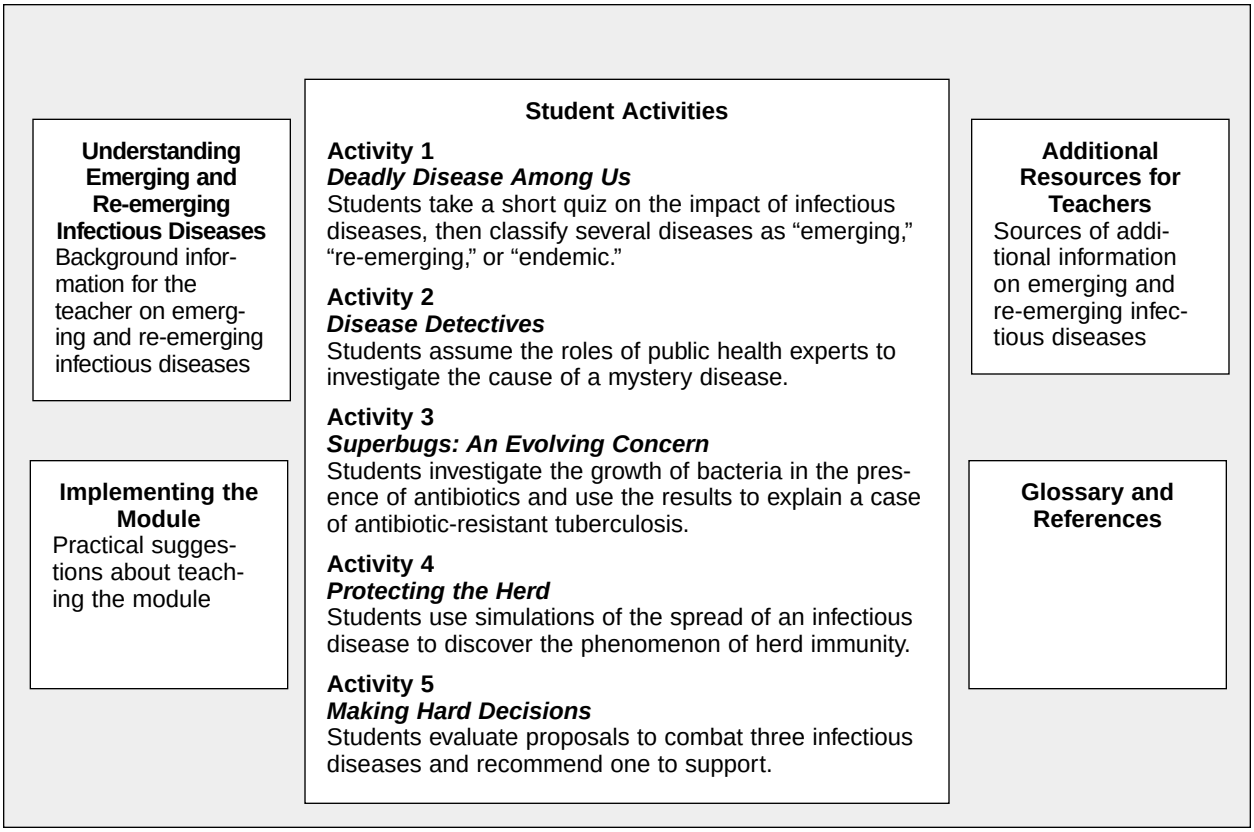
Science and medicine have made dramatic advances across the last two centuries in understanding, preventing, and treating infectious diseases. Despite

these advances, the last two decades have witnessed the emergence of a number of previously unrecog nized diseases and the re-emergence of several pre viously well-controlled ones. This phenomenon is intriguing from a biological standpoint, but is alarm ing from a public health standpoint.

In this module, students explore the biological fac tors 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 have chosen, with the help of a variety of experts in this field, a rela tively 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 iso lated 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 propor-

Figure 2 This diagram identifies the module's major sections and describes their contents.



tion 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 strate gies 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 five activities provided in this module (Figure 2) will be effective vehicles to carry these concepts to your students. Although the activities contain much interesting information about specific infectious diseases, we suggest that you focus your students' attention on the major concepts the mod ule was designed to convey. The concluding steps in each activity are intended to focus the students' attention on these concepts as the activity draws to a close.

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, 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 typically are found among groups such as the elderly (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

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 building the Aswan Dam; and legionellosis was identified after an outbreak of pneumonia among individuals attending a conference in Philadelphia.

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 bacteria 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. Their genomes are circular, double-stranded DNA that is associated with much less protein than 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 Kingdom Monera, there is a wide range of diversity among the bacteria.

There are a variety of morphologies among bacteria, but three of the most common are bacillus (rod-shaped), coccus (spherical), or 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, respiratory, and wound infections, and *Clostridium tetani*, which produces a toxin that can be lethal for humans.

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, 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, 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 very 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 two 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 (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 with 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 health care 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. 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.

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 also are 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 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

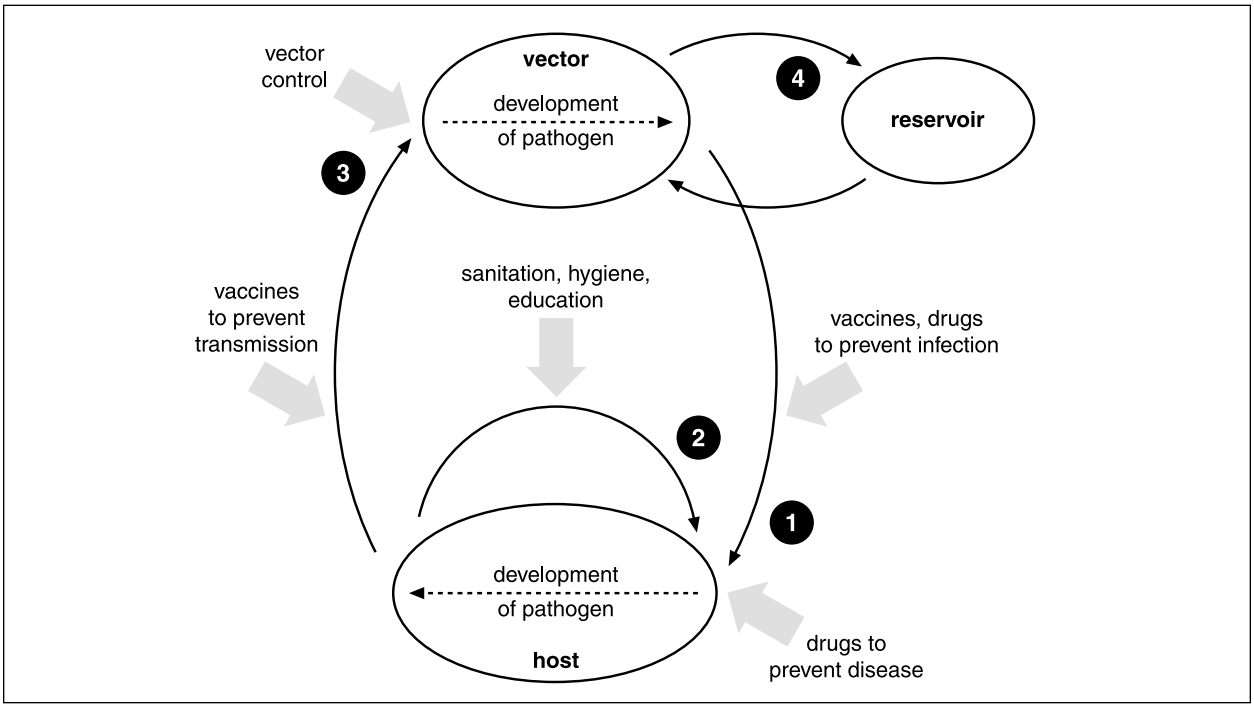


Figure 4 The black arrows illustrate a generalized infectious cycle; the shaded arrows indicate points where infectious diseases can be prevented. (1) A host is infected by the reservoir or a vector for the pathogen. This individual may infect (2) other hosts in a population or (3) new vectors. (4) The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

activities of the pathogen that cause disease (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 in order to identify 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 education. 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.

In some cases, the tools, including drugs, vaccines and vector control methods, are already available to deal with these 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 mankind. 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 also is 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 also are protected by a variety of physiological deterrents. For example, tears continually 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 tempera ture, and pain. Unfortunately, inflammation itself frequently causes tissue damage and, in severe cases, even death.

Finally, 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 pres ence of other microorganisms. These organisms protect the host by successfully competing with dis ease-causing organisms, preventing the latter from invading host tissues. When the growth of the nor mal flora is suppressed (for example, due to antibi otic 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 initi ates a second, specific line of defense. This specific immune response enables the body to target partic ular pathogens and pathogen-infected cells for destruction. It depends on specialized white blood cells called lymphocytes and includes T-cells (pro duced from lymphocytes that matured in the thy mus gland) and B-cells (produced from lympho cytes 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 effi cient 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 pro teins 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 lym phokines 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 anti-gens on the surface of the pathogens and signal attack by phagocytic cells and complement system. Other B-cells go on to become memory B-cells, which respond quickly by producing more anti-bodies 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 levels of lymphokines and antibod ies. 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 levels 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 weak ened (attenuated) strain of a particular pathogen, or a solution containing critical antigens from the

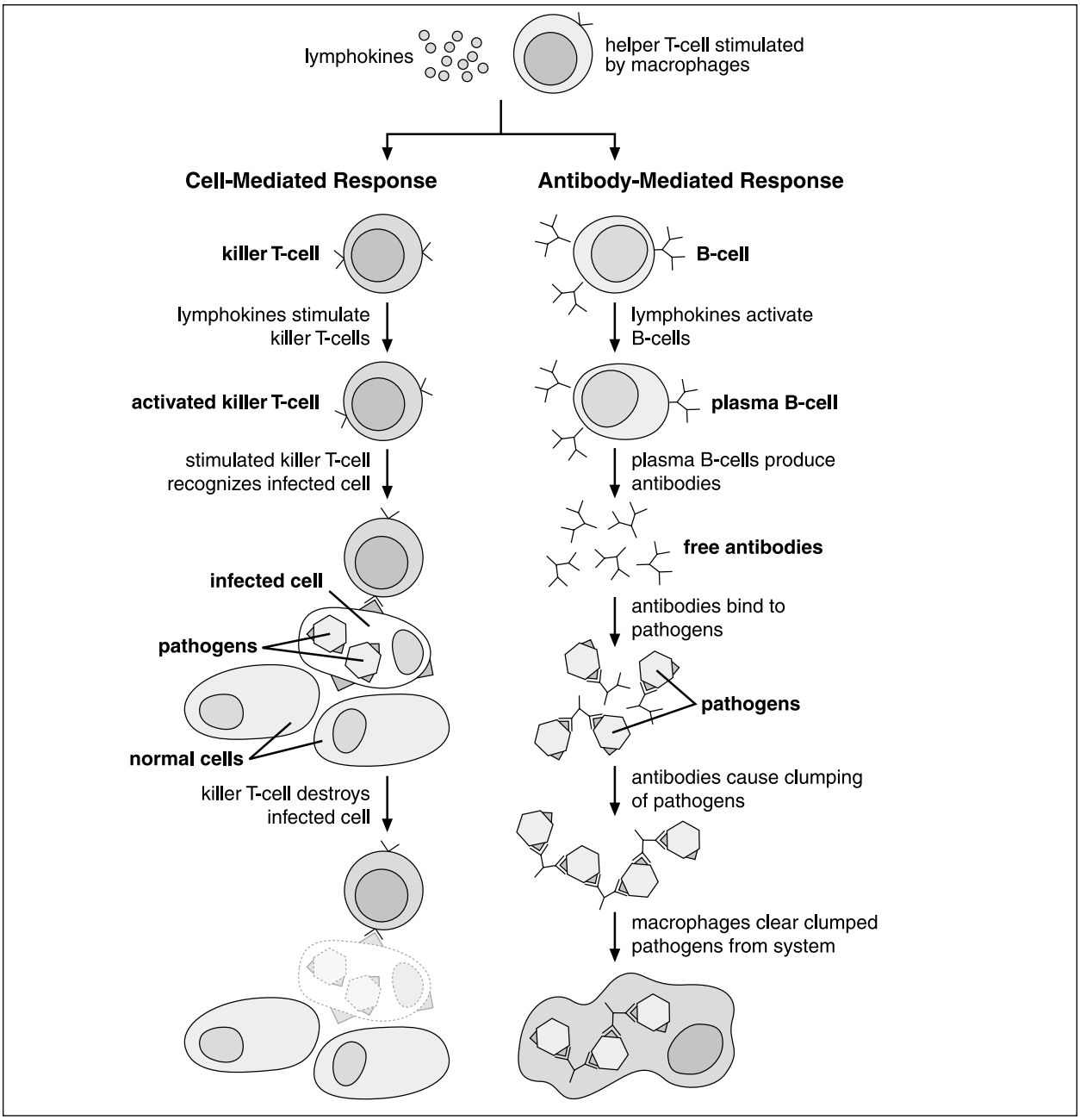


Figure 5 This diagram provides an overview of specific immunity.

pathogen. The body's immune system will respond to these vaccines as if they contain the actual pathogen, even though the 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.

Currently 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 cholera 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 run-off. These fluids may carry the pathogens for many waterborne diseases, including giardiasis and hepatitis A; therefore, 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. Meat-packing facilities are inspected regularly to detect and eliminate diseased animals, ensure that stan dards for processes such as meat cutting and refrig eration are observed, and detect residues from pes ticides and antibiotics as well as contamination by bacteria and other parasites. Restaurants and supermarkets are similarly inspected. Milk is pas teurized and dated for sale and is analyzed period ically for contamination. Industry standards for canning and preserving foods are maintained through periodic quality control checks and, if con tamination 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 domes-tic herd animals and abscesses of the liver, spleen, bone marrow, and lymph nodes in humans) has helped eliminate the threat of passing the pathogens for those diseases to humans in contam inated 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 man-dated 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 (a notable example is malaria). 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 ani mals 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 facil ities 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 dis ease in the population will be avoided. This phe nomenon is called **herd immunity**.

The threshold proportion varies depending on the disease and other conditions in the relevant popula tion. Vaccination programs led by public health offi cials 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 regu lations, provide public health services such as vac cination programs, and monitor and report the inci dence of particular diseases to state and federal

Figure 6 Vaccination programs are important compo nents of public health systems.

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 one of eight health agencies of the U.S. Public Health Service. It supports health-related research aimed at understanding, preventing, treating, and controlling infectious and other diseases of humankind. The Public Health Service 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) provides international surveillance and control of disease. Among other efforts, WHO 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. In general, 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.

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. 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. Alarmingly, 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 drugs' ability to bind to it; reduced permeability of the cell membrane to the drug, 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 extra-chromosomal 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*. Bacteria are subject to viral infection. When a bacteria cell is infected, the virus takes over the cell's metabolism, directing synthesis of its 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. Malaria, a protozoan disease, was successfully treated for many years with chloroquine, a drug that was widely available over the counter in regions where malaria was a problem. In recent decades, *Plasmodium* strains that are resistant to this drug have appeared and spread 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 two decades have shown the foolhardiness of that position. At least a dozen "new" diseases have been identified (such as AIDS, Legionnaire 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). Figure 7 lists several examples of infectious diseases that have emerged in the last three decades.

A review of Figure 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 insect 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 disease and hemolytic uremic syndrome include changing

Figure 7 Examples of Emerging Infectious Diseases

Disease	Infectious Agent	Year Recognized*	Contributing Factors
Lassa fever	*Arenaviridae* family (virus)	1969	urbanization and other conditions that favor the rodent host; nosocomial transmission
Ebola hemorrhagic fever	*Filoviridae* family (virus)	1977	unknown natural reservoir; nosocomial transmission
Legionnaire disease	*Legionella pneumophila* (bacterium)	1977	cooling and plumbing systems
hemolytic uremic syndrome	*Escherichia coli* 0157:H7 (bacterium)	1982	mass food production systems
Lyme borreliosis	*Borrelia burgdorferi* (bacterium)	1982	conditions favoring the tick vector and deer, such as reforestation near homes
AIDS	human immunodeficiency virus	1983	migration to cities, global travel, transfusions, organ transplants, intravenous drug use, multiple sexual partners
gastric ulcers	*Helicobacter pylori* (bacterium)	1983	newly recognized as due to infectious agent
cholera	*Vibrio cholerae* 0139 (bacterium)	1992	evolution of new strain of bacteria combining increased virulence and long-term survival in the environment
hantavirus pulmonary syndrome	*Bunyaviridae* family (virus)	1993	environmental changes favoring contact with rodent hosts
pandemic influenza	*Orthomyxoviridae* family (virus)	new viral strains emerge periodically	pig-duck agriculture (possibly)

Sources: Morse, S.S. 1995. Factors in the emergence of infectious diseases. *Emerging Infectious Diseases* [Serial online], 1(1). Available http://www.cdc.gov/ncidod/EID/index.htm. June 1999; Satcher, D. 1995. Emerging infections: Getting ahead of the curve. *Emerging Infectious Diseases* [Serial online], 1(1). Available http://www.cdc.gov/ncidod/EID/index.htm. 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.

*Year infectious agent was identified.

technologies: 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. Figure 8 lists examples of re-emerging infectious diseases.

A review of Figure 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

Figure 8 Examples of Re-emerging Infectious Diseases

Disease	Infectious Agent	Contributing Factors
cryptosporidiosis	*Cryptosporidium parvum* (protozoa)	inadequate control in water supply; international travel; increased use of child-care facilities
diphtheria	*Corynebacterium diptheriae* (bacterium)	interruption of immunization program due to political changes
malaria	*Plasmodium* species (protozoon)	drug resistance; favorable conditions for mosquito vector
meningitis, necrotizing fasciitis (flesh-eating disease), toxic shock syndrome, and other diseases	Group A *Streptococcus* (bacterium)	uncertain
pertussis (whooping cough)	*Bordetella pertussis* (bacterium)	refusal to vaccinate based on fears the vaccine is not safe; other possible factors: decreased vaccine efficacy or waning immunity among vaccinated adults
rabies	*Rhabdovirus* group (virus)	breakdown in public health measures; changes in land use; travel
rubeola (measles)*	*Morbillivirus* genus (virus)	failure to vaccinate; failure to receive second dose of vaccine
schistosomiasis	*Schistosoma* species (helminth)	dam construction; ecological changes favoring snail host
tuberculosis	*Mycobacterium tuberculosis* (bacterium)	antibiotic-resistant pathogens; immunocompromised populations (malnourished, HIV-infected, poverty-stricken)
yellow fever	*Flavivirus* group (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. April 17, 1998. *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.

*Following 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 has declined again, to an all-time low of 138 cases in 1997.

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, intro duction of the pathogen into the population leads to an outbreak of the disease.

Despite the challenges of emerging and re-emerg ing 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 han tavirus 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 inter-

vened between the advent of AIDS and the advent of HPS saw the development of polymerase chain reaction, a powerful new research technique that allows rapid identification of causative agents. Recommendations for avoiding and/or treating of 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 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.

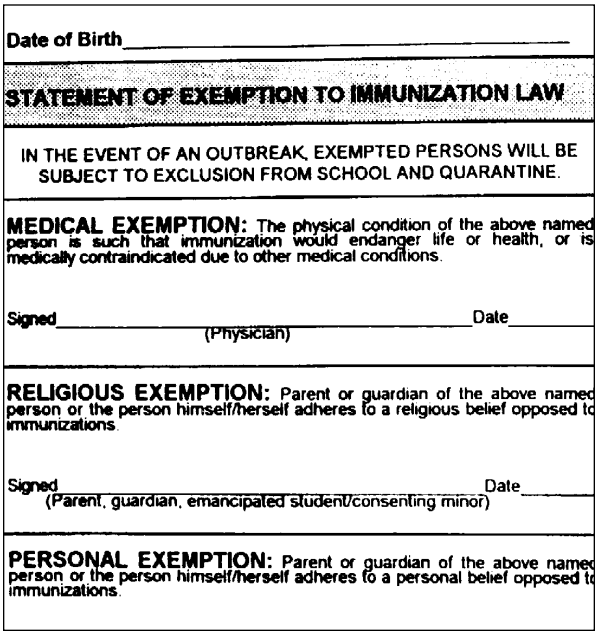
Infectious Diseases and Society

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 last 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, multifaceted, and 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 public health laws encourage their widespread use, individuals are permitted (in most, but not all, states) to choose not to be vaccinated.

Figure 9 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_____ Date_____
(Physician)

RELIGIOUS EXEMPTION: Parent or guardian of the above named person or the person himself/herself adheres to a religious belief opposed to immunizations.

Signed_____ Date_____
(Parent, guardian, emancipated student/consenting minor)

PERSONAL EXEMPTION: Parent or guardian of the above named person or the person himself/herself adheres to a personal belief opposed to immunizations.

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 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 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 health care 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 or those in the inner cities? 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 may 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 and is not known) + choice = power

power + behavior = increased 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.

Implementing the Module

The five activities 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 con cepts in biology. The following pages offer general suggestions about using these materials in the classroom; you will find specific suggestions in the support material provided for each activity.

Goals for the Program

Emerging and Re-emerging Infectious Diseases is designed to help stu dents develop the following major goals associated with biological literacy: (1) to understand a set of basic scientific principles related to emerging and re-emerging infectious diseases, (2) to experience the process of inquiry and develop an enhanced understanding of the nature and methods

Figure 10 Conceptual Flow of the Activities

Activity	Major Concept
Activity 1 *Deadly Disease Among Us*	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.
Activity 2 *Disease Detectives*	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).
Activity 3 *Superbugs: An Evolving Concern*	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).
Activity 4 *Protecting the Herd*	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.
Activity 5 *Making Hard Decisions*	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.

of science, and (3) to recognize the role of science in society and the relationship between basic science and personal and public health.

Conceptual Organization of the Activities

We have organized the activities 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*). Figure 10 illustrates the sequence of major concepts addressed by the five activities.

Although we encourage you to use the activities in the sequence outlined in Figure 10, many of the activities can be taught individually, to replace or enhance a more traditional approach to the same or related content. Figure 11 provides recommendations for inserting the activities into a standard high school curriculum in biology.

Correlation to 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*). Figure 12 lists the specific content and teaching standards that this module primarily addresses.

Active, Collaborative, and Inquiry-Based Learning

The activities in this module are designed to offer students the opportunity to participate in active, collaborative, and inquiry-based learning in biology. But what do these terms mean? Despite their current popularity, many teachers think of

Figure 11 Correlation Between Activities and Standard Curricula*

Topic	Module Activity					Biology Textbook** Chapter									
	1	2	3	4	5	DOL	AEE	LS	Blue	Green	Human	VL	P & E	Modern	TLS
infectious diseases (causes)	•	•	•	•	•	18, 21, 22, 23, 42	4, 5, 12	15	20	11	2	18, 19, 20, 25	20, 21	24, 25, 26, 28, 48	40
society and infectious diseases		•	•	•	•	42	–	15, 23	–	–	–	–	20	48, 53	21
antibiotics and antibiotic resistance			•		•	21, 42	4, 18	–	16	–	2	18	20	24, 25, 28	21
natural selection			•		•	18	29	12, 13	1, 16	9	2	10	12	15, 16	10
vaccination				•	•	42	4	23	20	11	6, essay	18, 33	10, 39	48	40

*The table indicates where topics addressed in the module are covered in a variety of current high school textbooks.

**DOL = *Biology: The Dynamics of Life* (Glencoe)
AEE = *Biology: An Everyday Experience* (Glencoe)
LS = *Biology: Living Systems* (Glencoe)
Blue = *BSCS Biology: A Molecular Approach* (D.C. Heath and Co./McDougal-Littel)
Green = *BSCS Biology: An Ecological Approach* (Kendall/Hunt)
Human = *BSCS Biology: A Human Approach* (Kendall/Hunt)
VL = *Biology: Visualizing Life* (Holt, Rinehart, Winston)
P & E = *Biology: Principles & Explorations* (Holt, Rinehart, Winston)
Modern = *Modern Biology* (Holt, Rinehart, Winston)
TLS = *Biology: The Living Science* (Prentice Hall)

Figure 12 Correlation to the *National Science Education Standards*

The Content Standards	
Standard A: As a result of activities in grades 9–12, all students should develop abilities necessary to do scientific inquiry and understandings about scientific inquiry.	**Correlation to *Emerging and Re-emerging Infectious Diseases***
• Identify questions and concepts that guide scientific investigations.	Activities 2 and 3
• Design and conduct scientific investigations.	Activity 3
• Use technology and mathematics to improve investigations and communications.	Activity 4
• Formulate and revise scientific explanations and models using logic and evidence.	Activities 2, 3, and 4
• Recognize and analyze alternative explanations and models.	Activities 2, 3, and 4
• Communicate and defend a scientific argument.	Activities 4 and 5
• Understandings about scientific inquiry.	Activities 2, 3, and 4
Standard C: As a result of their activities in grades 9–12, all students	**Correlation to *Emerging and Re-emerging Infectious Diseases***
should develop understanding of the molecular basis of heredity.	
• In all organisms, the instructions for specifying the characteristics of the organism are carried in DNA . . .	Activity 3
• Changes in DNA (mutations) occur spontaneously at low rates.	Activity 3
should develop understanding of biological evolution.	
• Species evolve over time.	Activity 3
should develop understanding of the interdependence of organisms.	
• Human beings live within the world's ecosystems.	Activity 2
Standard E: As a result of activities in grades 9–12, all students	**Correlation to *Emerging and Re-emerging Infectious Diseases***
should develop abilities of technological design and understandings about science and technology.	
• Scientists in different disciplines ask different questions, use different methods of investigation, and accept different types of evidence to support their explanations.	Activity 2
• Science often advances with the introduction of new technologies.	Activity 5
• Creativity, imagination, and a good knowledge base are all required in the work of science and engineering.	Activities 1–5
• Science and technology are pursued for different purposes.	Activities 1–5

Standard F: As a result of activities in grades 9–12, all students should develop understanding of	**Correlation to *Emerging and Re-emerging Infectious Diseases***
• personal and community health.	Activities 1–5
• natural and human-induced hazards.	Activities 1–5
• science and technology in local, national, and global challenges.	Activity 5
Standard G: As a result of activities in grades 9–12, all students should develop understanding of	**Correlation to *Emerging and Re-emerging Infectious Diseases***
• science as a human endeavor.	Activities 2 and 5
• nature of scientific knowledge.	Activities 3, 4, and 5
• historical perspectives.	Activity 1
The Teaching Standards	
Standard A: Teachers of science plan an inquiry-based science program for their students. In doing this, teachers	**Correlation to *Emerging and Re-emerging Infectious Diseases***
• develop a framework of yearlong and short-term goals for students.	Each activity provides short-term objectives for students. Figures 10 (Conceptual Flow of the Activities) and 16 (Timeline for Teaching the Module) also help teachers plan.
• select science content and adapt and design curricula to meet the interests, knowledge, understanding, abilities, and experiences of students.	Using the modules helps teachers update their curriculum in response to their students' interest in this topic.
• select teaching and assessment strategies that support the development of student understanding and nurture a community of science learners.	The focus on active, collaborative, and inquiry-based learning in the activities helps teachers meet this standard.
Standard B: Teachers of science guide and facilitate learning. In doing this, teachers	**Correlation to *Emerging and Re-emerging Infectious Diseases***
• focus and support inquiries while interacting with students.	All of the activities in the module encourage and support student inquiry.
• orchestrate discourse among students about scientific ideas.	All of the activities in the module promote discourse among students.
• challenge students to accept and share responsibility for their own learning.	All of the activities in the module challenge students to accept and share responsibility for their learning.
• recognize and respond to student diversity and encourage all students to participate fully in science learning.	Combining the 5E instructional model with active, collaborative learning is an effective way of responding to the diversity of student backgrounds and learning styles.
• encourage and model the skills of scientific inquiry, as well as the curiosity, openness to new ideas and data, and skepticism that characterize science.	Annotations for the teacher that occur throughout the activities provide many suggestions for how teachers can model these attributes.

Standard C: Teachers of science engage in ongoing assessment of their teaching and of student learning. In doing this, teachers	**Correlation to *Emerging and Re-emerging Infectious Diseases***
• use multiple methods and systematically gather data about student understanding and ability.	Each activity has a variety of assessment components embedded within its structure. Annotations draw teachers' attention to these opportunities for assessment.
• analyze assessment data to guide teaching.	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.
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	**Correlation to *Emerging and Re-emerging Infectious Diseases***
• display and demand respect for the diverse ideas, skills, and experiences of all students.	The answers provided in the annotations for teachers model these qualities.
• nurture collaboration among students.	All of the activities are designed to be com≠ pleted by students working in collaborative teams.
• structure and facilitate ongoing formal and informal discussion based on a shared understanding of rules of scientific discourse.	All of the discussions in the activities model the rules of scientific discourse.
• model and emphasize the skills, attitudes, and values of scientific inquiry.	The annotations for teachers provide many suggestions about how to model these skills, attitudes, and values.

active, collaborative, and inquiry-based learning rather generically. Defining these three key terms more specifically will provide a foundation on which we can build a detailed description of the instructional approach that the five activities in this module advocate and implement.

Conceptually the broadest of the three, **active learning** means that students are involved "in doing things and thinking about the things they are doing" (Bonwell and Eison, 1991, p. 2). These authors elabo rate by listing the following characteristics typically associated with strategies that deserve to be labeled "active."

- Students are involved in more than listening.
- Instructors place less emphasis on transmitting information and more emphasis on developing students' skills.
- Students are involved in higher-order thinking (for example, analysis, synthesis, and evaluation).
- Students are engaged in activities (for example, reading, discussing, and writing).
- Instructors encourage students' exploration of their own understandings, attitudes, and values.

Most teachers endorse the use of active learning. We know intuitively, if not experientially and explicitly, that learning does not occur through a process of passive absorption. But often we do not realize *how active* students must be for real learning to occur. Typically, the answer to this question is *more active* than we might expect.

The activities in this module were designed with the following assumptions about active learning (BSCS, 1999):

1. An activity promotes active learning to the degree to which *all students*, not simply a vocal few, are involved in mental processing related to the content.

2. An activity promotes active learning to the degree that it offers *extended opportunities* for students to become personally engaged with the content.
3. An activity promotes active learning to the degree that it involves students in thinking *deeply* about content.

The activities also make extensive use of **collaborative learning**. Most often occurring within the context of group work, collaborative and cooperative learning currently enjoy "favorite child" status among the many strategies available to teachers. Teachers are using group approaches across disciplines, for in- and out-of-class assignments, with large and small classes, and with beginning and advanced students. In fact, you will often find that collaborative activities go hand-in-hand with active learning.

Collaborative and cooperative learning, both with long theoretical and empirical histories, come out of different academic traditions, operate on different premises, and employ different strategies. But both approaches share a fundamental commitment to the notion that students learn from and with each other, "learning through joint intellectual effort," according to one expert (Brody, 1995, p. 134). In the interest of brevity, we will leave alone the finer distinctions between the two, offering in this curriculum a mix of strategies that put students together and engage them in tasks that encourage learning in collective contexts.

Finally, the activities in the module use **inquiry-based strategies**. All truly inquiry-based activities share the characteristics of active learning. In addition, inquiry-based strategies emphasize discovery: the process of observation, followed by analysis, that leads to explanation, to conclusion, or to the next question. Note that an activity need not involve students in active experimentation to be fundamentally an inquiry experience.

More than active or collaborative learning, inquiry-based strategies attempt to teach students how biologists see the world, how they think about what they see, and how they draw conclusions that are consistent with observations and current knowledge. Such strategies say to the student, in effect, "*This* is science as a way of knowing."

The 5E Instructional Model

The activities in the module also have been designed using an instructional model to organize and sequence the experiences offered to students. This model, called the 5E model, is based on **constructivism**, a term that expresses a view of the student as an active agent who "constructs" meaning out of his or her interactions with events (Perkins, 1992). According to this view, rather than passively absorbing information, the student redefines, reorganizes, elaborates, and changes his or her initial understandings through interactions with phenomena, the environment, and other individuals. In short, the student interprets objects and phenomena and then internalizes this interpretation in terms of previous experiences.

A constructivist view of learning recognizes that the development of ideas and the acquisition of lasting understandings take time and experiences (Saunders, 1992). In the typical classroom, this means that fewer concepts and subjects can be covered during the school year or, in this case, in five days of instruction. Nevertheless, research suggests that students who are given time and opportunity to thoroughly grasp a small number of important concepts do better on traditional tests than students who are exposed briefly to a large number of ideas (Sizer, 1992; Knapp, 1995). In fact, the intensive thinking involved in constructing a thorough understanding of a few major ideas appears to benefit all students, regardless of ability.

Figure 13 illustrates the key components of the 5E model, so-called because it takes students through five phases of learning that are easily described using five words that begin with the letter "E": Engage, Explore, Explain, Elaborate, and Evaluate.

This instructional model allows students to share common experiences related to emerging and re-emerging infectious diseases, to use and build on prior knowledge, to construct meaning, and to assess continually their understanding of a major concept. It avoids excessive use of lecture because research shows that 10 minutes of lecture is near

Figure 13 The Key Components of the 5E Model

Phase	What the Teacher Does That Is	
	***Consistent* with the 5E Model**	***Inconsistent* with the 5E Model**
Engage	Creates interest Generates curiosity Raises questions Elicits responses that uncover what students know or think about the concept/subject	Explains concepts Provides definitions and answers States conclusions Provides premature answers to students' questions Lectures
Explore	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	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	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	Accepts explanations that have no justification Neglects to solicit students' explanations Introduces unrelated concepts or skills
Elaborate	Expects students to use formal labels, defini≠ tions, and explanations provided previously Encourages students to apply or extend con≠ cepts 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 . . . ?"	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	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?"	Tests vocabulary words, terms, and isolated facts Introduces new ideas or concepts Creates ambiguity Promotes open-ended discussion unrelated to concept or skill

the upper limit of comfortable attention that students give to lecture material, whereas the attention span in an investigative activity is far longer (Project Kaleidoscope, 1991). In the 5E model, the teacher acts as facilitator and coach much more frequently than he or she acts as the disseminator ofÄ information.

The following paragraphs illustrate how the 5Es areÄ implemented across the activities in this module.Ä They also provide some suggestions about teachingÄ behaviors that help students experience each phaseÄ of the learning cycle.Ä

Activity 1, *Deadly Disease Among Us*, serves as theÄ

Engage phase of instruction for the students. This phase of the model initiates the learning sequence and introduces the major topic to be studied. Its primary purpose is to capture the students' attention and interest. The activity 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.

Activities 2, 3, and 4, *Disease Detectives*, *Superbugs: An Evolving Concern*, and *Protecting the Herd*, serve in a broad sense as the Explore and Explain phases of the model. Activity 2 helps students discover that ecological changes are a major factor in the emergence of new diseases worldwide. Likewise, Activities 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 the teacher introduces 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, the teacher's 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.

During the Elaborate and Evaluate phases of the model, exemplified in this module by Activity 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 of this activity 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 of the program. At this point, students see they can extend and apply their understanding of infectious disease to the real world. It also is important here that they receive feedback on the adequacy of their explanations and understandings. Elaborate and Evaluate activities are complex and challenging, and Activity 5 will stretch your students' abilities to listen, think, and speak.

Using the *Emerging and Re-emerging Infectious Diseases* CD-ROM in the Classroom

The *Emerging and Re-emerging Infectious Diseases* CD-ROM is a tool, like an overhead projector or a textbook, that you can use to help organize your use of the module, engage student interest in learning, and help orchestrate and individualize instruction. The CD-ROM contains the following major resources:

- an introduction to the National Institutes of Health and the National Institute of Allergy and Infectious Diseases;
- printable files of this module;
- printable files of the print-based alternatives for Activities 3 and 5;
- the video *Infectious Disease Then and Now*, an optional introduction to Activity 1, *Deadly Disease Among Us*;
- the video segments that are an optional introduction to Activity 2, *Disease Detectives*;
- an optional video demonstration of the laboratory exercise that explores antibiotic resistance, in Activity 3, *Superbugs: An Evolving Concern*;
- the video *Debi's Story* required to complete Activity 3, *Superbugs: An Evolving Concern*;
- the *Disease Transmission Simulation* required to complete Activity 4, *Protecting the Herd*; and
- the video clips and reference databases required to complete Activity 5, *Making Hard Decisions.*

The CD-ROM runs on Apple Macintosh and IBM-compatible personal computers. The recommended requirements for a Macintosh computer are the fol lowing: OS 7.1 operating system or higher, 68030 or Power Mac processor, 256 color monitor or higher, 8 megabytes RAM, QuickTime 4 for Macintosh, and a 2x CD-ROM.

The recommended requirements for IBM-compatible computers are the following: Windows 95 operating system or higher, Pentium 60 processor or higher, 256 color monitor or higher, 8 megabytes RAM, Soundblaster or Windows Sound System-compatible card, QuickTime 4 for Windows, and a 2x CD-ROM.

To use the CD-ROM, load it into the CD-ROM drive as you would any other CD. If you do not have QuickTime 4 loaded on your computer, you will see a dialogue box that will ask you if you want to install it. Click Yes to automatically load the program. Then, follow the installation instructions shown in Figure 14.

Figure 14 Loading Instructions for the *Emerging and Re-emerging Infectious Diseases* CD-ROM

IBM-Compatible Computers

Place the CD in the CD-ROM drive and close the door. The CD should automatically launch the program.

If you have turned off the autorun feature on your CD-ROM drive, you must run the setup program the first time you use the software. Click Start | Run and type the following into the dialog box:

d:\setup.exe (change "d:\" depending on the letter of your CD-ROM drive)

If you want to run the software without eject ing and re-inserting the disk each time you use the program, do one of the following:

- Click Start | Programs | NIH Supplements | NIH CD-ROM
- Click Start | Run and type the following in the dialog box:
  d:\hsplayer\hsplayer.exe home.stk
  (change "d:\" if necessary). Click OK.

Macintosh Computers

Place the CD in the CD-ROM drive and close the door.

Open the CD-ROM, then click on the NIAID icon.

Network Installation

A network installation of the entire program requires up to 250 to 450 megabytes of disk space. Performance of the videos will depend on the network speed and the processor speed of client stations. Each client computer must have QuickTime 4 or higher installed.

1. Place the disk in the CD-ROM drive and click on Quit if the program opens auto matically.
2. Create a folder on the network or local drive where you want to install the applica tion and name it Disease.
3. Copy all the folders and files in the root directory of the CD-ROM into the new folder. Note: Macintosh users cannot see files from the PC format on the CD-ROM, and vice versa. If you run both platforms from your network, you need to copy files from the CD to the network twice, once from a network PC and once from a net-work Mac. If you have room, create two complete copies of the software in differ ent folders, one for each platform. Because users will see both Mac and PC files on the network, be sure that Mac users open only Mac files and PC users open only PC files. Otherwise, there is a danger of acciden tally opening the home stack for the other platform.
4. To run the application, follow the proce dures described here for IBM-compatible or Macintosh computers by locating the local or network copy of the desired Hyper-Studio player files.

The ideal use of the CD-ROM requires one computer for each student team; the installation instructions explain how to make the information available over a network. However, if you have only one computer and CD-ROM drive available, you can still use the CD (for example, by using a suitable display device to show animations or videos to the whole class or by rotating teams through a computer station to access CD-ROM-based resources).

If you do not have the facilities for using the CD-ROM in your classroom, a print-based alternative for each activity that requires the CD is available for printing from the CD-ROM. To use this version, you will need to print out the activity lesson plan and its associated masters.

Before you use this CD-ROM or any other piece of instructional software in your classroom, it may be valuable to identify some of the benefits you expect the software to provide. For example, Roblyer (1997) suggests four major ways that instructional multimedia software can benefit students and teachers. First, well-designed multimedia software can **help motivate students**, help them enjoy learning, and help them want to learn more. Multimedia programs offer users a rich, interesting, and compelling environment in which to explore and learn, and it rewards users with a broader and more complex set of sensory experiences than print-based resources can provide. Well-designed multimedia resources can enliven content that students otherwise perceive as dull and uninteresting. The video clips provided on the *Emerging and Re-emerging Infectious Diseases* CD offer students this benefit. Because they often provide nonlinear access to a rich array of information and stimulation, multimedia programs also can encourage reluctant students to immerse themselves in a topic, creating, in effect, a positive feedback loop in which students learn as they "go their own way," wherever their interest or curiosity takes them.

Second, well-designed multimedia software also **offers unique instructional capabilities**. For example, such software can stimulate students to explore topics in greater depth and in more different dimensions than students often are willing or able to pursue. The reference databases that support Activity 5 have this effect. This benefit is related to the first, but it deepens and intensifies learning rather than stimulates students to investigate content they otherwise would not investigate. Part of this benefit derives from the power such software has to provide essentially immediate access to a wealth of ever more detailed and complex information on a topic, all presented in interesting and unusual ways. Part of the benefit, however, derives from the software's very design: A well-designed user interface provides an easy-to-use navigation system, stimulates curiosity, and encourages exploration of related areas.

Completing activities using instructional software can help students learn to organize and be responsible for their own learning rather than depend entirely on the teacher for direction and support. This goal is commonly cited by teachers and employers, most of whom explicitly desire students and employees who are self-directed and can structure and execute work independently.

Multimedia software can offer students learning experiences that are closer to actual field experiences than the experiences print-based resources offer. The video that supports Activity 3 allows students to listen to a high school student describe an actual disease situation that occurred in her life. Although the students' experience of the situation is vicarious, it is more realistic and memorable than the comparatively static and unchanging experience that a script of this story would offer. Because it engages more senses than simply sight, and because it requires more skills than simply understanding what one reads, well-designed instructional software also addresses many different learning styles and serves the needs of a wider population of students than most print-based resources.

Third, multimedia software can provide teachers with **support for experimenting with new instructional approaches**. The educational system in the United States is struggling to improve its ability to prepare students for the complex, collaborative, technology-rich workplace they will enter when they leave school. Technology can make possible new approaches to teaching. The simulation provided in support of Activity 4 illustrates this benefit.

By moving the responsibility for organizing learning from the teacher to the student, this simulation can help teachers move into the role of observer and facilitator of learning rather than dispenser of information. As students work independently or in small teams, teachers can circulate throughout the room, listening to students interact with one another, asking and answering questions, and challenging students to consider alternative lines of research and analysis. These behaviors are very different from the typical ones teachers are engaged in when they carry the primary responsibility for delivering and explaining content.

Instructional software also can be an effective tool for helping teachers organize discussions of controversial issues in the classroom. In Activity 5, using videos to present competing proposals lends greater credibility to these proposals than they may have if they each were presented by the teacher. It also depersonalizes the positions, allowing both teachers and students to focus on the substance of the issues rather than on the controversy itself.

Software programs on CD-ROM also offer teachers the opportunity to expand and enrich the number and depth of research-based projects they assign students, and to increase the scope and difficulty of problem- or case-based activities they use in their classrooms. Although basic mathematic and communication skills still are considered essential for students to develop, educators are becoming increasingly aware that curricula must place less emphasis on learning specific factual information, and more emphasis on the ability to locate and use information to solve problems and to think critically about issues. The reference databases for Activity 5 allow teachers to involve students in problem-solving and locating and using information while teaching the basic skills students are expected to acquire.

Finally, well-designed instructional software can **increase teacher productivity**. There are a variety of ways such software can accomplish these goals, such as helping teachers with assessment, record keeping, and classroom planning and management. Instructional software such as the CD-ROM enclosed with this module offers teachers the convenience of a full week of instruction that is stored and transported in the space of a single CD and this teacher's guide. Instructional software also can give teachers increased credibility in their students' eyes. Many of today's students have been raised in a technology-rich environment and often respond positively to the use of technology-based methods that streamline and enhance communication between teachers and students and, in so doing, increase the efficiency of both.

Organizing Collaborative Groups

All of the activities in this module are designed to be completed by groups of students working together. Although many of the specific steps can be completed by individual students working alone, this strategy will not stimulate the types of student-student interactions that are one of the goals of active, collaborative, inquiry-based learning. Therefore, we recommend that you organize collaborative groups of between two and six students each, depending on the number of computers equipped with CD-ROM drives you have available. Students in groups larger than this likely will have difficulty organizing the student-computer interactions equitably, which can lead to one or two students assuming the primary responsibility for the computer-based work. Although this type of arrangement can be efficient, it means that some students do not get the opportunity to experience the in-depth discovery and analysis that the enclosed CD-ROM was designed to stimulate.

If you are teaching all five activities as a unit, we recommend that you keep your students in the same collaborative groups for all of the activities. This will allow each group to develop a shared experience with the software and with the ideas and issues that the activities present. A shared experience also will enhance your students' perceptions of the activities as a conceptual whole. This will be particularly important in the activities toward the end of the module, as students consider some of the ethical and public policy implications of allocating funds to fight disease.

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 activities. For example, if you have only one computer available, you may want students to complete the CD-based work across an extended time period. You can do this in several ways. The most practical way is to use your computer as a center along with several other centers at which students complete other activities. In this strategy, students would rotate through the computer center, eventually completing the CD-based work that you have assigned.

A second way to structure the activities if you only have one computer available is to use an overhead projection system to display the computer monitor onto a screen for the whole class to see simultaneously. Giving selected students in the class the opportunity to manipulate the program in response to class suggestions and requests can give students some of the same type of autonomy over their learning that they would gain if they were working with the CD in small teams. Some activities require students to use the CD for extensive research; give the students printouts of selected portions of the program to work from. This strategy, however, will not give the students an opportunity to interact personally with the CD. We recommend that you use this strategy only if you have no other options.

Dealing with Values and Controversial Topics

Instructors sometimes feel that the discussion of values is inappropriate in the science classroom or that it "detracts" from the learning of "real" science. The activities in this module, however, are based upon 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. Opportunities to encounter and consider carefully some of these ways will reinforce and enrich those scientific principles that we desire to teach.

The activities provide a variety of opportunities for students to discuss, interpret, and evaluate basic science and public health issues in the light of values and ethics. Many issues that students will encounter—especially those having to do with public policies that force people to protect themselves and others from infectious diseases—are potentially controversial. How much controversy develops will depend on many factors, such as how similar your students are with respect to socioeconomic status, perspectives, value systems, and religious preferences. It also will depend on how you handle your role as facilitator of the discussion. Your language and attitude may be the most important factors to the flow of ideas and the quality of exchange among the students.

Neutrality may be the single most important characteristic of a successful discussion facilitator. The following suggestions may help you think about how to guide your students in discussions that balance factual information with feelings.

- Encourage your students to discover as much information about the issue as possible. Ask questions that will help your students distinguish between those components of an idea or issue scientific research can answer and those components that are a matter of values. Maintaining this distinction is particularly important as students discuss the issues that are related in Activity 5. Students should understand the importance of accurate information to any discussion and should recognize the importance of distinguishing factual information from opinions.
- Keep the discussion relevant and moving forward by questioning or posing appropriate problems or hypothetical situations. Invite your students to respond to or build on each other's ideas. Avoid asking questions that have exact answers unless the facts are important to the integrity of the discussion. 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. Point out that we cannot make intelligent decisions if we close ourselves off from some viewpoints. Even if we

cannot agree with or are offended by a viewpoint, we still must hear it so that we know that it exists and can consider it as we shape our own views.

- Use unbiased questioning to help the students critically examine all views presented. Help your students consider different points of view thoroughly by asking them to define the relevant arguments and counterarguments. Let the students help you promote the expression of alternative points of view.
- Allow for the discussion of all feelings and opinions. Avoid becoming a censor of views that are radical or shocking (as long as these views are consistent with the facts). When a student seems to be saying something for its shock value, see whether other students recognize the inappropriate comment and invite them to respond.
- Avoid seeking consensus on all issues. This is particularly important in Activity 5. The multifaceted issues that the students discuss result in the presentation of divergent views, and students should learn that this is acceptable.
- Keep your own views out of the discussion. Experts in science education recommend that teachers withhold their personal opinions from students. The position of teacher carries with it an authority that might influence students. The danger also exists that the discussion might slip into indoctrination into a particular value position, rather than an exploration of divergent positions. Either result misses the point of the discussion. If your students ask what you think, you may wish to respond with a statement such as "My personal opinion is not important here. We want to consider your views."
- Acknowledge all contributions in the same even-handed manner. If the class senses that you favor one idea over another, you will inhibit open debate and discussion. For example, avoid praising the substance or content of comments. Instead, acknowledge the willingness of students to contribute by making such comments as "Thanks for that idea" or "Thanks for those comments." As you display an open attitude, a similarly accepting climate will begin to develop within the class.
- 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. If necessary, remind them that there is a fine line between freedom and license. In general, freedom is a positive influence, whereas license usually generates negative results.
- Insist upon a nonhostile environment in the classroom. Do not allow your students to make *ad hominem* arguments (arguments that attack the person instead of the idea). Help your students learn to respond to ideas instead of to the individuals presenting those ideas.
- Respect silence. Reflective discussions often are slow. If you break the silence, your students may allow you to dominate the discussion.
- Finally, at the end of the discussion, ask your students to summarize the points that they and their classmates have made. Let your students know that your respect for them does not depend on their opinion about any controversial issue. If students feel that they must respond in particular ways to gain your approval, your class will not discuss issues openly and with forthrightness.

Following these general suggestions should help you stimulate meaningful student-to-student interaction with as little direct involvement by you as possible. Initially, some students may have difficulty responding without specific direction. It is important, however, that you resist the temptation to intervene extensively in the initial, sometimes uncomfortable phase of long silences and faltering responses. Unless students are given opportunities to evaluate ideas and values in the context of a larger problem, they may never learn to do so.

Assessing Student Progress

Because we expect this module to be used in a variety of ways and at a variety of points in an individual teacher's curriculum, we believe the most appropriate mechanism for assessing student learning is one that occurs informally at various points within the activities, rather than something that happens more formally just once at the end of the module. Accordingly, we have integrated a variety

of specific assessment components throughout the activities within the module. These "embedded assessment" opportunities include one or more of the following strategies:

- performance-based activities (for example, structured discussions of potentially controversial issues);
- written assignments (for example, answering questions or writing magazine or newspaper articles, letters, and short reports); and
- written summaries of laboratory activities.

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.

An assessment icon and an annotation that describes the aspect of learning you can assess using a particular strategy appear in the margin beside the step in which each embedded assessment occurs.

Student Activities

The heart of this module is the set of five activities that follow. These activities are the vehicles that we hope will carry important concepts related to dis ease and public health to your students. To review the concepts in detail, refer to Figure 10 in *Implementing the Module*.

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

At a Glance gives you a convenient overview of the activity.

- The **Focus** provides a one- to two-sentence sum mary of what students do.
- **Major Concepts** state the central idea(s) the activity is designed to convey.

Figure 15 A Möbius strip is a one- sided, one-edged loop. Test this by making a loop with five twists. With a marker, draw a continuous line around the strip, start ing 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 num bers of twists are Möbius strips; loops with even num bers of twists are not. In this module, we use a five-twist Möbius strip as a metaphor for the relationship between basic science and personal and public health.

- **Objectives** lists three to five specific understand ings or abilities students should have after com pleting the activity.
- **Prerequisite Knowledge** alerts you to the understandings and skills students should have before beginning the activity.
- The **Basic Science-Public Health Connection** describes how the activity illustrates the rela tionship 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 activity in a context and provides a short overview of its key compo nents.

Materials and Preparation provides instructions for collecting and preparing the materials required to complete the activity.

Procedure outlines the activity's steps and provides implementation suggestions and answers to ques tions. Annotations in the margins, identified by icons, provide specific hints about helping students see connections between basic science and personal and public health (the Möbius strip icon), assessing student understanding (the checkmark icon), and focusing students' attention on the activity's major concepts during its closing steps (the "completing the-puzzle" icon).

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

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

Three of the activities (*Superbugs: An Evolving Concern*, *Protecting the Herd*, and *Making Hard Decisions*) use the enclosed *Emerging and Re-emerging Infectious Diseases* CD-ROM. For information about using the CD, see the section "Using the Emerging and Re-emerging Infectious Diseases CD-ROM in the Classroom" in *Implementing the Module*. If you do not have enough computers equipped with CD-ROM drives available to conduct these activities with your students, you can use the print-based alternatives. To view and print the instructions and masters for these alternate activities, load the CD onto a computer and click the Print button on the main menu screen. The computer will display a screen showing the resources available for printing from the CD; click on the button labeled Non-CD Lesson Plan from the choices available for the relevant activity. This will reveal the lesson plan and the masters for the alternate, non-CD-based lesson. Click Print again to print these resources.

Figure 16 outlines a plan for preparing for and completing the five activities that follow. The page references in the caption indicate the pages on which you will find specific preparation instructions. The plan assumes you will teach the activities on consecutive days. If this is not your plan, adjust the timing of your preparation accordingly.

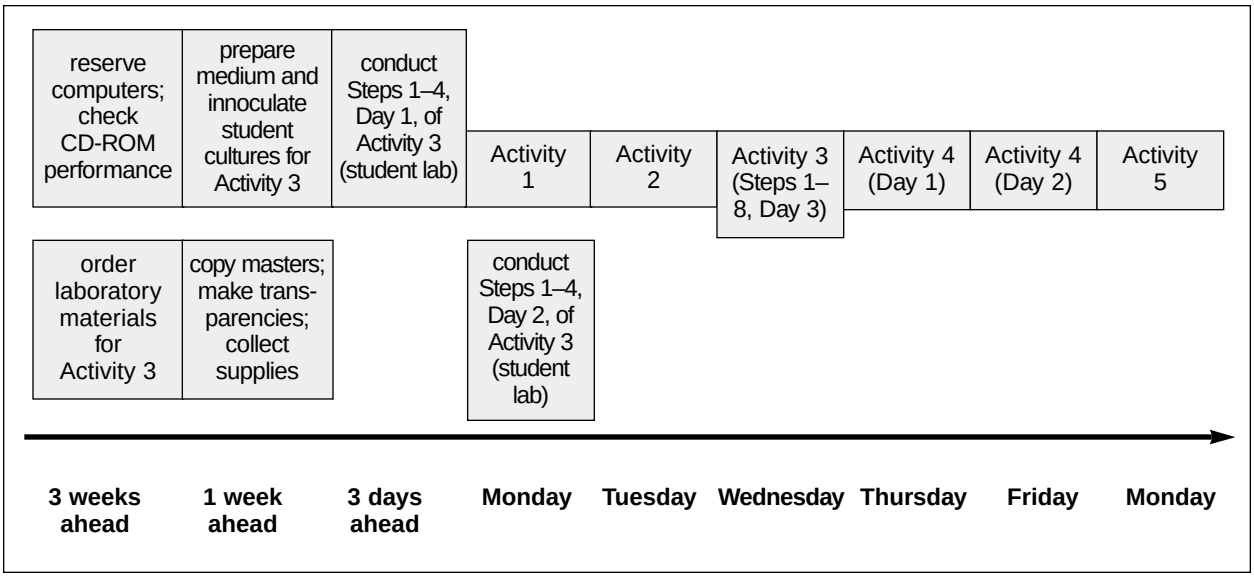


Figure 16 Timeline for teaching the module. Before you begin teaching this module, review this timeline. Instructions for computer set-up are on page 31, for laboratory preparation, page 64; and for preparing other required materials, see Materials and Preparation in each activity.

Activity 1

Deadly Disease Among Us

At a Glance Ä

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

Major Concepts: Infectious diseases continue to be a major cause of humanÄ suffering and death, both in the United States and around the world. EmergingÄ infectious diseases are diseases that have not occurred in humans before or thatÄ occurred only in small numbers in isolated places. Re-emerging infectious dis Ä eases are diseases that once were major health problems globally or in a partic Ä ular country, and then declined dramatically, but are again becoming healthÄ problems for a significant proportion of the population. Ä

Objectives: After completing this activity, students will Ä

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

Prerequisite Knowledge: Students should be familiar with bacteria andÄ viruses and understand that infectious diseases are due to infection of the bodyÄ by an external agent.Ä

Basic Science-Public Health Connection: This opening activity introducesÄ emerging and re-emerging infectious diseases as a public health issue that canÄ be examined using the methods of science (for example, collecting and organiz Ä ing data into categories).Ä

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 suc cessful 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 0157:H7 caused severe vomiting and diarrhea among patrons of Jack in the Box restaurants in Washington State in 1993 and among children swimming in public pools in Atlanta, Georgia, in 1998. And 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. 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 "tradi tional" 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. Among the dis eases "re-emerging" as a consequence of microbial resistance are tuberculosis and malaria, leading causes of death from infectious diseases worldwide.

This activity engages students in the seriousness of infectious diseases by help ing them become aware of the widespread impact of such diseases. Students discover that some diseases are relatively new to humankind (emerging dis eases), 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).

Materials and Preparation

You will need to prepare the following materials before conducting this activity:

- Master 1.1, *Causes of Death Quiz* (make 1 transparency)
- Master 1.2, *Disease Cards* (make a classroom set)

  To 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.

- Master 1.3, *Disease Classifications* (make 1 transparency)
- red transparency pen

Note to teachers: Activity 3 includes a bacterial growth experiment. If you are teaching the activities on consecutive days, students will need to complete Steps 5 to 8 on Master 3.1a, *Bacterial Growth Experiment,* during this class ses sion. See Master 3.1a for details.

Procedure

1. **Introduce the module and this activity 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 sev- eral responses and entertain a brief discussion about the diseases stu- dents perceive as threats and why.**

List students' responses on the board or a transparency.

Heart disease was the top killer globally in 1998. AIDS and cancer are likely to be two of the top threats students perceive. According to the World Health Organization (WHO), in 1998 AIDS was the fourth high est killer worldwide, while cancer of the trachea, bronchus, or lung was the ninth highest killer. Also in the top 10 killers globally were cere brovascular disease (second), pneumonia (third), chronic obstructive pulmonary disease (fifth), diarrheal diseases such as cholera (sixth), perinatal conditions (seventh), tuberculosis (eighth), and traffic acci dents (tenth).

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.**

   If you have the equipment to project the video *Infectious Disease Then and Now* on the CD-ROM for the whole class, you can substitute this video for the quiz. Follow the instructions on page 31 to load the CD-ROM into the computer you will use. 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 activity 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 they are ingested, the 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 stimu late 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 ori gin of the caduceus symbol that represents the medical profession. Students will learn as they complete this activity that Legionnaire dis ease 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 dis ease never develops. Any condition that compromises the immune system, such as HIV infection, will allow the bacteria to grow, result ing 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, mos quito 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 nutri tion, and generally poor living conditions probably contributed to the rapid spread of the flu around the world. The 1918 flu was particu larly virulent and, unlike typical flu epidemics, caused death more frequently among young adults than among children and the elderly.

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 Activity 3, *Superbugs: An Evolving Concern*.

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

(d) Pneumonia was the third highest killer in 1998, behind heart dis ease and 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 activity they will learn about some infectious diseases that cause problems in the world today.**

   You may need to distinguish *infectious* diseases from *noninfectious* dis eases. Ask students to review the *Causes of Death Quiz* and identify some of the infectious and noninfectious diseases listed there. If neces sary, point out that noninfectious diseases such as cancer, 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 previ ously considered noninfectious, chronic conditions. For example, there is evidence that gastric ulcers are caused by *Helicobacter pylori* bacteria. Similarly, infection by *Chlamydia pneumoniae* may contribute to the development of cardiovascular disease, leading some people to ques tion whether heart disease might be infectious.

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

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

Circulate among the teams while they catego rize their diseases in Steps 5, 8, and 10 for an informal assessment of students' skills in orga nizing information.

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 1.3, *Disease Classifications*, and direct the teams to review their disease cards and sort them into piles that represent different types 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.

6. **Solicit titles for the categories identified from several teams and write them on the appropriate place on *Disease Classifications*. Then, ask the other teams to name one or more diseases they classified in the categories and write these into the appropriate columns. Ask students to describe the symptoms of each disease as they do so.**

The discussion in Steps 7 and 9 are opportunities to point out the contribu tion 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 inter rupting the organism's reproductive cycle. Continuing research likely will lead to effec tive treatment and pre ventive measures in the future for diseases like AIDS that are currently incurable.

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 the evidence (symptoms) that occur in each. 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 dif ferent types of agents. It is useful to classify diseases by the type of infectious agent because that indicates the type of treatment that may be effective better than does a review of symptoms.

8. **Reveal the next classification criterion on *Disease Classifications* and ask students to re-sort their disease cards based on this criterion (the mecha nism 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 mea sure. For example, the spread of diseases such as AIDS and Ebola hemor rhagic 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 reduce the size of the vector population or that limit contact between humans and the vector.

10. **Reveal the last classification criterion, history of the occurrence of the disease, and repeat Steps 5, 6, and 7.**

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

    If this is the case, fill these headings into the first two columns on *Disease Classifications* and list the diseases named by students. Then challenge them to re-examine the "old" diseases they listed and to sub divide that category. Assist 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 dis tinction, add the new headings for the second and third columns on *Disease Classifications* and relist the diseases accordingly.

    Students should note that whereas all of 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 two categories from the subdi vided "old" category could be renamed "Old and Increasing" and "Old and Remaining Constant."

11. Supply the labels "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 columns.

This step focuses stu dents' 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 dis eases.

The disease cards provide examples of all three types of diseases, as shown in Figure 17.

Both polio and guinea worm disease are diseases that have declined dramatically and, hopefully, are on their way to global eradication. Cholera and influenza are more complicated examples that are less eas ily classified. Based on the information on their cards, students will likely classify cholera as 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 strain *Vibrio cholerae* 0139. This strain combines the greater virulence of the classic *V. cholerae* strain with the long-term survivability of the *V. cholerae* strain called El Tor.

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

Figure 17 History of Occurrence

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

been recognized as due to an infectious pathogen (gastric ulcers caused by *Helicobacter pylori* is an example that falls into this subcate gory). Many researchers include re-emerging diseases as a subcategory of emerging diseases.

12. **Conclude the activity 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 activities.**

Potential Extensions

Internet Web sites maintained by both the Centers for Disease Control and Prevention (www.cdc.gov/) and the World Health Organization (www.who.org/) include health topic sections that provide 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.

Activity 2

Disease Detectives

At a Glance

Focus: 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 environ mental change (for example, human encroachment into wilderness areas and increased human traffic through previously isolated areas).

Objectives: After completing this activity, 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 activity demonstrates how scien tists use ecological, biochemical, and medical research to investigate infectious disease outbreaks. The activity 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.

Introduction

When local health care 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 evi dence about environmental factors that might be involved. Their goal is to pro tect public health by identifying the disease as rapidly as possible and recom mending 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 mortal ity 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 activity. HPS was first rec ognized in 1993; Lyme disease first came to the attention of public health work ers 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 out-break 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 north-east United States, 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 these new diseases "emerged" as a result of environmental changes and / or move ment of humans into areas inhabited by the organism that serves as reservoir for the pathogen. The two activities that follow, Activity 3, *Superbugs: An Evolving Concern*, and Activity 4, *Protecting the Herd*, help students understand two factors involved in the re-emergence of infectious diseases.

Materials and Preparation

You will need to prepare the following materials before conducting this activity:Ä

- blank transparenciesÄ
- Master 2.1, *Three Mysterious Diseases* (make 1 copy per student)Ä
- Master 2.2, *Documents from Physician's Investigation File* (make a classroom set)Ä
- Master 2.3, *Documents from Laboratory Scientist's Investigation File* (make a class-Ä room set)
- Master 2.4, *Documents from Field Researcher's Investigation File (make a classroom set)*

  To make 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 stu dents (one student from each of three or four different teams) study the docu ments in the file together. For example, for a class of 30 students (10 teams), pre-pare three sets of each type of file.

- Master 2.5, *Notes from the Physician's Investigation* (make 1 copy per team)
- Master 2.6, *Notes from the Laboratory Scientist's Investigation* (make 1 copy per team)
- Master 2.7, *Notes from the Field Researcher's Investigation* (make 1 copy per team)

- Master 2.8, *Mystery Disease 1 Final Report* (make 1 copy per team)
- Master 2.9, *Mystery Disease 2 Final Report* (make enough copies for half the teams)
- Master 2.10, *Mystery Disease 3 Final Report* (make enough copies for half the teams)
- Master 2.11, *Mystery Diseases Summary Table* (make 1 copy per student and 1 transparency)

Procedure

1. **Introduce the activity 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 impor tant to leave these questions on the board or the overhead projector so that students can refer to them as they complete the activity.

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 activity students will follow in the footsteps of public health officers to answer some of the questions they have listed about a mystery disease. Distribute 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.

   You can use the *Mystery Diseases* video on the CD-ROM to introduce the activity if you have the equipment to project the video for the whole class. Follow the instructions on page 31 to load the CD-ROM

into the computer you will use.

3. **Organize students in teams of three and tell them they will spend the next 30 minutes investigating the first mystery disease. Direct them to assign each team 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 his or her team answer the questions the class listed in Step 1.**

   We suggest that you use the same teams as in Activity 1.

4. **Identify stations in the room that have investigation documents for the physicians, laboratory scientists, and field researchers. Distribute one copy each 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* to each team. 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 teams. 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.

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.

   Tip from the field test. To save time and reduce confusion, place three or four copies of Masters 2.3, 2.6, and 2.7 at the appropriate stations prior to class time. Then tell students they will find a copy of the form they need to complete at the station.

5. **Reconvene the original teams and distribute one copy of Master 2.8, *Mystery Disease 1 Final Report*, to each student. Allow students 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 teams 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 teams 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, *Mystery Diseases Summary Table*, and ask several teams to report one piece of information as you complete the first row of the table. Ask the remaining teams whether they have additional information and whether they disagree with any of the information provided by the other teams. 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* ticks)
   - Mystery Disease 3—contact with rat (*Mastomys natalensis*) urine and feces, and close contact with victims of the disease

   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 to *M. natalensis* 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

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.

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
- 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 health care workers, just as they were to students in this activity.

In this step, students are challenged to synthesize in their own words the discussion from Step 9. Completing the sen tences requires them to state and elaborate the activity's major concept.

10. Ask students individually to complete, in writing, the sentences at the bottom of *Mystery Diseases Summary Table*.

11. Collect students' assignments from Step 10 and close the activity 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 activity should lead students to recognize that chang ing environmental conditions create opportunities for new or previ ously 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 advan tages of economic development outweigh the risks of emerging dis eases? 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 con struction of dams. Although this was known before the Aswan Dam

was constructed, the officials involved in the decision felt that the economic advantages of the dam outweighed the disease conse quences. Before the dam was built, about 1 percent of the school chil dren 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 chemother apy campaign against schistosomiasis.

This example also shows that the incidence of "old" diseases may be affected by environmental changes. Schistosomiasis is not a "new" dis ease, 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 activities.

PotentialÄ ExtensionsÄ

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 booksÄ such as *The Hot Zone* by Richard Preston (which describes outbreaks of EbolaÄ hemorrhagic fever) and *The Coming Plague* by Laurie Garrett (which describesÄ the efforts of scientists and policymakers regarding a variety of emerging andÄ re-emerging diseases, including HPS, Lassa fever, malaria, and LegionnaireÄ disease). Ä

Activity 3

Superbugs: Ä An Evolving ConcernÄ

At a Glance

Focus: Students investigate the growth of bacteria in the presence of antibiotics and use the results to explain a case of antibiotic-resistant tuberculosis, pre sented in a CD-ROM-based interview.

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

Objectives: After completing this activity, 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 activity, students learn that the evolution of antibiotic resistance among bacteria observed in laboratory experi ments occurs in the natural environment as well, and that such evolution has serious consequences for the effectiveness of treatments for some diseases.

Introduction

In 1943, penicillin was introduced as the “magic bullet” for curing many infec tious 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 peni cillin-resistant.

After the introduction of penicillin, additional antibiotics were rapidly isolated and developed, including streptomycin and the tetracylines. Today, there are more than 100 antibiotics available. Nevertheless, some strains of at least three bacterial species (*Enterococcus faecium, Mycobacterium tuberculosis, Pseudomonas aeruginosa*) are resistant to all of these antibiotics, and health care workers fear 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 evolution. When mutant genes arise that make a bacterium less sensitive to an antibiotic, that bacterium survives and produces descendants in an environment rich in antibi otics. That is, the process of natural selection operates. Multiple mutations may be required to result in 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, nor even in every species of pathogen, but can simply be acquired from another organism).

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

Materials and Preparation

You will need to prepare the following materials before conducting this activity:

- Master 3.1, *Bacterial Growth Experiment* (make 1 copy per student)Ä
- Master 3.2, *Discussion Questions for the Bacterial Growth Experiment* (make 1 copyÄ per student)
- Master 3.3, *Debi's Story: Explaining What Happened* (make 1 copy per student)
- Master 3.4, *Antibiotic Concerns* (make 1 per team)
- *Emerging and Re-emerging Infectious Diseases* CD-ROM (1 per team)

Students complete this activity across a five-to-seven day period. You will need to prepare the materials for the laboratory exercise. Ordering information and preparation directions are on page 64, immediately following the activity.

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. A number of leaders in infectious diseases, including scientists from NIH, contributed to the Web site. *Pseudomonas fluorescens*, the organism used in the laboratory exercise in this activity, is included on the list of microorganisms considered appropriate for students in grades 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 activity:

> *Pseudomonas fluorescens*, the bacteria 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 weak ened immune system for these or any other reasons, let me know and I will provide you with 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 CD-ROM as described in the following paragraphs.

They can rejoin the class in Day 3 of the activity, after the other students have recorded their results and discarded their bacterial cultures.

If you do not have the time or facilities for conducting the laboratory exercise, you will need only one day to complete this activity. 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* CD-ROM. Students will need copies of Master 3.1 to help them follow the steps in the demonstration. Then move to Day 3 of the activity.

Follow the instructions on page 31 to load the CD-ROMs into the computers students will use.

Note to teachers: If you do not have enough computers equipped with CD-ROM drives to conduct this activity, you can use the print-based alternative. To view and print the instructions and masters for this alternate activity, load the CD onto a computer and click the Print button on the main menu screen. The computer will display a screen showing the resources available for printing from the CD; click on the button labeled Non-CD Lesson Plan from the choices available for Activity 3, *Superbugs: An Evolving Concern*. This will reveal the lesson plan and the masters for the alternate, non-CD-based lesson. Click Print again to print these resources.

Procedure

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

1. **Remind students of the theory of evolution by natural selection and tell them that a powerful feature of theories is that they lead to hypotheses that can be experimentally tested.**

   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 teams of three and challenge the teams 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 a 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 teams 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 of 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 team 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*, which shows students using aseptic techniques as they prepare the initial cultures in the experiment.

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

1. **Direct teams to complete the remaining steps on *Bacterial Growth Experiment*.**

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

   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 teams 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 antibi otic 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 bacter ial 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 expla nation, suggest that they use their understanding of natural selection to explain the difference in the results on the plates for the two cul tures. They should be able to explain that the environment in culture B (which contained kanamycin) *selected for* the growth of those bacte ria that were resistant to kanamycin. By the time students plated a sample from that culture, all of the bacteria in the sample were resis tant, 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 they 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 selec tion 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 resis tant to kanamycin, even though there was no kanamycin present. Similarly, a few bacteria in culture A were resistant to kanamycin even though no antibiotic was present. When the resistant and nonre sistant 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 of the bacteria in the culture—the prog eny 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.**

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. Instruct teams to take their copies of the flow chart and *Discussion Questions* with them to the computer stations.**

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 expla nations for disease and for the success or failure of disease treatment. This understanding leads scientists to pro- pose further research and policies directed at improving public health.

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 bacte rial 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 3.3*, 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 teams at individual computer stations to view Debi French's story will allow them to complete this part of the activity at their own pace. An alternative, if you have the equipment to project the

video from the CD-ROM 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 teams. After the teams have discussed and written answers to the first set of questions on *Debi's Story*, reconvene the class to watch the second part of the video. Instruct students to return to their teams 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 Activity 1.

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

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.

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

Question 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.

Question 2

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

Question 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.

Question 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.

Question 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 contin ued 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, was resistant.

Question 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 antibi otic taken by a person who has a bacterial infection doesn't kill all of the disease-causing bacteria? What can you say about the bacteria that sur vive?" 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 for treating more diseases than TB. For exam ple, many strains of the organism that causes the sexually transmitted disease gonorrhea (*Neisseria gonorrohoeae*) and most strains of a com mon 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 Activity 5, *Making Hard Decisions*.

8. **Distribute one copy of Master 3.4, *Antibiotic Concerns*, to each team and assign one of the three statements to each team. Explain that each statement describes an example of an inappropriate or potentially inappropriate use of antibiotics. Instruct the teams 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.**

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

Laboratory Preparation for Activity 3

1. *Four weeks before conducting the activity*. Order the following materials from Carolina Biological Supply:

   • *Pseudomonas fluorescens* culture, catalog #AA-15-5255Ä
   • nutrient broth, catalog #AA-78-5360Ä
   • nutrient agar, catalog #AA-78-5300Ä
   • kanamycin, catalog #AA-21-6881Ä

   Allow two weeks for delivery. Carolina Biological Supply will onlyÄ ship live or perishable materials on Mondays, Tuesdays, andÄ Wednesdays.Ä

2. *Two days before conducting the activity*. Prepare the following additional materials:

   • petri dishesÄ
   • capped test tubesÄ
   • sterile 1-ml pipetsÄ
   • pipet pumps or bulbsÄ
   • glass rod spreadersÄ
   • Bunsen burnersÄ
   • alcohol (for sterilizing the glass spreaders)Ä
   • facilities for sterilizing and preparing growth mediaÄ

3. Prepare a stock solution of 25 mg/ml kanamycin in water and filter-steril ize 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 con taining kanamycin for each team. You will also need 3 nutrient agar plates and 3 nutrient agar plates containing kanamycin for each team. We recom mend preparing extras to allow for contamination and errors.

6. Inoculate 1 nutrient broth tube with *P. fluorescens* for each team 2 days before Day 1 of the activity (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. You may want to demonstrate these techniques by showing the Day 1 segment of *Bacterial Growth Experiment* on the CD-ROM. 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. Hands, equipment, and counter tops should be washed with a commercial, microbiological 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.

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 refrig erate 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.

All cultures should be decontaminated when students have completed their work. Used cultures should be placed in an autoclave at 1 atmosphere pressure for 15 minutes to kill bacteria. Plastic petri dishes should be placed in heat-resistant plastic bags prior to autoclaving because the dishes will melt and leak. A kitchen pressure cooker can also be used to kill bacterial cultures.

Activity 4
Protecting the Herd

At a Glance

Focus: Students use in-class and CD-ROM-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 activity, 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 activity 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.

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 in some parts of the world, however, vaccination programs must be maintained everywhere, because an infected individual 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 age 4–6 or 11–12.

This activity and Activity 3, *Superbugs: An Evolving Concern,* both provide explanations for the re-emergence of some infectious diseases. Activity 3 explained that some re-emerging diseases are due to the evolution of antibiotic resistance among pathogens. Activity 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 activity, 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 activity. 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.

Materials and Preparation

You will need to prepare the following materials before conducting this activity:

- Master 4.1, *Measles Outbreak at Western High* (make 1 per student)
- Master 4.2, *A Little Sleuthing* (make 1 per student)
- Master 4.3, *Following an Epidemic* (make 2 per student and 2 transparencies)
- red, pink, and black cards (make 1 of each per student)
- folded pieces of paper labeled "immune" and "susceptible" (make enough of each for half the students)

If you do Day 2 of the activity, you will also need the following materials:

- Master 4.4, *Disease Transmission Simulation Record* (make 1 per student)
- Master 4.5, *Characteristics of Smallpox, Polio, and Measles* (make 1 transparency)
- Master 4.6, *Cases of Smallpox in Niger and Bangladesh* (make 1 transparency)
- blank transparencies
- *Emerging and Re-emerging Infectious Diseases* CD-ROM

Follow the instructions on page 31 to load the CD-ROMs on the computers students will use.

Note to teachers: If you do not have enough computers equipped with CD-ROM drives, you will not be able to conduct the optional Day 2 of this activity.

Procedure

DAY 1

1. **Introduce the activity 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 is based on an outbreak of measles that occurred in Washington State in 1996.

   An alternate way to introduce the activity 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 activity, 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.

2. **After students have read *Measles Outbreak*, 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 likely will 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 didn't 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." Distribute 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 page 77, immediately following the activity.**

This is an opportunity to point out that research in microbiology and related disciplines in the last 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.

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 it 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, in particular the second simulation in which half of 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 of 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 effectively transmitted.**

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.

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.

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.

DAY 2 (Optional)

1. **Open the activity by reminding students about two-day disease and the simulation that 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 also may 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 that they will use a computer simulation to investigate the likelihood of an epidemic when they vary one of the four characteristics they just discussed. Distribute one copy of Master 4.5, *Disease Transmission Simulation Record,* to each student and ask students to organize into their teams. Assign each team one of the four characteristics to investigate and direct students to circle this characteristic on the master.**

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

4. **Explain briefly how to access and use the simulation, then direct students to use it to test their assigned characteristic. Explain that teams 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 teams that are assigned the virulence characteristic select four levels from the low end of the available range (less than .1 or .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.

Note to teachers: The simulation will allow students to enter values for the disease characteristics that are outside the indicated range. However, the results of those simulations may not be reasonable.

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 teams that investigated the effect of varying virulence level to read its summary statement to the class. Invite other teams 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 teams 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 those 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 (50–90 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.

Level of immunity: 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 of an epidemic occurring in a particular population or to estimate the level of vaccination coverage they must achieve to prevent epidemics in the population.**

7. **Challenge students to work in their teams to use the simulation to estimate the level of immunization required to prevent epidemics of three real diseases: smallpox, polio, and measles. Assign each team one of the diseases and display Master 4.5, *Characteristics of Smallpox, Polio, and Measles*, which provides the settings they need for the simulation. Tell teams 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 teams for their results and add them to the appropriate column of *Characteristics of Smallpox, Polio, and Measles*. 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.**

   Based on 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 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 (.23 cases per square kilometer) but not in Niger (.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 are 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 of 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 activity 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.

Potential Extensions

The World Health Organization maintains a Web site that includes information on infectious diseases that are 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 health care workers for meeting that goal, and (3) the strategies epidemiologists are using to meet their goals.

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

Simulating the Transmission of Two-Day Disease

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, they are 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.

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 *Following an Epidemic*.
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 two 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 onto 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 *Following an Epidemic*. 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 a folded card that says "immune" and 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 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 are newly immune 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 will reveal who is immune and who is susceptible and may influence the choices students make as they transmit the disease. Tell students to record the number 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 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 onto 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.

Activity 5
Making Hard Decisions

At a Glance

Focus: Students explore several CD-ROM-based resources to evaluate proposals to combat AIDS, VRSA, and measles and recommend one proposal to support.

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 dif ferent diseases raises complex ethical questions. Understanding the relevant biological principles can help in making these difficult decisions.

Objectives: After completing this activity, 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 control- ling infectious diseases, such as the evolution of drug resistance and the chal lenge 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 activ ity students see that implementing these measures is challenging, both finan cially and logistically, and requires that difficult decisions be made. 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 that money be spent to better understand the factors involved in infec tious diseases and their spread, to alleviate suffering, and to prevent disease where possible. Much of the money spent in the United States to fight infec tious diseases is federal money, allocated through well-established and closely monitored agencies and programs. Some of the money, however, is private money—money that is made available through the beneficence of private foun dations 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 the reviewers, the requests meet the funding criteria that have been established for use of the money.

In this activity, students consider three proposals for spending $5 million that a private foundation has made available to combat infectious diseases. Each pro posal addresses a different infectious disease (AIDS; measles; and vancomycin resistant *Staphylococcus aureus*, or VRSA) and proposes different actions. Students use three reference databases on the CD-ROM 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 effective ness (how likely it is that the proposed project will address the situation suc cessfully). Finally, students recommend which proposal to fund, provide rea sons for their recommendations, and discuss differences in their evaluations as a way to understand how complex such decisions can be.

Materials and Preparation

You will need to prepare the following materials before conducting this activity:

- Master 5.1, *Proposal Criteria Matrix* (make 1 copy per student)
- Master 5.2, *Proposal Summary Matrix* (make 1 copy per student)
- Master 5.3, *Reflection Questions* (make 1 transparency)
- *Emerging and Re-emerging Infectious Diseases* CD-ROM (1 per team)

Follow the instructions on page 31 to load the CD-ROMs on the computers stu dents will use.

Note to teachers: If you do not have enough computers equipped with CD-ROM drives to conduct this activity, you can use the print-based alternative. To view and print the instructions and masters for this alternate activity, load the CD onto a computer and click the Print button on the main menu screen. The computer will display a screen showing the resources available for printing from the CD; click on the button labeled Non-CD Lesson Plan from the choices available for Activity 5, *Making Hard Decisions*. This will reveal the lesson plan and the masters for the alternate, non-CD-based lesson. Click Print again to print these resources.

Procedure

1. **Introduce the activity 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 pre vious activities 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 consid ering 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.

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

2. **Continue the discussion by saying something like, "Fighting infectious diseases requires money as well as knowledge. There is a limit, however, to the money that is available for this purpose. 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 recomendations also must include reasons for funding one proposal but not the other two.**

   In the first video segment (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 5.1, *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 poten tial for this burden to increase in the future. Effectiveness refers to how well the proposal will alleviate the serious consequences of the disease.

   A third criterion—means—often is used to make decisions about plans to address societal problems. Means refers to how well we can accom plish 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 team judges a proposed project to have high "effectiveness," the team believes there are means available to accomplish it.

   Most funding agencies have an established review process and evalua tion 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.

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.

3. **Organize students into their teams and direct them to watch the video segments *Introducing the Proposals* and *Proposal 1*, *Proposal 2*, and *Proposal 3* on the CD-ROM, then to proceed directly into their research using the databases on the CD-ROM. Tell the teams that they have 30 minutes to complete their work.**

4. **Distribute Master 5.1, *Proposal Criteria Matrix*, and Master 5.2, *Proposal Summary Matrix* as students begin their work and tell them that at the end of the 30 minutes, each team should be prepared to announce its recommendation and explain its rationale to the class.**

   While the student teams 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 team to identify a spokesperson to tell the class which proposal the team recommends and the reason it selected that proposal. As the teams 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 team 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 teams gave more weight to the "magnitude" criterion and others gave more weight to the "effectiveness" criterion.

   If all teams 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 5.3, *Reflection Questions*, and ask each team to work together to list as many responses to each question as they can. Conclude the activity by asking each team 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 yu consider in making you decisions?

Students may say that they felt it was important to consider the num ber 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 pro ductivity 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 spend ing money to combat infectious diseases is complex and there is typically no one "right" decision. Students also should recognize that understanding the biol ogy underlying such dis eases can help inform the decisions that ultimately are made.

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 World Wide Web

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. In addition, the following site has links to publications from the institute: http://www.niaid.nih.gov/eidr/cover.htm.

ProMED: The Program for Monitoring Emerging Diseases
http://www.healthnet.org/programs/promed.html#intro

The Federation of American Scientists (FAS) sponsors the Program for Monitoring Emerging Diseases (ProMED), a global electronic network of scientists, physicians, teachers, students, and laypersons interested in learning about and discussing emerging disease concerns. In addition to information posted on the Web site, you can subscribe free of charge to the ProMED-mail electronic conference. Subscribers receive one or two postings a day that report the incidence of and circumstances surrounding cases of emerging infectious diseases. The reports are edited and moderated by a group of experts in areas such as viral diseases, animal diseases, plant diseases, and emerging infectious diseases.

United States Public Health Service
http://phs.os.dhhs.gov/phs/

This is the Web site for the United States Public Health Service. Information here includes descriptions of the work of the Public Health Service, press releases and fact sheets from the service, and links to the Web sites for the various Public Health Service agencies.

Centers for Disease Control and Prevention
http://www.cdc.gov/

The Centers for Disease Control and Prevention (CDC), a branch of the U.S. Public Health Service, operates this Web site. It contains information about CDC activities; recent press releases; fact sheets on more than 150 diseases, injuries, and disabilities in the United States and around the world; and links to many CDC centers and offices of interest, such as The National Immunization Program, the National Center for Infectious Diseases, and the Global Health Odyssey. The Global Health Odyssey provides information on the history of the CDC and a connection to EXCITE (Excellence in Curriculum Integration through Teaching Epidemiology), a collection of teaching materials on the science of epidemiology.

This site also has a link to the CDC's electronic journal, *Emerging Infectious Diseases*, a valuable resource for anyone interested in research in this field. The direct URL for the journal is www.cdc.gov/eid.

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)

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 (1998)

Glossary

acquired immune deficiency 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 amoebae. 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.

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*.

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*.

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 protozoon *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 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 that is associated with the onset of AIDS.

immune: Protected against a particular disease by either nonspecific or specific immune defenses.

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 disease: Pulmonary form of disease caused by infection with *Legionella pneumophila*.

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 protozoon *Plasmodium*. 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 health care 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.*

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.*

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 is 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.

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

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Masters

Activity 1, *Deadly Disease Among Us*

Activity 2, *Disease Detectives*

Activity 3, *Superbugs: An Evolving Concern*

Activity 4, *Protecting the Herd*

Activity 5, *Making Hard Decisions*

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 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 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 more deaths in 1998 than the others?

a. AIDS

b. diabetes

c. lung cancer

d. pneumonia

Disease Cards

AIDS	
Infectious Agent:	virus (human immunodeficiency virus)
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 appropriate hospital procedures to prevent accidental spread of HIV
History:	first recognized in 1979; currently a global epidemic

Cholera	
Infectious Agent:	bacteria (*Vibrio cholerae*)
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 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; 18 outbreaks since then

Guinea Worm Disease (Drancunculiasis)	
Infectious Agent:	helminth (the roundworm *Dracunculus medinensis*)
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; has 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:	vaccine against current strains; wash hands frequently
History:	present from antiquity; epidemics occur at regular intervals

Legionnaire Disease	
Infectious Agent:	bacteria (*Legionella pneumophilia*)
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 waters
History:	first recognized in 1976; occasional outbreaks since then

Lyme Disease	
Infectious Agent:	bacteria (*Borrelia burgdorferi*)
Evidence of the Disease:	initially an expanding, ringlike rash, fever, fatigue, and headache; followed weeks or months later by chronic arthritis
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 *Plasmodium* species)
Evidence of the Disease:	cyclic fever and chills, anemia
Treatment:	antiprotozoan drugs
Transmission:	bites from infected mosquitos
Preventive Measures:	follow procedures to reduce mosquitos such as eliminating standing water and spraying with insecticides; follow procedures to limit contact between humans and mosquitos such as installing screens and bed nets and using insect repellant
History:	present from antiquity; has increased in recent years

Streptococcal Pharyngitis (“Strep Throat”)	
Infectious Agent:	bacteria (*Streptococcus pyogenes*)
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 (*Yersinia pestis*)
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 the elderly

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 *Schistosoma*)
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:	*Schistosoma* 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 (*Mycobacterium tuberculosis*)
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/early 1990s

Disease Classifications

Infectious Agent

Mechanism of Transmission

History of Occurrence

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. Anytime 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 co-workers, 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 informa tion and find parallel cases—which might tell me what the disease is, where it's coming from, why it's hap pening, 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.

Physician's Notes and Database Searches

10-17

Assisted in treatment of farmer with acute respiratory distress syndrome (ARI last week – he died 2 days ago. We were unable to determine the cause, so death was listed as due to "ARDS of unknown cause." The case was particula 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 beginning of an epidemic & took the following actions:

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

* 10-23

10-27

Results of these actions collected in this file

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

Call Mary – 520-879-4592 No. AZ – Record

10-18

Began calling hospitals in NM, AZ & CO - requested info. on deaths due to "ARDS of unknown cause"

Results –

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

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

SEARCH	acute respiratory distress syndrome (ARDS)	SCREEN	Southwest United States

4 matches
results printed below

Begin Search

Bacterial Pneumonia

Incidence	throughout the world; in temperate zones, highest incidence in winter and spring; often accompanies epidemics of influenza
Infectious Agent	90% of U.S. cases due to 1 of more than 80 strains of *Streptococcus pneumoniae*; other bacteria that cause pneumonia include *Hemophilus influenzae* (usually in children), *Klebsiella pneumoniae* (typically among alcoholics, diabetics, or those with cardiopulmonary disease), *Pseudomonas aeruginosa* (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, 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
Reservoir	humans; possibly other warm-blooded animals
Treatment	treat symptoms

Plague

Incidence	10 to 20 cases per year, usually in the Southwest
Infectious Agent	bacterial—*Yersinia pestis*
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 *Y. pestis* 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 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	▼

2. Identify additional characteristics:

Symptoms	Acute respiratory distress syndrome	▼

3. Click here:

Begin search

2 matches
Results printed 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

Results of Laboratory Analyses from National Laboratory

INTEROFFICE-

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	*Streptococcus pneumoniae*	all samples negative
influenza	myxovirus	sample from Victim 4 positive; all other samples negative
plague	*Yersinia pestis*	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 - R. Kauffman

DATE: 10-27

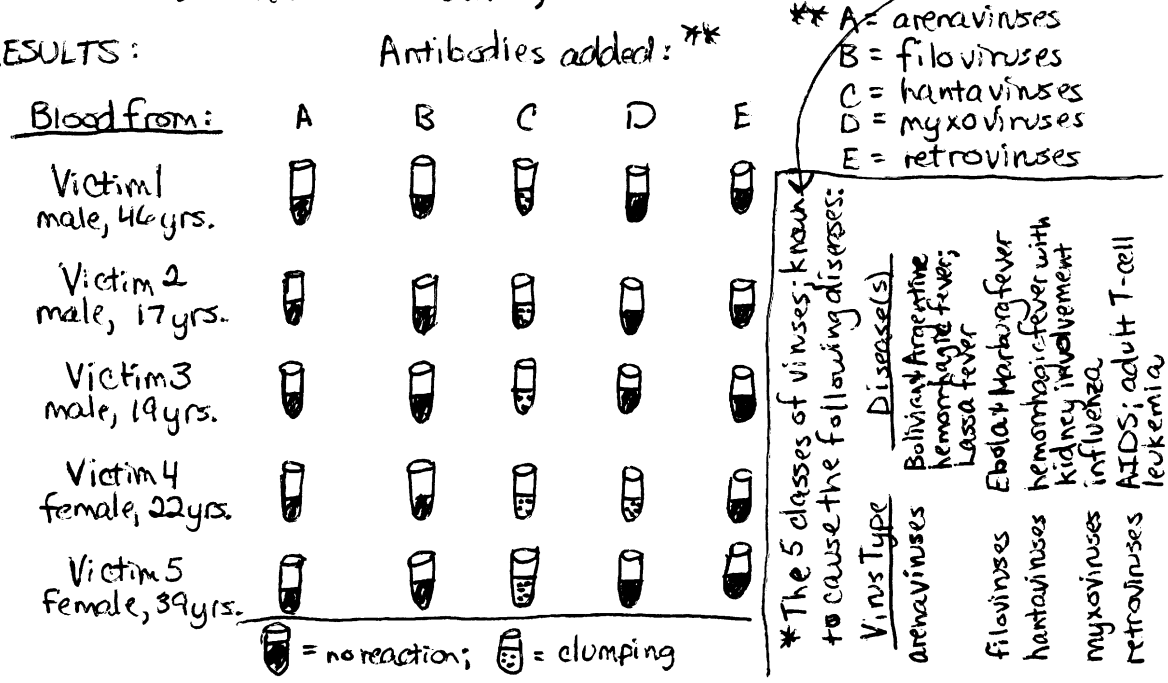
PURPOSE: Received autopsy samples (blood) from 5 victims of acute respiratory distress syndrome (ARDS) of unknown cause to test against antibodies for viruses we have in stock.

PROCEDURE: ① Placed each victim's blood into 5 test tubes labeled: "Arenaviruses," "Filoviruses," "Hantaviruses," "Myxoviruses," and "Retroviruses." *

② Added antibodies against each of viral types above to the appropriate tubes.

③ Examined for clumping (indicates reaction of virus in patient's blood with antibodies added).

RESULTS:



INTEROFFICE-

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:

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

Mario

Epidemiology Reports and Other Notes

Phone Call

Southwest Regional Public Health Office

For: D. Martinez **Date:** 10-20 **Time:** 10:00 a.m.

From: Western CO Health Center **Phone:** 970-555-1212

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 surviv ing 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 ❐

Epidemiology Report Form E763 **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 hos pital . . . 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 mouse traps. 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?

A.G. - 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?

Epidemiology Report Form E4

Investigation of Victim's Home

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 board, seeds & 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

Epidemiology Report Form E763

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 fin ished 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.

Epidemiology Report Form E4

Investigation of Victim's Home

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, w/ newspapers scattered on ottoman. Kitchen was clean, w/ 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 reroofed 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. Morton

Epidemiology Report Form E4

Investigation of Victim's Home

Victim's sex and age: male, 19 years
(female, 24 years)

1. Description of dwelling
The first victim lived with his mother in a trailer 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 - ~~lead~~ to good harvests

10-25
3:30 Meet Sally

10-24 - Talked c 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 researd survey team *Mike Lee 970-893-4582 - Call him *

10-25 - Mike Lee

Said most interesting finding of past yr was size of deer mice pop. - 10x higher than any previous yr. of records.

Notes from the Physician's Investigation

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

Work with your fellow experts to review the investigation documents and complete this form. When your team 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, or 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 investigation documents and complete this form. When your team 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 investigation documents and complete this form. When your team 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

Pool the information from all members of your team 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 against 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

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, in order to reduce the chances of new epidemics among people, we should . . .

Bacterial Growth Experiment

Pseudomonas fluorescens, the bacteria 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 immunosuppres sive 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 the last page provides an overview of the experiment.

Hypothesis:

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 label ing, 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 demon strate 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" and 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 for three days.

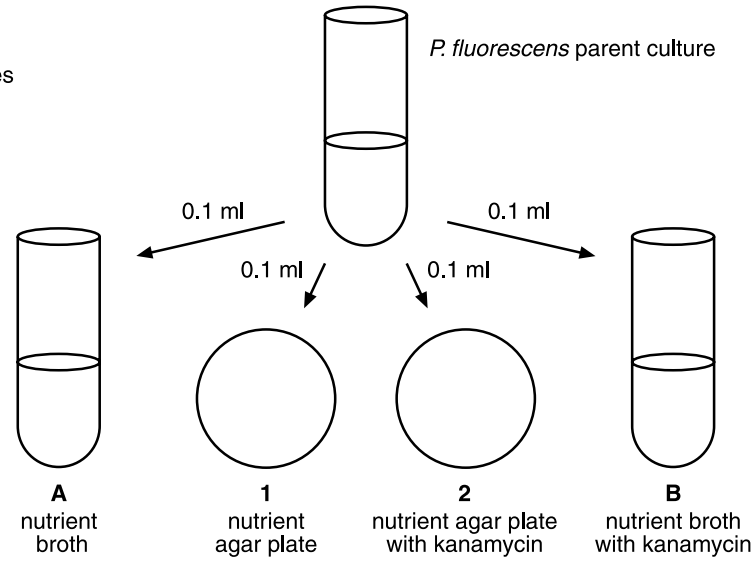
DAY 2 (3 days later)

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 plates, 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.

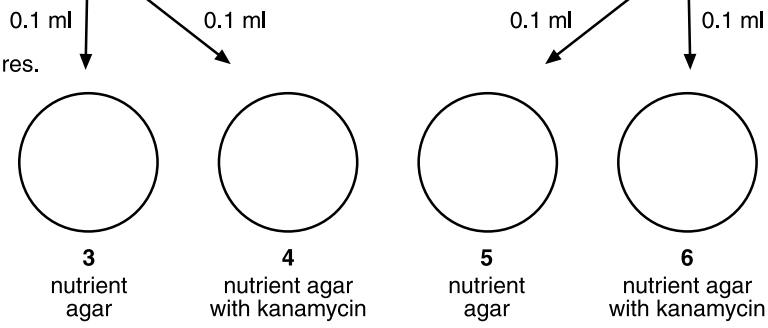
DAY 3 (2–3 days later)

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.

Discussion Questions for the Bacterial Growth Experiment

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: Explaining What Happened

Follow the steps below to explain what happened to Debi French.

1. Click on *The Diagnosis* and view Debi's description of her initial diagnosis. Summarize what you learned by completing the following sentences:

   Debi contracted tuberculosis (TB) from

   The symptoms Debi had were

2. Click on *The Initial Treatment* to hear Debi describe the treatment prescribed by her doctor and its outcome. 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

4. Click on *The Treatment Fails* to learn what happened to Debi next. 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. Click on *A Happy Ending* to learn what finally happened to Debi. 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

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 a 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 devel oped 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 follow ing 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. But there is another question:

In the 1950s and 1960s (before the measles vaccine was developed), most people got this disease as preschool children or as elementary school students. 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?

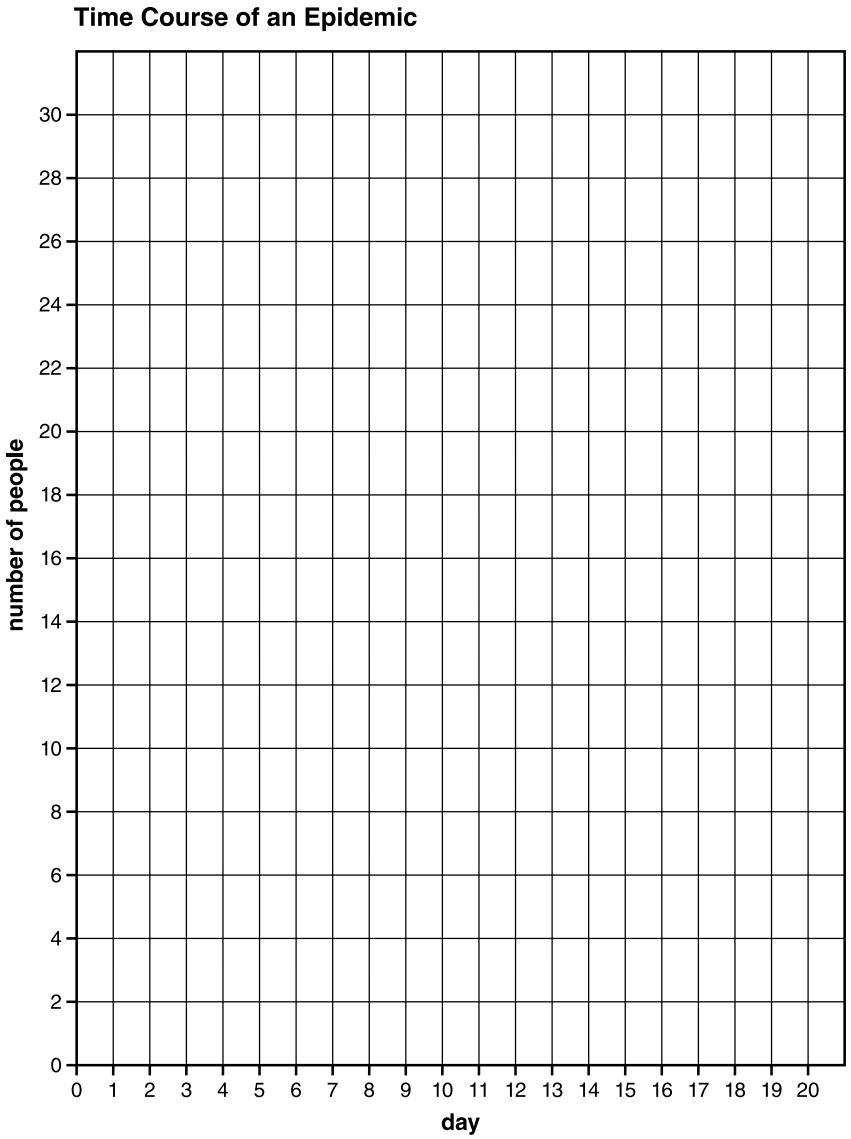
Following an Epidemic

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 simula tions? How long did it last? Did everyone get sick at some point?

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 illnesses _____

Disease Transmission Simulation Record

Use the computer simulation of disease transmission to investigate the effect of changing a disease charac teristic on the occurrence of an epidemic.

1. Run the computer simulation of disease transmission first with the Disease Characteristics values set for two-day disease: virulence = 0; duration of infection = 2; rate of transmission = 1; initial percent immune = 0. Record the results below.

   Did an epidemic occur? Y N

   Maximum number of sick _____

   Maximum percentage sick _____

   Maximum occurred on day _____

2. Circle the disease characteristic you were assigned to investigate:

   virulence duration of infection rate of transmission immunity level

3. 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.

Simulation 1		**Simulation 2**	
Characteristic tested set at	_____	Characteristic tested set at	_____
Did an epidemic occur?	Y N	Did an epidemic occur?	Y N
Maximum number sick	_____	Maximum number sick	_____
Maximum percent sick	_____	Maximum percent sick	_____
Maximum occurred on day	_____	Maximum occurred on day	_____
Simulation 3		**Simulation 4**	
Characteristic tested set at	_____	Characteristic tested set at	_____
Did an epidemic occur?	Y N	Did an epidemic occur?	Y N
Maximum number sick	_____	Maximum number sick	_____
Maximum percent sick	_____	Maximum percent sick	_____
Maximum occurred on day	_____	Maximum occurred on day	_____

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., & May, R.M. 1992. *Infectious diseases of humans.* New York: Oxford University Press, p. 89.

Proposal Criteria Matrix

View the video segments on the CD-ROM and use the databases to learn about the three infectious diseases addressed by the proposal. Make notes in the table below about the magnitude of each situation and the effectiveness of each plan.

Proposal Criteria Matrix

Proposal	Criteria	
	What Is the Magnitude of the Situation?*	**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 *Staphylococcus aureus*.		

***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

Review the notes you made on the *Proposal Criteria Matrix*. Place checkmarks in the matrix below to indi cate 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 recom mending that proposal instead of the others.

Proposal Summary Matrix

Proposal	Criteria	
	What Is the Magnitude of the Situation?	**How Effective Is the Plan?**
Proposal 1—AIDS		
Proposal 2—Measles		
Proposal 3—VRSA Infections		

Proposal recommended for funding:

Reasons for recommendation:

Reflection Questions

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

2. What else did you consider in making your decision?