SEVENTH EDITION

INTRODUCTION TO Epidemiology

Ray M. Merrill

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SEVENTH EDITION

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To Beverly, Sara, and Todd.

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PREFACE

The field of epidemiology has come a long way since the days of infectious disease investigations by scientists such as Louis Pasteur, Robert Koch, and John Snow. Historically, the main causes of death were due to a single pathogen, a single cause of disease. Epidemiologists had the challenge of isolating a single bacterium, virus, or parasite. In modern times, advances in nutrition, housing conditions, sanitation, water supply, antibiotics, and immunization programs have resulted in a decrease in various infectious diseases but an increase in many noninfectious diseases and conditions. Consequently, the scope of epidemiology has expanded to include the study of acute and chronic noninfectious diseases and conditions. Advances in biology, medicine, statistics, and social and behavioral sciences have greatly aided epidemiologic study.

This book was written as an introductory epidemiology text for the student who has minimal training in the biomedical sciences and statistics. *Introduction to Epidemiology* is based on the premise that the advanced analyses of empirical research studies, using advanced statistical methods, are more akin to biostatistics than to epidemiology and, therefore, receive less attention in this book. Many recent books bearing the title of epidemiology are in fact biostatistics books, with limited information on the basics of epidemiological investigations or the study of epidemics. Epidemiology is unique from biostatistics in that emphasis is placed on completing the causal picture in human populations. Identifying causal factors and modes of transmission, with the assistance of statistical tools and biomedical information, reflect the primary aim of epidemiology. This book maintains that focus.

Chapter 1 presents the foundations of epidemiology, including definitions, concepts, and applications. Chapter 2 covers historical developments in epidemiology. Chapter 3 looks at several important disease concepts in epidemiology. Chapters 4 through 6 focus on descriptive epidemiology and present several design strategies and statistical measures. Chapter 7 presents design strategies and statistical methods used in analytic epidemiology. Chapter 8 covers design strategies and ethical issues relevant to experimental studies. Chapter 9 considers the basics of causal inference. Chapter 10 focuses on basic concepts and approaches used in field epidemiology. Chapter 11 presents chronic disease epidemiology. Chapter 12 presents epidemiology in clinical settings.

INTRODUCTION

Epidemiology is a fun and challenging subject to study, as well as an interesting field to pursue as a career. Most undergraduate and graduate degree programs in public health, environmental health, occupational health and industrial hygiene, health education and health promotion, health services administration, nursing, and other health-related disciplines require a basic introductory course in epidemiology.

Introduction to Epidemiology covers the fundamentals of epidemiology for students and practitioners. It is hoped that this book will be a useful and practical source of information and direction for students of epidemiology in the classroom and for those practicing epidemiology in the field. Readers of this book may be specialists in international projects in developing countries, industrial hygienists within major industrial plants, infectious disease nurses in hospitals and medical centers, chronic disease epidemiologists in government agencies, behavioral scientists conducting health epidemiological investigations, or staff epidemiologists in local public health departments.

ABOUT THE AUTHOR

Ray M. Merrill, PhD, MPH, received his academic training in statistics and public health. In 1995, he was named a Cancer Prevention Fellow at the National Cancer Institute, where he worked in the Surveillance Modeling and Methods Section of the Applied Research Branch. In 1998, he joined the faculty of the Department of Health Science at Brigham Young University in Provo, Utah, where he has been active in teaching and research. In 2001, he spent a sabbatical working in the Unit of Epidemiology for Cancer Prevention at the International Agency for Research on Cancer Administration in Lyon, France. He has won various awards for his research and is a Fellow of the American College of Epidemiology and of the American Academy of Health Behavior. He is the author of more than 250 peer-reviewed publications, including *Environmental Epidemiology, Reproductive Epidemiology, Principles of Epidemiology Workbook, Fundamentals of Epidemiology and Biostatics, Behavioral Epidemiology,* and *Statistical Methods in Epidemiologic Research* (all with Jones & Bartlett Learning). Dr. Merrill teaches classes in epidemiology and biostatistics and is a full professor in the Department of Health Science, College of Life Sciences, at Brigham Young University.

NEW TO THE *SEVENTH EDITION*

The seventh edition of this classic text, like its previous editions, continues its mission of providing a comprehensive introduction to the field of epidemiology. Emphasis is placed on application of the basic principles of epidemiology according to person, place, and time factors in order to solve current, often unexpected, serious public health problems. Direction is given for how to identify and describe public health problems, formulate research hypotheses, select appropriate research study designs, manage and analyze epidemiologic data, interpret study results, and apply the results in preventing and controlling disease and health-related events. Real-world public health problems involving both infectious and chronic diseases and conditions are presented throughout the text.

Additions to this edition include a greater emphasis on epidemiology in international settings, causality, disease transmission, as well as updated tables, figures, examples, and conclusions throughout the text. News Files are now included in each chapter. A section on modern epidemiology was added, which presents a number of statisticians who helped advance several sound methods of scientific investigation.

This seventh edition offers an easy and effective approach to learning epidemiology, and the case reports (Appendix I) and current News Files represent applications of commonly used research designs in epidemiology. The chapter topics were selected to represent the fundamentals of epidemiology. Learning objectives are presented at the beginning of each chapter, and the chapters are divided into concise sections with several examples. Figures and tables are used to summarize and clarify important concepts and information. Key terms are bolded in the text and defined. A glossary of these terms is included. Study questions are provided at the end of each chapter.

CHAPTER 1

Foundations of Epidemiology

OBJECTIVES

After completing this chapter, you will be able to:

- Define epidemiology.
- Define descriptive epidemiology.
- Define analytic epidemiology.
- Identify selected activities performed in epidemiology.
- Explain the role of epidemiology in public health practice and individual decision making.
- Define epidemic, endemic, and pandemic.
- Describe common source, propagated, and mixed epidemics.
- Describe why a standard case definition and adequate levels of reporting are important in epidemiologic investigations.
- Describe disease transmission concepts.
- Describe the epidemiology triangle for infectious disease.
- Describe selected models for chronic diseases and behavioral disorders.
- Define the three levels of prevention used in public health and epidemiology.
- Understand the basic vocabulary used in epidemiology.

Public health is concerned with threats to the population's health. Important subfields of public health include epidemiology, biostatistics, and health services. Epidemiology is commonly referred to as the foundation of public health because it is a study that aids our understanding of the nature, extent, and cause of public health problems and provides important information for improving the health and social conditions of people. Epidemiology has a population focus in that epidemiologic investigations are concerned with the collective health of a group of individuals who share one or more observable personal or observational characteristic. Geographic, social, family (marriage, divorce), work and labor, and economic factors may characterize populations. In contrast, a clinician is concerned for the health of an individual. The clinician focuses on treating and caring for the patient, whereas the epidemiologist focuses on identifying the source or exposure of disease, disability or death, the number of persons exposed, and the potential for further spread. The clinician treats the patient based on scientific knowledge, experience, and clinical judgment, whereas the epidemiologist uses descriptive and analytical epidemiologic methods to provide information that will ultimately help determine the appropriate public health action to control and prevent the health problem.

Suppose you are experiencing fever, chills, severe aches, and chest discomfort. Is this a common cold or the flu (influenza)? Your physician can quickly distinguish between a cold and the flu and provide the appropriate treatment. In general, the onset of a cold is gradual, but that of the flu is acute. Although a cold is sometimes accompanied by fatigue, aches, and fever, these symptoms are often present with the flu. A sore throat, sneezing, or a stuffy nose are common symptoms with a cold but are rare with the flu. Standard treatment for the flu includes antihistamines, decongestants, nonsteroidal anti-inflammatories, extra rest, and extra fluids. Antibiotics are useless in fighting the flu virus, but antiviral and other medications may be prescribed to improve patient comfort. On a population level, the flu virus is highly infectious, with the potential of affecting all populations; children younger than age 2, adults older than 65, and individuals with chronic health problems or weakened immune systems are most vulnerable to the virus. Annual attack rates for children, as well as estimated number of cases of severe illness and deaths worldwide, are obtained through surveillance methods. Each season flu vaccine contains antigens representing three or four influenza virus strains, and epidemiologists monitor the rate and the effectiveness of the vaccine.

Epidemiology is the study of the distribution and determinants of health-related states or events in human populations and the application of this study to the prevention and control of health problems.[1] The word *epidemiology* is based on the Greek words *epi*, a prefix meaning "on, upon, or befall"; *demos*, a root meaning "the people"; and *logos*, a suffix meaning "the study of." In accordance with medical terminology, the suffix is read first and then the prefix and the root. Thus, the word epidemiology taken literally refers to the study of that which befalls people. As such, epidemiology is commonly referred to as the basic science or foundation of public health.

Epidemiology involves sound methods of scientific investigation. Epidemiologic investigations involve descriptive and analytic methods that draw on statistical techniques for describing data and evaluating hypotheses, biological principles, and causal theory. **Descriptive epidemiology** involves characterization of the distribution of health-related states or events. **Analytic epidemiology** involves finding and quantifying associations, testing hypotheses, and identifying causes of health-related states or events.[2]

The study of the distribution of health-related states or events involves identifying the frequency and pattern of the public health problem among people in the population. Frequency refers to the number of health-related states or events and their relationship to the size of the population. Typically, the number of cases or deaths is more meaningful when considered in reference to the size of the corresponding population, especially when comparing risks of disease among groups. For example, despite differences in population sizes across time or among regions, meaningful comparisons can be made of the burden of HIV/AIDS by using proportions or percentages. In 2008, HIV prevalence was 7.8% in Kenya, 16.9% in South Africa, and 25% in Botswana.[3]

Pattern refers to describing health-related states or events by who is experiencing the health-related state or event (person), where the occurrence of the state or event is highest or lowest (place), and when the state or event occurs most or least (time). In other words, epidemiologists are interested in identifying the people involved and why these people are affected and not others, where the people are affected and why in this place and not others, and when the state or event occurred and why at this time and not others.

For example, in 1981 the Centers for Disease Control and Prevention (CDC) reported that five young men went to three different hospitals in Los Angeles, California, with confirmed *Pneumocystis carinii* pneumonia. These men were all identified as homosexuals.[4] On July 27, 1982, this illness was called AIDS, and in 1983, the Institute Pasteur in France found the human immunodeficiency virus, which causes AIDS.[5]

Identifying the determinants or causes of health-related states or events is a primary function of epidemiology. A **cause** is a specific event, condition, or characteristic that precedes the health outcome and is necessary for its occurrence. An adverse health outcome can be prevented by eliminating the exposure. The presence of a given exposure may be necessary for a specific health outcome to occur, but it alone may not be sufficient to cause the adverse health outcome. For example, a mother's exposure to rubella virus (*Rubivirus*) is necessary for rubella to occur, but exposure to rubella virus is not sufficient to cause rubella because not everyone infected develops the disease.

Identifying causal associations is complex and typically requires making a "judgment" based on the totality of evidence, such as a valid statistical association, time sequence of events, biologic credibility, and consistency among studies. A step toward understanding causation is to identify relevant risk factors. A **risk factor** is a behavior, environmental exposure, or inherent human characteristic that is associated with an important health condition.[6] In other words, a risk factor is a condition that is associated with the increased probability of a health-related state or event. For example, smoking is a risk factor for chronic diseases such as heart disease, stroke, and several cancers (including cancers of the oral cavity and pharynx, esophagus, pancreas, larynx, lung and bronchus, urinary bladder, kidney and renal pelvis, and cervix).[7–10] A risk factor is typically not sufficient to cause a disease; other contributing factors, such as personal susceptibility, are also required before a disease occurs.

The term "health-related states or events" is used in the definition of epidemiology to capture the fact that epidemiology involves more than just the study of disease (e.g., cholera, influenza, and pneumonia); it also includes the study of events (e.g., injury, drug abuse, and suicide) and of behaviors and conditions associated with health (e.g., physical activity, nutrition, seat belt use, and provision and use of health services).

Epidemiology involves the study of the distribution and determinants of health-related states or events in human populations, and also the application of this study to prevent and control health problems. Results of epidemiologic investigations can provide public health officials with information related to who is at greatest risk for disease, where the disease is most common, when the disease occurs most frequently, and what public health programs might be most effective. Such information may lead to more efficient resource allocation and to more appropriate application of health programs designed to educate the public and prevent and control disease. Epidemiologic information can also assist individuals in making informed decisions about their health behavior.

Activities in Epidemiology

An epidemiologist studies the occurrence of disease or other health-related events in specified populations, practices epidemiology, and controls disease.[1] Epidemiologists may be involved in a range of activities, such as:

- Identifying risk factors for disease, injury, and death
- Describing the natural history of disease
- Identifying individuals and populations at greatest risk for disease
- Identifying where the public health problem is greatest
- Monitoring diseases and other health-related events over time
- Evaluating the efficacy and effectiveness of prevention and treatment programs
- Providing information that is useful in health planning and decision making for establishing health programs with appropriate priorities
- Assisting in carrying out public health programs
- Being a resource person
- Communicating public health information

The interdependence of these activities is evident. For example, carrying out an intervention program requires clearance from an institutional review board and often other organizations and agencies. As is also the case for funding agencies, these groups require quantifiable justification of needs and of the likelihood of success. This presupposes that the risk factors are known, that there is an understanding of the natural history of the disease, that there are answers to the questions of person, place, and time, and that there is evidence of the probable success of the intervention. Being a resource person in this process requires a good understanding of the health problem as it relates to the individual and community; the rationale and justification for intervention, along with corresponding goals and objectives; and an ability to communicate in a clear and concise manner.[11] All of this requires a good understanding of epidemiologic methods.

In their professional work, the focus of epidemiologists may be on the environment, social issues, mental health, infectious disease, cancer, reproductive health, and so on. They are employed by the appropriate health agencies at all levels of local, state, and federal government. They find careers in health care organizations, private and voluntary health organizations, hospitals, military organizations, private industry, and academics.

Role of Epidemiology in Public Health Practice

Epidemiologic information plays an important role in meeting public health objectives aimed at promoting physical, mental, and social well-being in the population. These findings contribute to preventing and controlling disease, injury, disability, and death by providing information that leads to informed public health policy and planning as well as to individual health decision making. Some useful information provided to health policy officials and individuals through epidemiology is listed in **TABLE 1-1**.

Public health assessment identifies if, where, and when health problems occur and serves as a guide to public health planning, policy making, and resource allocation. The state of health of the population should be compared with the availability, effectiveness, and efficiency of current health services. Most areas of the United States have surveillance systems that monitor the morbidity and mortality of the community by person, place, and time. Public health surveillance has been defined as the ongoing systematic collection, analysis, interpretation, and dissemination of health data.[12] Surveillance information about disease epidemics, breakdowns in vaccination or prevention programs, and health disparities among special populations is important for initiating and guiding action.

Identifying the determinants (or causes) of health-related states or events is a central aim in epidemiology in order to prevent and control health problems. The connection between human health and physical, chemical, biological, social, and psychosocial factors is based on conclusions about causality. Although we may not be able to prove with certainty that a causal association exists, the totality of evidence can help us make informed decisions.

Table 1-1 Epidemiologic Information Useful for Public Health Policy and Planning and Individual Decision Making

1. Assessment
    - Identify who is at greatest risk for experiencing the public health problem
    - Identify where the public health problem is greatest
    - Identify when the public health problem is greatest
    - Monitor potential exposures over time
    - Monitor intervention-related health outcomes over time
2. Cause
    - Identify the primary agents associated with disease, disorders, or conditions
    - Identify the mode of transmission
    - Combine laboratory evidence with epidemiologic findings
3. Clinical picture
    - Identify who is susceptible to the disease
    - Identify the types of exposures capable of causing the disease
    - Describe the pathologic changes that occur, the stage of subclinical disease, and the expected length of this subclinical phase of the disease
    - Identify the types of symptoms that characterize the disease
    - Identify probable outcomes (recovery, disability, or death) associated with different levels of the disease
4. Evaluate
    - Identify the efficacy of the public health program
    - Measure the effectiveness of the public health program

We know through epidemiologic research that young children, older adults, pregnant women, residents living in nursing homes or long-term care facilities, and individuals with chronic health problems or weakened immune systems are at greatest risk for developing flu-related complications. We also know that there are three types of influenza viruses with subtypes, the symptoms of flu, and that getting a flu vaccine can protect against flu viruses that are the same or related to the viruses in the vaccine.

When evaluating a prevention or control program, both the efficacy and the effectiveness of the program should be considered. Although these terms are related, they have distinct meanings. **Efficacy** refers to the ability of a program to produce a desired effect among those who participate in the program compared with those who do not.[13] **Effectiveness**, on the other hand, refers to the ability of a program to produce benefits among those who are offered the program.[13] For example, suppose a strict dietary intervention program is designed to aid in the recovery process of heart attack patients. If those who comply with the program have much better recoveries than those who do not, the program is efficacious; however, if compliance is low because of the amount, cost, and types of foods involved in the program, for example, the program is not effective. Similarly, a physical activity program involving skiing could be efficacious, but the cost of skiing and the technical skills associated with it may make it ineffective for the general public. Finally, it must be taken into account that the administration of some interventions might require the presence of individuals with advanced medical training and technically advanced equipment. In certain communities, a lack of available health resources may limit the availability of such programs, making them ineffective even though they may be efficacious.

Epidemics, Endemics, and Pandemics

Historically, epidemiology was developed to investigate epidemics of infectious disease. An **epidemic** is the occurrence of cases of an illness, specific health-related behavior, or other health-related events clearly in excess of normal expectancy in a community or region.[1] Public health officials often use the term "outbreak" synonymously with epidemic, but an outbreak actually refers to an epidemic that is confined to a localized area.[6] An epidemic may result from exposure to a common source at a point in time or through intermittent or continuous exposure over days, weeks, or years. An epidemic may also result from exposure propagated through a gradual spread from host to host. It is possible for an epidemic to originate from a common source and then, by secondary spread, be communicated from person to person. The 2014 Ebola epidemic in West Africa gained world recognition as threats of it reaching pandemic levels ensued.

A **pandemic** is an epidemic affecting or attacking the population of an extensive region, country, or continent.[1] **Endemic** refers to the ongoing, usual, or constant presence of a disease in a community or among a group of people; a disease is said to be endemic when it continually prevails in a region.[1] For example, although influenza follows a seasonal trend with the highest number of cases in the winter months, it is considered endemic if the pattern is consistent from year to year.

Several epidemics of cholera have been reported since the early 1800s. In 1816, an epidemic of cholera occurred in Bengal, India, and then became pandemic as it spread across India, extending as far as China and the Caspian Sea before receding in 1826.[14] Other cholera epidemics that also became pandemic involved Europe and North America (1829–1851), Russia (1852–1860), Europe and Africa (1863–1875), Europe and Russia (1899–1923), Indonesia, El Tor, and Bangladesh (India), and the Union of Soviet Socialist Republics (1961–1966).[14] Examples of case reports of cholera, provided by John Snow, along with descriptions of two cholera epidemics investigated by Snow, are presented in Case Study I: Snow on Cholera (**Appendix I**).

In the United States, cholera is now classified as an endemic disease. From 1992 to 1999, the annual numbers of cases reported were 103, 25, 39, 23, 4, 6, 17, and 6, respectively.[15] Other examples of diseases classified now as endemic in the United States include botulism, brucellosis, and plague.

Epidemics are often described by how they spread through the population. Two primary types of infectious-disease epidemics are common-source and propagated epidemics. **Common-source epidemics** arise from a specific source, whereas **propagated epidemics** arise from infections transmitted from one infected person to another. Transmission can occur through direct or indirect routes. Common-source epidemics tend to result in cases occurring more rapidly during the initial phase than do

NEWS FILE

Ebola Virus Disease

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West Africa: The Largest Ebola Outbreak in History

In 2014, many Americans were on high alert due to a small number of cases—four to be exact—of the Ebola virus disease (EVD) reported in the United States. Once it was confirmed that there were no longer any cases of EVD in the United States, the hysteria subsided and thoughts of the virus faded from American minds. Although Ebola had been eradicated in the United States, it continued to have a devastating effect on the people of West Africa, particularly the countries of Sierra Leone, Guinea, and Liberia. The *Zaire ebolavirus,* the species of Ebola virus responsible for this particular outbreak,[2] is infecting and killing people at unprecedented rates, making the West African 2014 Ebola outbreak the largest in the history of the disease.

The Ebola virus disease (family *Filoviridae*, genus *Ebolavirus*), formerly known as Ebola hemorrhagic fever, was first discovered in the Democratic Republic of the Congo near the Ebola River in 1976, and has since been causing periodic outbreaks of Ebola in Africa.[3] In Africa, it is thought that an outbreak starts when a person comes into contact with an infected wild fruit bat or handles bushmeat.[3] The first person to be infected with the virus (the index case or "patient zero") then transmits the disease to other people through person-to-person transmission; this involves direct contact with an infected person's bodily fluids (blood, urine, feces, saliva, vomit, semen, or sweat[3]) and can lead to an outbreak. After a person has been exposed to the virus, the individual will begin to experience Ebola-related symptoms within 2 to 21 days; these symptoms include fever, sore throat, diarrhea, weakness, and muscle pain. As the disease progresses, a person will experience vomiting, abdominal pain, and unexplained hemorrhaging, which results in death.[3] Ebola has an average case fatality rate of 50%, making it one of the deadliest viruses known to man.[1]

The West African Ebola outbreak of 2014 was the worst Ebola outbreak in the history of the virus; as of July 2015, there have been a total of 27,609 people infected and 11,261 deaths due to the Ebola virus in West Africa[3]—more than in all of the past Ebola outbreaks combined. This outbreak was the worst in the virus's history because West Africa possesses ideal conditions for the virus to spread to a large number of people in a short amount of time. The first reason the West African Ebola outbreak was much larger than previous outbreaks in central Africa is because it occurred in a much more populated region of the continent.[2] The outbreak originated in the West African country of Guinea, and quickly spread to neighboring countries, primarily Sierra Leone and Liberia. These countries are home to many large urban areas and cities that are densely populated—conditions that allowed the virus to spread faster and to more people than in rural central Africa. The second factor that contributed to the immense size of the West African outbreak was the locals' traditional burial practice of washing the body of a deceased family member before burial.[2] This practice is of special concern regarding the transmission of the virus because Ebola is most communicable just after an infected person has died, and those who are washing the corpse will undoubtedly contract the disease. The final factor that had a role in this particular outbreak was the meager public health infrastructure in West African countries. There are fewer than 10 doctors per 100,000 people in West Africa[2]—not nearly enough to tend to all those infected with the virus and requiring treatment. The hospitals located in this region are not well equipped to deal with a virus as lethal as the Ebola virus; they do not possess the protective equipment or the sanitation practices needed to control the virus's spread, and they often do not have medications stocked at the hospital, which places the responsibility of finding and funding the medication necessary for treatment on the patient or the patient's family.

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host-to-host epidemics. Identifying the common source of exposure and removing it typically causes the epidemic to abate rapidly. On the other hand, host-to-host epidemics rise and fall more slowly. Some examples of common-source epidemic diseases are anthrax, traced to milk or meat from infected animals; botulism, traced to soil-contaminated food; and cholera, traced to fecal contamination of food and water. Some examples of propagated epidemic diseases are tuberculosis, whooping cough, influenza, and measles.

In some diseases, natural immunity or death can decrease the susceptible population. Resistance to the disease can also occur with treatment or immunization, both of which reduce susceptibility. Disease transmission is usually a result of direct person-to-person contact or of contact with a fomite or vector. Syphilis and other sexually transmitted infections (STIs) are examples of direct transmission. Hepatitis B and HIV/AIDS in needle-sharing drug users are examples of **vehicle-borne transmission**. Malaria spread by mosquitoes is an example of vector-borne transmission.

Some disease outbreaks may have both common-source and propagated epidemic features. A **mixed epidemic** occurs when victims of a common-source epidemic have person-to-person contact with others and spread the disease, resulting in a propagated outbreak. In some cases, it is difficult to determine which came first. During the mid-1980s, at the beginning of the AIDS epidemic in San Francisco, HIV spread rapidly in bathhouses. Homosexual men had sexual contact before entering the bathhouses, yet the bathhouses would be considered the common source aspect of the epidemic, and the person-to-person spread through sexual intercourse would be the source of direct transmission. Direct disease transmission from person-to-person contact occurred in some individuals before and after entering a bathhouse. The bathhouses (the common source) were clearly a point for public health intervention and control, so the bathhouses were closed in an attempt to slow the epidemic.

Case Concepts in Epidemiology

When an epidemic is confirmed and the epidemiology investigation begins, one activity of the epidemiologist is to look for and examine cases of the disease. A **case** is a person in a population who has been identified as having a particular disease, disorder, injury, or condition. A standard set of criteria, or **case definition**, ensures that cases are consistently diagnosed, regardless of where or when they were identified and who diagnosed the case. Higher levels of reporting ensure accurate representation of the health problem; however, even low levels of reporting can provide important information as to the existence and potential problems of a given health state or event. A clinical record of an individual, or someone identified in a screening process, or from a survey of the population or general data registry can also be an epidemiologic case. Thus, the epidemiologic definition of a case is broader than the clinical definition because a variety of criteria can be used to identify cases in epidemiology.

In an epidemic, the first disease case in the population is the **primary case**. The first disease case brought to the attention of the epidemiologist is the **index case**. The index case is not always the primary case. Those persons who become infected and ill after a disease has been introduced into a population and who become infected from contact with the primary case are **secondary cases**. A **suspect case** is an individual (or a group of individuals) who has all of the signs and symptoms of a disease or condition yet has not been diagnosed as having the disease, or has the cause of the symptoms connected to a suspected **pathogen** (i.e., any virus, bacteria, fungus, or parasite).[1] For example, a cholera outbreak could be in progress, and a person could have vomiting and diarrhea, symptoms consistent with cholera. This is a suspect case as the presence of cholera bacteria in the person's body has not been confirmed, and the disease has not been definitely identified as cholera because it could be one of the other gastrointestinal diseases, such as salmonella food poisoning.

Because epidemics occur across time and in different places, each case must be described in exactly the same way each time to standardize disease investigations. As cases occur in each separate epidemic, they must be described and diagnosed consistently—and with the same diagnostic criteria—from case to case. When standard disease diagnosis criteria are used by all the people assisting in outbreak investigations, the epidemiologist can compare the numbers of cases of a disease that occur in one outbreak (numbers of new cases in a certain place and time) with those in different outbreaks of the same disease (cases from different epidemics in different places and times). Computerized laboratory analysis that is now available, even in remote communities, has enhanced the ability of those involved to arrive at a case-specific definition. With advanced computer-assisted support directly and quickly available from the CDC, case definitions of almost all diseases have become extremely accurate and specific.

Different levels of diagnosis (suspect, probable, or confirmed) are generally used by the physician who is assisting in epidemic investigations. As more information (such as laboratory results) becomes available to the physician, the physician generally upgrades the diagnosis. When all criteria are met for the case definition, the case is classified as a confirmed case. If the case definition is not matched, then the exposed person is labeled "not a case," and other possible diseases are considered until the case definition fits. Elaborate diagnoses are not always needed in those epidemics in which obvious symptoms can be quickly seen, such as measles and chicken pox.

If people become ill enough to require hospitalization, the severity of the illness is of concern. **Case severity** is found by looking at several variables that are effective measures of it. One such measure is the average length of stay in a hospital. The longer the hospital stay, the greater the severity of the illness. Subjectively, severity is also measured by how disabling or debilitating the illness is, the chances of recovery, how long the person is ill, and how much care the person needs.[16–19]

The Epidemiology Triangle

When the colonists settled America, they introduced smallpox to the Native Americans. Epidemics became rampant and entire tribes died as a result. In the 1500s, the entire native population of the island of Jamaica died when smallpox was introduced. Poor sanitation and little basic knowledge of disease, low levels of immunity, various modes of transmission, and environmental conditions all allowed such epidemics to run wild and wipe out entire populations. A multitude of epidemiologic circumstances allowed such epidemics to happen. The interrelatedness of four epidemiologic factors often contributed to an outbreak of a disease: (1) the role of the host; (2) the agent or disease-causing organism; (3) the environmental circumstances needed for a disease to thrive, survive, and spread; and (4) time-related issues.

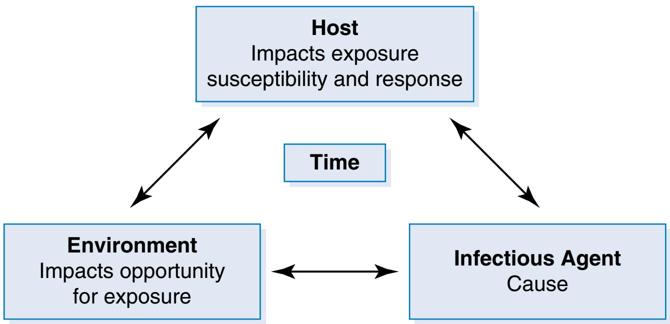

FIGURE 1-1 The triangle of epidemiology.

The traditional triangle of epidemiology is shown in **FIGURE 1-1**. This triangle is based on the infectious disease model and is useful in showing the interaction and interdependence of the agent, host, environment, and time. The **agent** is the cause of the disease; the **host** is a human or an animal that is susceptible to the disease (e.g., health care workers, patients, unvaccinated individuals); the **environment** includes those surroundings and conditions external to the human or animal that cause or allow disease transmission; and **time**, which represents the incubation period, life expectancy of the host or the pathogen, and duration of the course of the illness or condition.

Agents of infectious disease may be bacteria, viruses, parasites, fungi, and molds. A host offers subsistence and lodging for a pathogen and may or may not develop the disease. The level of immunity, genetic makeup, level of exposure, state of health, and overall fitness of the host can determine the effect a disease organism will have on it. Host characteristics include age, sex, race, genetic profile, immune status, occupation, and previous diseases. Environment involves external factors that influence the opportunity for disease exposure or transmission (e.g., temperature, humidity, housing, crowding, neighborhood, sanitation, standing water, or health care setting). The surroundings in which a pathogen lives and the effect the surroundings have on it are a part of the environment. Finally, time includes severity of illness in relation to how long a person is infected or until the condition causes death or passes the threshold of danger toward recovery. Delays in time from infection to when symptoms develop, duration of illness, and threshold of an epidemic in a population are time elements with which the epidemiologist is concerned.

In the epidemiologic triangle model of infectious disease causation, the environment allows the agent and host to interact. For example, the environment may be a watery breeding site conducive to mosquitoes. Mosquitoes are capable of conveying disease-causing organisms to human or animal hosts. A primary mission of epidemiology is to influence the environment that brings together agent and host. One common approach is to spray the watery breeding places (environment) of mosquitoes in an effort to kill the vector of diseases such as malaria, St. Louis encephalitis, and yellow fever.

Some Disease Transmission Concepts

Several disease transmission concepts that relate to or influence the epidemiology triangle are fomites, vectors, reservoirs, and carriers.

A **fomite** is an object such as a piece of clothing, a door handle, or a utensil that can harbor an infectious agent and is capable of being a means of transmission.[1] Fomites are common routes of infection in hospital settings. Routes in which pathogens are passed between people may include a stethoscope, an IV drip tube, or a catheter. Sterilization of these types of objects can help prevent hospital-acquired infections.

A **vector** is an invertebrate animal (e.g., tick, mite, mosquito, bloodsucking fly) that transmits infection by conveying the infectious agent from one host to another.[1] A vector can spread an infectious agent from an infected animal or human to other susceptible animals or humans through its waste products, bite or body fluids, or indirectly through food contamination. A vector does not cause disease itself, but it can be part of the infectious process.

Transmission may be either mechanical (i.e., the agent does not multiply or undergo physiologic changes in the vector) or biological (i.e., the agent undergoes part of its life cycle inside the vector before being transmitted to a new host).

A **reservoir** is the habitat (living or nonliving) in or on which an infectious agent lives, grows, multiplies, and on which it depends for its survival in nature.[1,2] Reservoirs are humans, animals, or certain environmental conditions or substances (e.g., food, feces, decaying organic matter) that are conducive to the growth of pathogens. Two types of human or animal reservoirs are generally recognized: symptomatic (ill) persons who have a disease and carriers who are asymptomatic and can still transmit the disease. As infectious organisms reproduce in the reservoir, they do so in a manner that allows disease to be transmitted to a susceptible host. Humans often serve as both reservoir and host.

Zoonosis is an infectious organism in vertebrate animals (e.g., rabies virus, bacillus anthracis, Ebola virus, influenza virus) that can be transmitted to humans through direct contact, a fomite, or a vector. The World Health Organization states that zoonoses are those diseases and infections that can be naturally transmitted between vertebrate animals and humans.[20] For example, the rabies virus is transmitted from an infected animal (e.g., dog, cat, skunk, raccoon, monkey, bat, coyote, wolf, fox) to a human host through saliva by biting, or through scratches.

A **vehicle** is a nonliving intermediary such as a fomite, food, or water that conveys the infectious agent from its reservoir to a susceptible host.

A **carrier** contains, spreads, or harbors an infectious organism. The infected person (or animal) harboring the disease-producing organism often lacks discernible clinical manifestation of the disease; nevertheless, the person or animal serves as a potential source of infection and disease transmission to other humans (or animals). For example, rodents or coyotes are often carriers of Bubonic plague. Fleas serve as vectors in transmitting this disease to humans. The carrier condition can exist throughout the entire course of a disease if it is not treated, and its presence may not be apparent because the carrier may not be sick (healthy carriers). Some people can even be carriers for their entire lives. An example of this is Mary Mallon (Typhoid Mary), who was an asymptomatic carrier of the pathogen typhoid bacilli. Unfortunately, she worked as a cook, thereby contaminating the food she prepared. She was responsible for 51 cases and 3 deaths. Had she lived in modern times, antibiotics would have been effective treatment for Mary Mallon.[21,22] Tuberculosis is another example of a disease that is commonly known to have carriers.

Carriers have been found to have several different conditions or states. Traditionally, five types of carriers have been identified by the public health and medical fields:

1. **Active carrier**. Individual who has been exposed to and harbors a disease-causing organism (pathogen) and who has done so for some time, even though the person may have recovered from the disease.
2. **Convalescent carrier**. Individual who harbors a pathogen and who, although in the recovery phase of the course of the disease, is still infectious.
3. **Healthy carrier** (also called **passive carriers**). Individual who has been exposed to and harbors a pathogen but has not become ill or shown any of the symptoms of the disease. This could be referred to as a subclinical case.