CHAPTER 1

History and Scope of Epidemiology

LEARNING OBJECTIVES

By the end of this chapter the reader will be able to:

- define the term epidemiology
- define the components of epidemiology (determinants, distribution, morbidity, and mortality)
- name and describe characteristics of the epidemiologic approach
- discuss the importance of Hippocrates' hypothesis and how it differed from the common beliefs of the time
- discuss Graunt's contributions to biostatistics and how they affected modern epidemiology
- explain what is meant by the term natural experiments, and give at least one example

CHAPTER OUTLINE

I. Introduction
II. Epidemiology Defined
III. Foundations of Epidemiology
IV. Historical Antecedents of Epidemiology
V. Recent Applications of Epidemiology
VI. Conclusion
VII. Study Questions and Exercises

Introduction

Controversies and speculations regarding the findings of epidemiologic research are frequent topics of media reports; these findings sometimes arouse public hysteria. Examples of the questions raised by media reports include: "Is it more dangerous to vaccinate an entire population against smallpox (with resulting complications from the vaccine) or to risk infection with the disease itself through a terrorist attack?" "Is Ebola virus a danger to the general public?" "Should I give up eating fatty foods?" "Is it safe to drink coffee or alcoholic beverages?" "Will chemicals in the environment cause cancer?" "Should one purchase bottled water instead of consuming tap water from public drinking supplies?" "Will medications for *chronic diseases* (long-standing illnesses that are difficult to eradicate) such as diabetes cause harmful side effects?" "Will the foods that I purchase in the supermarket make me sick?" "When can we expect the next global pandemic influenza and what shall be the response?"

Consider the 2009–2010 episode of influenza first identified in the United States[1] and eventually called 2009 H1N1 influenza. Ultimately the 2009 H1N1 outbreak threatened to become an alarming pandemic that public health officials feared could mimic the famous 1918 "killer flu." In April 2009, 2 cases of 2009 H1N1 came to the attention of the Centers for Disease Control and Prevention (CDC), which investigates outbreaks of infectious diseases such as influenza. Thereafter, the number of cases expanded rapidly in the United States and then worldwide. When the epidemic eventually subsided during summer 2010, an estimated 60 million cases had occurred in the United States. According to the CDC, people in the age range of 18–64 years were most heavily affected by the virus; less affected were those 65 years of age and older. **Exhibit 1–1** provides an account of the pandemic.

EXHIBIT 1–1

The 2009 H1N1 Pandemic

During spring 2009, a 10-year-old California child was diagnosed with an unusual variety of influenza. Soon afterwards a case of the same flu strain was identified in an 8-year-old who lived approximately 130 miles from the first patient. This was an alarming event

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EXHIBIT 1–1 *continued*

in several respects. The type of influenza virus was usually found among swine. However, the newly identified virus appeared to have been transmitted among humans. Secondly, the appearance of these two unusual cases raised public health officials' suspicions that a deadly flu pandemic similar to the 1918 pandemic might be under way.

Scientists named the new virus 2009 H1N1. The agent was ". . . a unique combination of influenza virus genes never previously identified in either animals or people."[1] The genes of the new virus were closely related to North American swine-lineage H1N1 influenza viruses. Before this outbreak, human-to-human spread of swine-origin influenza viruses was highly unusual. During the previous three years (from December 2005 to January 2009), only 12 U.S. cases of swine influenza had been reported. The vast majority (n = 11) had indicated some contact with pigs. One of the unusual features of infections with the 2009 H1N1 virus were reports of a high prevalence of obesity among influenza-affected patients in intensive care units.

Following the identification of the initial cases in California, swine flu spread across the United States and jumped international borders. In response to a potential widespread epidemic, some schools and public health officials implemented pandemic preparedness plans, which included school closures and social distancing. In June, the World Health Organization (WHO) declared that a global pandemic was under way. Here is a brief chronology of the events that transpired during the pandemic.

- April 15, 2009—first case of pandemic influenza (2009 H1N1) identified in a 10-year-old California patient.
- April 17—eight-year-old child living 130 miles away from first case develops influenza.
- April 21—Centers for Disease Control and Prevention (CDC) began work on a vaccine against the virus.
- April 22—three new cases are identified in San Diego County and Imperial County.
- April 23—two new cases identified in Texas.

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EXHIBIT 1–1 *continued*

- April 23—seven samples from Mexico were positive for 2009 H1N1.
- April 25—WHO declares a "Public Health Emergency of International Concern."
- April 25—cases diagnosed in New York City, Kansas, and Ohio.
- April 29—WHO raises the influenza pandemic alert from phase 4 to phase 5.
- May 6—CDC recommends prioritized testing and antiviral treatment for people at high risk of complications from flu.
- June 11—WHO raises the worldwide pandemic alert level to phase 6 and declares the global pandemic is under way.
- June 11—more than 70 countries have reported cases of pandemic influenza.
- June through July—the number of countries reporting influenza has nearly doubled; all 50 states in the U.S. have reported cases.
- Summer and fall—extraordinary influenza-like illness activity reported in the U.S.
- September 30—initial supplies of 2009 H1N1 vaccine distributed on a limited basis.
- December—vaccine made available to all who wanted it.
- Summer 2010—flu activity reaches normal summer time levels in the U.S.

According to the CDC approximately 60 million people became infected with 2009 H1N1 between April 2009 and March 13, 2010. The estimated range of the number of cases was between 43 million and 88 million. The process of estimating the number of flu cases is imprecise because many patients who become ill do not seek medical care, and those who do are not tested for the virus. **Figure 1–1** reports CDC estimates of 2009 H1N1 cases in the US by age group. ■

Source: Data from Centers for Disease Control and Prevention. The 2009 H1N1pandemic: summary highlights, April 2009—April 2010. Available at: http://www.cdc.gov/h1n1flu/cdcresponse.htm. Accessed July 19, 2012.

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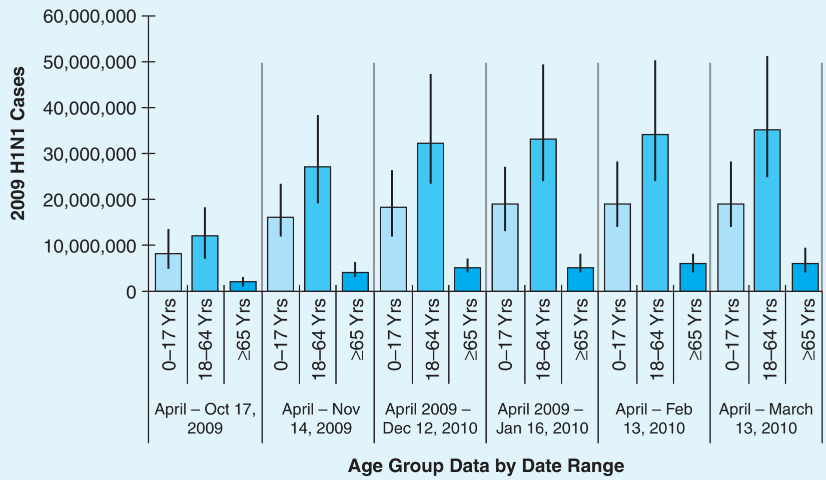

FIGURE 1–1 CDC estimates of 2009 H1N1 cases in the United States by age group. *Source:* Reproduced from Centers for Disease Control and Prevention. The CDC Estimates of 2009 H1N1 Influenza Cases, Hospitalizations and Deaths in the United States, April 2009–March 13, 2010. Available at: http://www.cdc.gov/h1n1flu/estimates/April_March_13.htm. Accessed August 23, 2012.

Another example of a disease that elicited public hysteria was the outbreak of *Escherichia coli* (*E. coli*) infections during late summer and fall 2006. The outbreak affected multiple states in the United States and captured media headlines for several months. Known as *E. coli* O157:H7, this bacterial agent can be ingested in contaminated food. The agent is an enteric pathogen, which can produce bloody diarrhea, and in some instances, the hemolytic-uremic syndrome (HUS), a type of kidney failure. Severe cases of *E. coli* O157:H7 can be fatal.

The 2006 outbreak was a mysterious event that gradually unfolded over time. The outbreak sickened 199 persons across United States and caused 3 deaths (as of October 6, 2006, when the outbreak appeared to have subsided). **Figure 1–2** shows the affected states. The 2006 outbreak caused 102 (51%) of the ill persons to be hospitalized; in all, 31 patients (16%) were afflicted with HUS. The majority of cases (141, 71%) were female. A total of 22 children 5 years of age and younger were affected.[2]

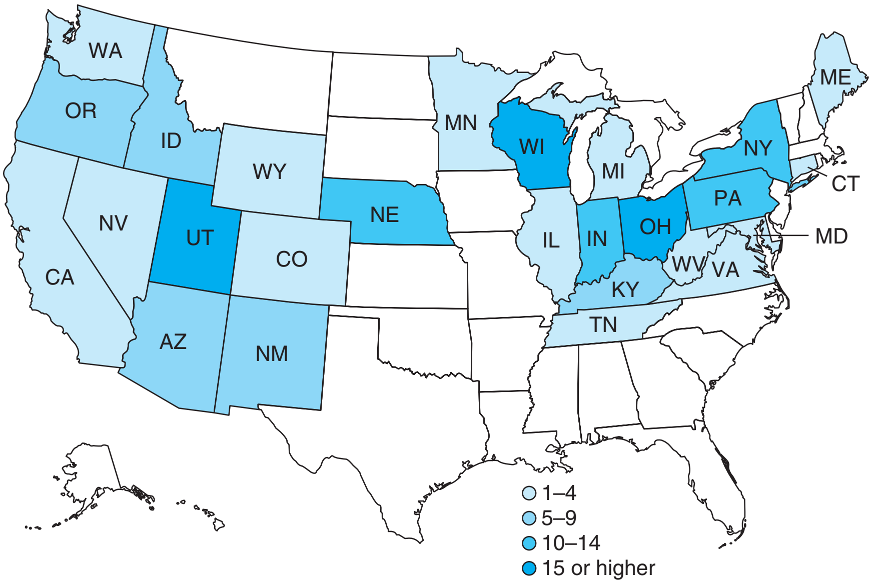

FIGURE 1–2 Distribution of *Escherichia coli* serotype O157:H7 cases across the United States, September 2006. *Source:* Reproduced from Centers for Disease Control and Prevention. Ongoing multistate outbreak of *Escherichia coli* serotype O157:H7 infections associated with consumption of fresh spinach—United States, September 2006. MMWR. 2006;55:1045–1046.

Tracking down the mysterious origins of the outbreak required extensive detective work. The outbreak was linked to prepackaged spinach as the most likely vehicle. Investigators traced the spinach back to its source, Natural Selection Foods near Salinas, California. The producer announced a recall of spinach on September 15, 2006.[3] The FDA and State of California conducted a traceback investigation, which implicated four ranches in Monterey and San Benito Counties. Cattle feces from one of the four ranches contained a strain of *E. coli* O157:H7 that matched the strain that had contaminated the spinach and also matched the strain found in the 199 cases.[4] The mechanism for contamination of the spinach with *E. coli* bacteria was never established definitively.

Noteworthy is the fact that subsequent to this major outbreak, *E. coli* O157:H7 continues to threaten the food supply of the United States, not only from spinach but also from other foods.[5] During November and December 2006, Taco Bell restaurants in the northeastern United States experienced a major outbreak that caused at least 71 persons to fall ill. Contamination of Topp's brand frozen ground beef patties and Totino's or Jeno's brand frozen pizzas with *E. coli* O157:H7 is believed to have sickened more than 60 residents of the eastern half of the United States during summer and early fall 2007. In 2008 and 2009, *E. coli* outbreaks were associated with ground beef and prepackaged cookie dough. Ground beef, cheese, romaine lettuce, bologna, and hazelnuts caused outbreaks during 2010 and 2011. A major outbreak of *E. coli* O104 occurred in Germany in 2011; 6 travelers from the United States were made ill, with one of the six dying. During summer 2012, a multistate outbreak caused by *E. coli* O145 sickened 18 persons and caused 9 deaths.

In summary, the 2009 H1N1 flu pandemic (Exhibit 1–1) and the *E. coli* spinach-associated outbreak illustrate that epidemiologic research methods are a powerful tool for studying the health of populations. In many instances, epidemiology resembles detective work, because the causes of disease occurrence are often unknown. Both examples raise several issues that are typical of many epidemiologic research studies:

- When there is a linkage or association between a factor (i.e., contaminants in food and water; animal reservoirs for disease agents) and a health outcome, does this observation mean that the factor is a cause of disease?
- If there is an association, how does the occurrence of disease vary according to the demographic characteristics and geographic locations of the affected persons?
- Based on the observation of such an association, what practical steps should individuals and public health departments take? What should the individual consumer do?
- Do the findings from an epidemiologic study merit panic or a measured response?
- How applicable are the findings to settings other than the one in which the research was conducted? What are the policy implications of the findings?

In this chapter we answer the foregoing questions. We discuss the stages that are necessary to unravel mysteries about diseases, such as those due to environmental exposures or those for which the cause is entirely unknown.

Epidemiology is a discipline that describes, quantifies, postulates causal mechanisms for diseases in populations, and develops methods for the control of diseases. Using the results of epidemiologic studies, public health practitioners are aided in their quest to control health problems such as foodborne disease outbreaks and influenza pandemics. The investigation into the spinach-associated *E. coli* outbreak illustrates some of the classic methods of epidemiology; first, describing all of the cases, enumerating them, and then following up with additional studies. Extensive detective work was involved in identifying the cause of the outbreak. The hypothesized causal mechanism that was ultimately linked to contaminated spinach was the bacterium *E. coli*. All of the features described in the investigation are hallmarks of the epidemiologic approach. In this example, the means by which *E. coli* contaminated the spinach remains an unresolved issue.

The 2009 H1N1 pandemic demonstrated the use of epidemiologic data to identify the source of the initial outbreaks, describe pandemic spread, and mount a public health response to control a pandemic. Officials created public awareness of the need to be vaccinated against the virus and to prevent spread of the virus by covering up one's mouth when coughing and washing one's hands frequently.

Epidemiology Defined

The word *epidemiology* derives from *epidemic*, a term that provides an immediate clue to its subject matter. Epidemiology originates from the Greek words *epi* (upon) + *demos* (people) + *logy* (study of). Although some conceptions of epidemiology are quite narrow, we suggest a broadened scope and propose the following definition:

> Epidemiology is concerned with the occurrence, distribution, and determinants of "health-related states or events"[6] (e.g., health and diseases, morbidity, injuries, disability, and mortality in populations). Epidemiologic studies are applied to the control of health problems in populations. The key aspects of this definition are determinants, distribution, population, and health phenomena (e.g., morbidity and mortality).

Determinants

Determinants are factors or events that are capable of bringing about a change in health. Some examples are specific biologic agents (e.g., bacteria) that are associated with infectious diseases or chemical agents that may act as carcinogens. Other potential determinants for changes in health may include less specific factors, such as stress or adverse lifestyle patterns (lack of exercise or a diet

Case 1: Intentional Dissemination of Bacteria That Cause Anthrax

After the United States experienced its worst terrorist attack on September 11, 2001, reports appeared in the media about cases of anthrax in Florida beginning in early October. In the United States, anthrax usually affects herbivores (livestock and some wild animals);

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CASE 1 *continued*

human cases are unusual. Anthrax is an acute bacterial disease caused by exposure to *Bacillus anthracis*. Cutaneous anthrax affects the skin, producing lesions that develop into a black scab. Untreated cutaneous anthrax has a case-fatality rate of 5–20%. The much more severe inhalational form, which affects the lungs and later becomes disseminated by the bloodstream, has a high case fatality rate.[7] Observations of an alert infectious disease specialist along with the support of laboratory staff led to the suspicion that anthrax had been deliberately sent through the postal system.[8] The CDC, in collaboration with officials at the state and local levels, identified a total of 21 anthrax cases (16 confirmed and 5 suspected) as of October 31, 2001. The majority of the cases occurred among employees located in four areas: Florida, New York City, New Jersey, and the District of Columbia.[9–12] **Figure 1–3** portrays the distribution of the 21 cases in 4 geographic areas of the United States.

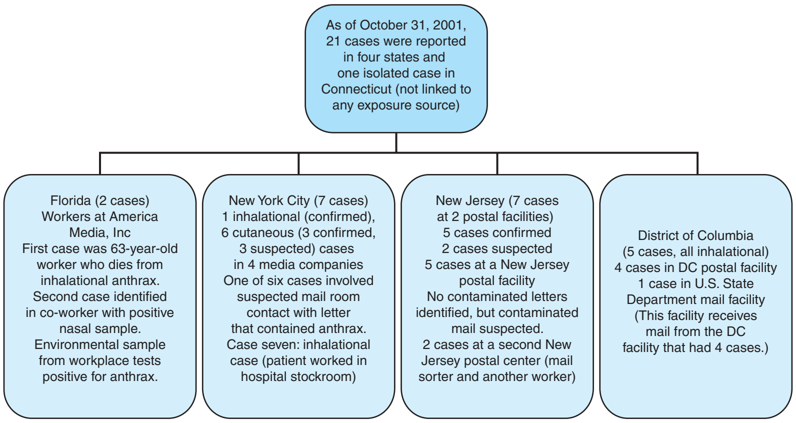

FIGURE 1–3 Occurrence of anthrax cases during the 2001 terrorist incident according to the investigation by the Centers for Disease Control and Prevention.

high in saturated fats). The following four vignettes illustrate the concern of epidemiology with disease determinants. For example, consider the steps taken to track down the source of the bacteria that caused anthrax and were sent through the mail; contemplate the position of an epidemiologist once again. Imagine a possible scenario for describing, quantifying, and identifying the determinants for each of the vignettes.

Case 2: Outbreak of Fear

When a 36-year-old lab technician known as Kinfumu checked into the general hospital in Kikwit, Zaire, complaining of diarrhea and a fever, anyone could have mistaken his illness for the dysentery that was plaguing the city. Nurses, doctors, and nuns did what they could to help the young man. They soon saw that his disease wasn't just dysentery. Blood began oozing from every orifice in his body. Within 4 days he was dead. By then the illness had all but liquefied his internal organs.

That was just the beginning. The day Kinfumu died, a nurse and a nun who had cared for him fell ill. The nun was evacuated to another town 70 miles to the west where she died—but not until the contagion had spread to at least three of her fellow nuns. Two subsequently died. In Kikwit, the disease raged through the ranks of the hospital's staff. Inhabitants of the city began fleeing to neighboring villages. Some of the fugitives carried the deadly illness with them. Terrified health officials in Kikwit sent an urgent message to the World Health Organization. The Geneva-based group summoned expert help from around the globe: a team of experienced virus hunters composed of tropical-medicine specialists, microbiologists, and other researchers. They grabbed their lab equipment and their bubble suits and clambered aboard transport planes headed for Kikwit.[13] ■

Case 3: Fear on Seventh Avenue

On normal workdays, the streets of New York City's garment district are lively canyons bustling with honking trucks, scurrying buyers, and sweating rack boys pushing carts loaded with suits, coats, and dresses. But during September 1978 a tense new atmosphere was evident. Sanitation trucks cruised the side streets off Seventh Avenue flushing pools of stagnant water from the gutters and spraying out disinfectant. Teams of health officers drained water towers on building roofs. Air conditioners fell silent for inspection, and several chilling signs appeared on 35th Street: "The New York City Department of Health has been advised of

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CASE 3 *continued*

possible cases of Legionnaires' disease in this building." By the weekend, there were 6 cases of the mysterious disease, 73 more suspected, and 2 deaths. In the New York City outbreak, three brothers were the first victims. Carlisle, Gilbert, and Joseph Leggette developed the fever, muscle aches, and chest congestion that make the disease resemble pneumonia. Joseph and Gilbert recovered; Carlisle did not. "He just got sick and about a week later he was dead," said John Leggette, a fourth brother who warily returned to his own job in the garment district the next week. "I'm scared," he said. "But what can you do?"[14] ■

Case 4: Red Spots on Airline Flight Attendants

From January 1 to March 10, 1980, Eastern Airlines received 190 reports of episodes of red spots appearing on the skin of flight attendants (FAs) during various flights. Complaints of symptoms accompanying the spots were rare, but some FAs expressed concern that the spots were caused by bleeding through the skin and might indicate a serious health hazard. On March 12, investigators from the CDC traveled to Miami to assist in the investigation. No evidence of damage to underlying skin was noted on these examinations, nor was any noted by consultant dermatologists who examined affected FAs after the spots had disappeared. Chemical tests on clinical specimens for the presence of blood were negative. Airline personnel had investigated the ventilation systems, cleaning materials and procedures, and other environmental factors on affected aircraft. Airflow patterns and cabin temperatures, pressures, and relative humidity were found to be normal. Cleaning materials and routines had been changed, but cases continued to occur. Written reports by FAs of 132 cases occurring in January and February showed that 91 different FAs had been affected, 68 once and 23 several times. Of these cases, 119 (90%) had occurred on a single type of aircraft. Of the 119 cases from implicated aircraft, 96% occurred on north- or southbound flights between the New York City and Miami metropolitan areas, flights that are partially over water. Only rarely was a case reported from the same airplane when flying transcontinental or other east-west routes.[15] ■

Solution to Case 4: Red Spots

The investigation then concentrated on defining the clinical picture more clearly. An Eastern Airlines (EAL) physician, a consultant dermatologist, and a physician from the National Institute for Occupational Safety and Health (NIOSH) rode on implicated flights on March 14 and examined three new cases considered by the EAL physician and other flight attendants (FAs) to be typical cases. Although the spots observed consisted of red liquid, they did not resemble blood. To identify potential environmental sources of red-colored material, investigators observed the standard activities of FAs on board implicated flights. At the beginning of each flight FAs routinely demonstrated the use of life vests, required in emergency landings over water. Because the vests used for demonstration were not actually functional, they were marked in bright red ink with the words "Demo Only." When the vests were demonstrated, the red ink areas came into close contact with the face, neck, and hands of the demonstrator. Noting that on some vests the red ink rubbed or flaked off easily, investigators used red material from the vests to elicit the typical clinical picture on themselves. On preliminary chemical analyses, material in clinical specimens of red spots obtained from cases was found to match red-ink specimens from demonstration vests. On March 15 and 16, EAL removed all demonstration model life vests from all its aircraft and instructed FAs to use the standard, functional, passenger-model vests for demonstration purposes. The airline . . . continue[d] to request reports of cases to verify the effectiveness of this action. Although all demonstration vests were obtained from the same manufacturer, the vests removed from specific aircraft were noted to vary somewhat in the color of fabric and in the color and texture of red ink, suggesting that many different production lots may have been in use simultaneously on any given aircraft.[15] ■

Health departments, the CDC in Atlanta, and epidemiologic researchers frequently confront a problem that has no clear determinants or etiologic basis. The methods and findings of epidemiologic studies may direct one to, or suggest, particular causal mechanisms underlying health-related events or conditions, such as the four examples cited in the vignettes: anthrax, the suspected outbreak of Ebola virus, Legionnaires' disease, and red spots on airline flight attendants. Read the solution to Case 4 to clear up the mystery of Case 4.

Distribution

Frequency of disease occurrence and mortality rates vary from one population group to another in the United States. For example, in 2006 death rates from coronary heart disease (CHD) and stroke were higher among African-Americans (blacks) than among American Indians/Alaskan natives, Asian/Pacific islanders, or whites.[16] In comparison with other racial/ethnic groups, Hispanics have lower mortality rates for CHD than non-Hispanics.[16,17] Such variations in disease frequency illustrate how disease may have different *distributions* depending upon the underlying characteristics of the populations being studied. Population subgroups that have higher occurrence of adverse health outcomes are defined as having health disparities, which need to be targeted for appropriate interventions.

Population

Epidemiology examines disease occurrence among population groups rather than among individuals. Lilienfeld[18] noted that this focus is a widely accepted feature of epidemiology. For this reason, epidemiology is often referred to as "population medicine." As a result, the epidemiologic and clinical descriptions of a disease are quite different. Sometimes, when a new disease is first recognized, clinical descriptions of the condition are the first data available. These initial clinical descriptions can lead to subsequent epidemiologic investigations.

Note the different descriptions of toxic shock syndrome (TSS), a condition that showed sharp increases during 1980 in comparison with the immediately previous years. TSS is a severe illness that in the 1980 outbreak was found to be associated with vaginal tampon use. The clinical description of TSS would include specific signs and symptoms, such as high fever, headache, malaise, and other more dramatic symptoms, such as vomiting and profuse watery diarrhea. The epidemiologic description would indicate which age groups would be most likely to be affected, time trends, geographic trends, and other variables that affect the distribution of TSS.

A second example is myocardial infarction (MI; heart attack). A clinical description of MI would list specific signs and symptoms, such as chest pain, heart rate, nausea, and other individual characteristics of the patient. The epidemiologic description of the same condition would indicate which age groups would be most likely to be affected, seasonal trends in heart attack rates, geographic variations in frequency, and other characteristics of persons associated with the frequency of heart attack in populations.

Referring again to the vignettes, one may note that the problem that plagued Kinfumu in Case 2 was recognized as a particularly acute problem for epidemiology when similar complaints from other patients were discovered and the disease began to spread. If more than one person complains about a health problem, the health provider may develop the suspicion that some widespread exposure rather than something unique to an individual is occurring. The clinical observation might suggest further epidemiologic investigation of the problem.

Health Phenomena

As indicated in the definition, epidemiology is used to investigate many different kinds of health outcomes. These range from infectious diseases to chronic diseases and various states of health, such as disability, injury, limitation of activity, and mortality.[19] Other health outcomes have included individuals' positive functioning and active life expectancy as well as adverse health-related events, including mental disorders, suicide, substance abuse, and injury. Epidemiology's concern with positive states of health is illustrated by research into active life expectancy among geriatric populations. This research seeks to determine the factors associated with optimal mental and physical functioning as well as enhanced quality of life and ultimately aims to limit disability in later life.

Morbidity and Mortality

Two other terms central to epidemiology are *morbidity* and *mortality*. The former, morbidity, designates illness, whereas the latter, mortality, refers to death. Note that most measures of morbidity and mortality are defined for specific types of morbidity or causes of death.

Aims and Levels

The preceding sections hinted at the complete scope of epidemiology. As the basic method of public health, epidemiology is concerned with efforts to describe, explain, predict, and control. The term *levels* denotes the hierarchy of tasks that epidemiologic studies seek to accomplish (e.g., description of the occurrence of diseases is a less-demanding task and therefore ranks lower on the hierarchy of levels than explaining the causes of a disease and predicting and controlling them). More information will be provided later in the chapter.

- To *describe* the health status of populations means to enumerate the cases of disease, to obtain relative frequencies of the disease within subgroups, and to discover important trends in the occurrence of disease.
- To *explain* the etiology of disease means to discover causal factors as well as to determine modes of transmission.
- To *predict* the occurrence of disease is to estimate the actual number of cases that will develop as well as to identify the distribution within populations.

Such information is crucial to planning interventions and allocation of healthcare resources.

- To *control* the distribution of disease, the epidemiologic approach is used to prevent the occurrence of new cases of disease, to eradicate existing cases, and to prolong the lives of those with the disease.

The implication of these aims is that epidemiology has two different goals: one related to the distribution of health outcomes and the second to controlling diseases. The first goal is to achieve an improved understanding of the natural history of disease and the factors that influence its distribution. With the knowledge that is obtained from such efforts, one can then proceed to accomplish the second goal, which is control of disease via carefully designed interventions.

Foundations of Epidemiology

Epidemiology Is Interdisciplinary

Refer to **Figure 1–4**, which characterizes the interdisciplinary foundations of epidemiology. As an interdisciplinary field, epidemiology draws from biostatistics and the social and behavioral sciences as well as from the medically related fields such as toxicology, pathology, virology, genetics, microbiology, and clinical medicine. Terris[20] pointed out that epidemiology is an extraordinarily rich and complex science that derives techniques and methodologies from many disciplines. He wrote that epidemiology "must draw upon and synthesize knowledge from the biological sciences of man and of his parasites, from the numerous sciences of the physical environment, and from the sciences concerned with human society."[20(p 203)]

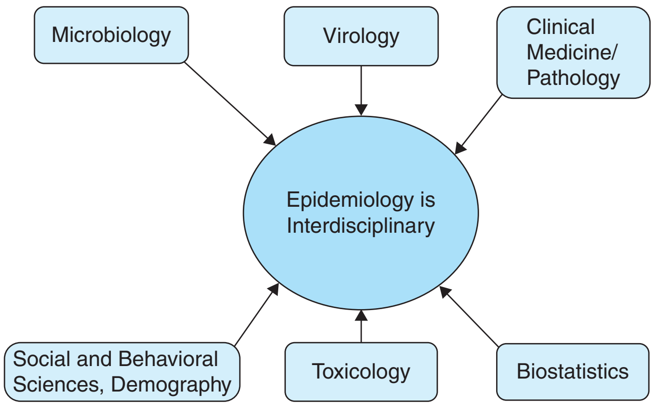

FIGURE 1–4 The interdisciplinary foundations of epidemiology.

Here are some illustrations of the contributions of other disciplines to epidemiology. Microbiology, the science of microorganisms, yields information about specific disease agents, including their morphology and modes of transmission. Related fields are bacteriology and virology. The previously discussed investigations of anthrax, Legionnaires' disease, and TSS utilized microbiologic techniques to identify possible infectious agents. Another example is epidemiologic studies of foodborne illnesses (e.g., *E. coli*); these studies apply microbiologic procedures to reveal the commonalities of bacteria involved in an outbreak in order to define whether it was caused by a common source.

Clinical medicine is involved in the diagnosis of the patient's state of health, particularly when defining whether the patient has a specific disease or condition. A pathologist's expertise may help differentiate between normal and diseased tissue. From our previous examples, clinical medicine diagnosed the individuals' symptoms or signs of ill health. Astute physicians and nurses may suggest epidemiologic research on the basis of clinical observations.

Toxicology, the science of poisons, is concerned with the presence and health effects of chemical agents, particularly those found in the environment and the workplace. A crucial issue for the United States is the fate of hazardous chemicals once they have performed their function. In the past, numerous toxic chemicals (e.g., pesticides) were deposited in an unsafe manner into waste sites that were later designated as hazardous. Toxicologic knowledge helps determine the presence of noxious chemical agents in hazardous waste sites and whether any health effects observed are consistent with the known effects of exposure to toxic agents. When responses to exogenous agents vary from person to person, geneticists may become part of the research team via the disciplines of molecular and genetic epidemiology. Frequently, toxicologists and epidemiologists collaborate in environmental and occupational investigations.

Social and behavioral sciences elucidate the role of race, social class, education, cultural group membership, and behavioral practices in health-related phenomena. Social and behavioral science disciplines, that is, sociology and psychology, are devoted respectively to the development of social theory and the study of behavior. The special concern of social epidemiologic approaches is the study of social conditions and disease processes.[21] Furthermore, the social sciences provide a great deal of the methodology on sampling; measurement; questionnaire development, design, and delivery; and group comparisons. Increasingly, community interventions have drawn upon the fund of knowledge from the social sciences. *Demography* is the study of data related to the structure of human populations.

Finally, the field of biostatistics is critical to the evaluation of epidemiologic data, especially when one is trying to separate chance from meaningful observations. Epidemiology profits from the interdisciplinary approach because the causality of a particular disease in a population may involve the interaction of multiple factors. The contributions of many disciplines help unravel the factors associated with a particular disease.

Methods and Procedures

The empirical dimensions of epidemiologic studies require quantification of relevant factors. Quantification refers to the translation of qualitative impressions into numbers. Qualitative sources of information about disease may be, for example, a physician's observations derived through medical practice about the types of people among whom a disease seems to be common. Epidemiologists enumerate cases of disease to objectify subjective impressions; the standard epidemiologic measures often require counting the number of cases of disease and examining their distribution according to demographic variables, such as age, sex, race, and other variables as well as exposure category and clinical features. The following quotation

The Language of Quantification: Severe Acute Respiratory Syndrome (SARS) in the United States

As of March 26, [2003] CDC has received 51 reports of suspected SARS cases from 21 states . . . identified using the CDC updated interim case definition . . . The first suspected case was identified on March 15, in a man aged 53 years who traveled to Singapore and became ill on March 10. Four clusters of suspected cases have been identified, three of which involved a traveler who had visited Southeast Asia (including Guangdong province, Hong Kong, or Vietnam) and a single family contact. One of these clusters involved suspected cases in patients L and M . . . who had stayed together at hotel M during March 1–6, when other hotel guests were symptomatic. Patient L became sick on March 13 after returning to the United States. His wife, patient M, became ill several days after the onset of her husband's symptoms, suggesting secondary transmission.

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Three patients in the United States with suspected SARS (patients I, L, and M) reported staying at hotel M when other persons staying in the hotel were symptomatic. The fourth cluster began with a suspected case in a person who traveled in Guangdong province and Hong Kong. Two [healthcare workers] subsequently became ill at the U.S. hospital where this patient was admitted.[22(p 244)] ■

illustrates a summary of the characteristics of 51 suspected cases of severe acute respiratory syndrome (SARS) that were reported to the CDC as of early 2003.

Sometimes epidemiologists present quantified information as tables, maps, charts, and graphs. Both charts and graphs are pictorial illustrations of the frequency of disease. (Refer to the later section on John Snow for an example of a map.) Quantification facilitates the epidemiologic investigation of the sources of variation of a disease by the characteristics of time, place, and person: When did the case occur? Where was it located? Who was affected?

Key methods for the graphic presentation of data are the use of pie charts, bar graphs, and line graphs. **Figure 1–5** shows an example of each type: a pie chart (A, admission diagnoses of discharged hospice care patients); a bar graph (B, diabetes prevalence among adults); and a line graph (C, obesity among children). Epidemiologists use these types of graphs to describe characteristics of data, such as subgroup differences and time trends.[23]

Use of Special Vocabulary

Epidemiology employs a unique vocabulary of terms to describe the frequency of occurrence of disease. Examples from this vocabulary are the words epidemic and pandemic.

Dorland's Illustrated Medical Dictionary defines the word *epidemic* as "attacking many people at the same time, widely diffused and rapidly spreading." More precisely, an epidemic refers to an excessive occurrence of a disease: "Most current definitions [of epidemic] stress the concept of excessive prevalence as its basic implication in both lay and professional usage."[24(p 2)] The following passage illustrates this notion by defining an epidemic as:

> The occurrence, in a defined community or region, of cases of an illness (or an outbreak) with a frequency clearly in excess of normal expectancy. The number of cases indicating presence of an epidemic varies according to the infectious agent, size and type of population exposed, previous experience or lack of exposure to the disease, and time and place of occurrence; epidemicity is thus relative to usual frequency of the disease . . .[25(p 705)]

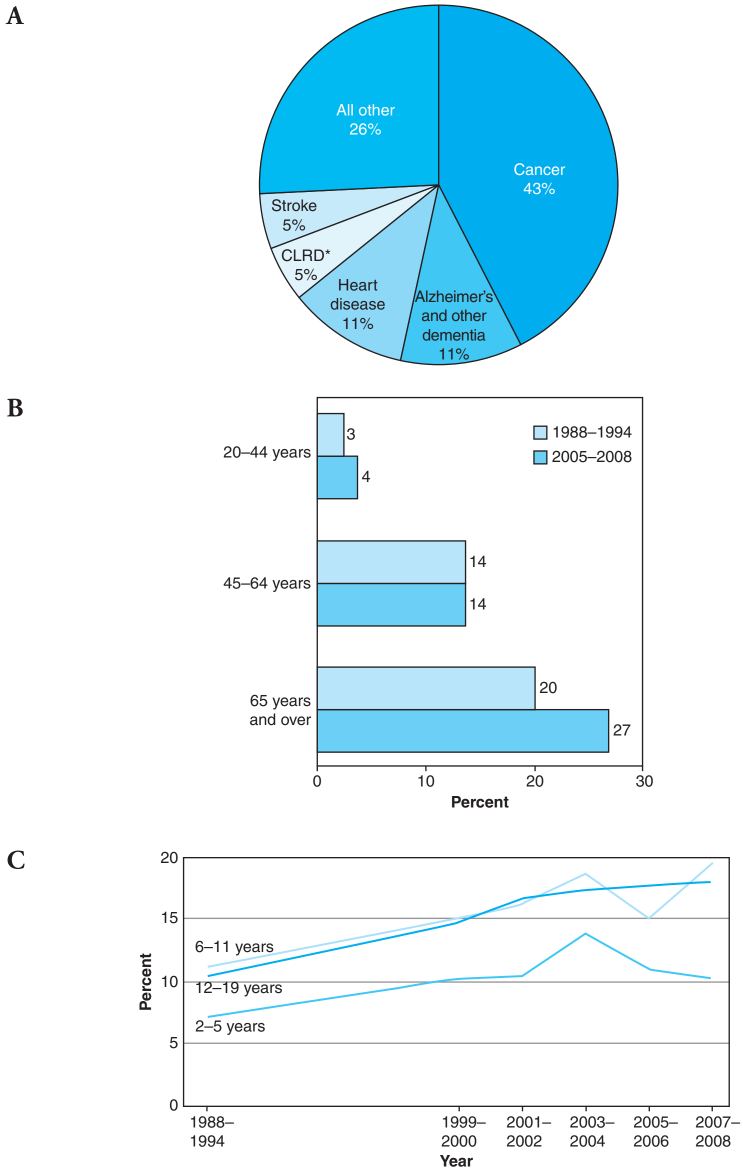


FIGURE 1–5 Examples of three different presentations of epidemiologic data. (A) Pie chart. Primary admission diagnoses of discharged hospice care patients: United States, 2007 (B) Bar graph. Diabetes prevalence among adults 20 years of age and over, by age: United States, 1988–1994 and 2005–2008. (C) Line graph. Obesity among children, by age: United States, 1988–1994 through 2007–2008. *Source:* Adapted and Reprinted from National Center for Health Statistics. Health, United States, 2010: with Special Feature on Death and Dying. Hyattsville, MD, 2011.

*Chronic lower respiratory disease.

The "usual frequency" means the disease's typical occurrence at the same time, within the same population, and in the same geographic area. Further, when a communicable disease has disappeared and a single case reappears, that event represents an epidemic. Also, the occurrence of two cases of a new disease ("first invasion") linked in time and place may be considered to be an epidemic, as this happening suggests disease transmission.

Explanation of Key Terms Used in the Definition of "Epidemic"

Communicable disease—An illness caused by an infectious agent that can be transmitted from one person to another.
Infectious disease—A synonym for a communicable disease.
Outbreak—A localized disease epidemic (e.g., in a town or healthcare facility). ■

In current thinking, an epidemic is not confined to infectious diseases. Take, for example, the Love Canal incident that generated spirited public debate and media attention during the late 1970s. Love Canal was a toxic waste disposal site located in Niagara Falls, New York. It was the destination for burial of thousands of chemical-filled drums deposited by the Hooker Chemicals & Plastics Corporation. Eventually, the waste disposal site was covered and converted into a housing tract. Subsequently, residents of the area reported several different types of health effects, including miscarriages, birth defects, and impaired cognitive functioning. The Love Canal site was the focus of extensive health effects studies and epidemiologic research. The threat posed by Love Canal and other hazardous waste sites led to the creation of the Superfund in 1980. Its purpose was to promote the cleanup of hazardous wastes.

By referring to the case studies reported in this text, you have seen additional examples—red spots among airline FAs and TSS—that illustrate two instances in which epidemiologic methodology was employed to study noninfectious conditions. TSS and red spots among airline FAs both represented apparent epidemics because the usual or expected rate was nil. Epidemiologic methods also are used to investigate occupationally associated illness (e.g., brown lung disease among textile workers and asbestosis among shipyard workers), environmental health hazards (e.g., toxic chemicals and air pollution), and conditions associated with lifestyle (e.g., unintentional injuries, ischemic heart disease, and certain forms of cancer).

Related to the term epidemic is the term *pandemic*, which refers to an epidemic on a worldwide scale; during a pandemic, large numbers of persons may be affected and a disease may cross international borders. Examples are flu pandemics, such as the pandemic of 1918 and more recent flu pandemics that occur periodically. The term endemic is used to characterize a disease that is habitually present in a particular geographical region. To illustrate, malaria is endemic to some tropical areas of Asia, and cholera is endemic to less developed countries where sanitation is lacking. Previously, during the 19th century, cholera was endemic to Western countries, such as England and the United States. However, cholera is no longer endemic to these two countries because of the introduction of sanitation and other public health measures.

Methods for Ascertainment of Epidemic Frequency of Disease

The CDC and vital statistics departments of state and local governments gather surveillance data on a continuing basis to determine whether an epidemic is taking place. The word *surveillance* denotes the systematic collection of data pertaining to the occurrence of specific diseases, the analysis and interpretation of these data, and the dissemination of consolidated and processed information to contributors to the surveillance program and other interested persons. Common surveillance activities include monitoring foodborne disease outbreaks, collecting information on communicable and infectious diseases, and tracking influenza.

As noted previously, an epidemic refers to the occurrence of disease in excess of normal expectancy. In order to ascertain epidemic trends, one must have data about the usual occurrence of a disease. Providing such information is the function of surveillance. For example, suppose a health practitioner states that 500 CHD deaths were reported in an upstate New York community during a particular year and that an epidemic is taking place. This information by itself would be insufficient to justify the assertion that an epidemic of CHD deaths has occurred. The usual frequency of CHD deaths would need to be determined via ongoing surveillance programs in the same community at some prior time. In addition, the size, age, and sex distribution of the population would need to be known. With this information at hand, one could determine whether or not an epidemic of CHD deaths has occurred.

A second example of determining epidemic frequency is shown in **Figure 1–6** for influenza and pneumonia deaths. The figure displays weekly pneumonia and influenza deaths in the United States from winter 2007 to spring 2012. The chart demonstrates that influenza (flu) has an underlying seasonal baseline, reflected in cyclic seasonal increases and declines in mortality. In the United States and other countries in the Northern hemisphere, flu occurs most frequently during the winter months (i.e., from October through April).[26] Therefore, the flu season spans the latter part of one calendar year and the early part of the following year (e.g., the 2011–2012 flu season). In the figure, the lower line denotes the usual number of total deaths to be expected from pneumonia and influenza during each week of the year. An upper parallel line indicates the frequency of disease at the epidemic threshold, that is, the minimum number of deaths that would support the conclusion that an epidemic was under way. The epidemic threshold is based on statistical projections. Figure 1–6 demonstrates that the combined pneumonia and influenza deaths peaked substantially above the epidemic threshold during early 2008, late 2009, and early 2011.

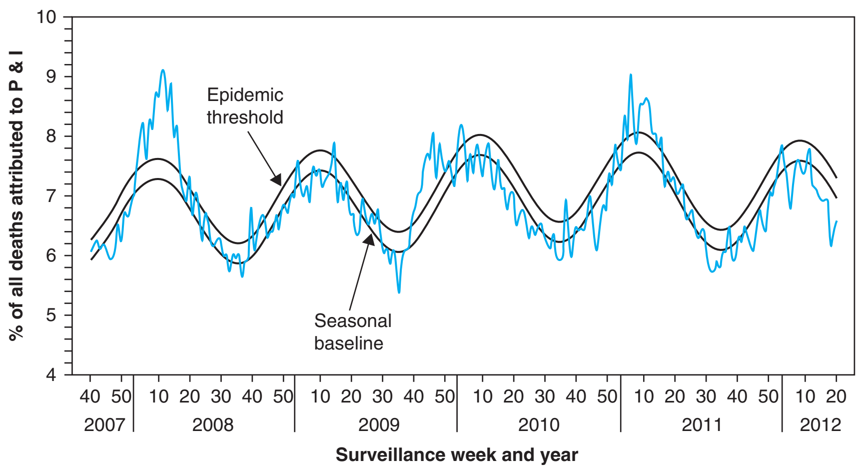


FIGURE 1–6 Percentage of all deaths attributable to pneumonia and influenza (P&I), by surveillance week and year—122 Cities Mortality Reporting System, United States, 2007–May 19, 2012. *Source:* Reproduced Centers for Disease Control and Prevention. Update Influenza Activity—United States, 2011–12 Season and Composition of the 2012–13 Influenza Vaccine. MMWR. 2012;61:418.

Historical Antecedents of Epidemiology

Epidemiology is often thought of as a relatively new discipline. However, this viewpoint is not entirely correct. The history of epidemiology began with the classical period of the Greeks and Romans and included major developments that occurred during later eras: the medieval period, the Renaissance, the late 1800s and early 1900s, and more recently the mid- to late 20th century, when the pace of epidemiologic activities exploded.

It may be said that epidemiology began with the Greeks, who in their concern for the ancient epidemics and deadly toll of diseases, attributed disease causality to environmental factors. Early causal explanations for epidemics included the wrath of the gods, the breakdown of religious beliefs and morality, the influence of weather, and "bad air." During the medieval period, the Black Death caused by plague killed more than 25% of the European population. Another terrible scourge was smallpox: Edward Jenner's work led to the development of an effective vaccination against smallpox. During the late Renaissance, pioneering biostatisticians quantified morbidity and mortality trends.

When the 19th century arrived, deadly cholera epidemics impacted Europe and the United States The disease is thought to have been spread along trade routes from India to Asia, the Middle East, and Russia. Cholera is a life-threatening condition caused by a bacterium; victims retch from severe (but painless) vomiting and diarrhea and eventually die from dehydration and electrolyte disturbances. An example that memorializes the assault of cholera on Europe is the Cholera Fountain (Cholera Brunnen) in Dresden, Germany. Residents constructed the fountain in the mid-1800s to express their gratitude for having escaped a cholera epidemic that threatened the city. (See **Figure 1–7**.) Often cited as a major historical development is John Snow's investigations of London cholera outbreaks, reported in *Snow on Cholera*.[27]

A contemporary of Snow, William Farr, promoted innovative uses of vital statistics data. During the 19th century, early microbiologists formalized the germ theory of disease, which attributed diseases to specific organisms. At the beginning of the 20th century, a flu pandemic killed more than 50 million people worldwide. Each of these historical developments that contributed to the genesis of epidemiology is discussed in turn below.

Environment as a Factor in Disease Causation

The following account by Thucydides records, in detail, the ravages produced by a deadly disease, "Thucydides' plague"[28]; such graphic descriptions of major

FIGURE 1–7 The Cholera Fountain in Dresden, Germany.

epidemics in history indicate this early author's concern with the causality of these remarkable phenomena:

> Others, who were in perfect health, were taken suddenly, without any apparent cause, with violent heats in their heads, and with redness and inflammations in their eyes. Their tongues and throats within became immediately bloody; their breath in great disorder and offensive. A sneezing and a hoarseness ensued; and, in a short time, the pain descended into the breast, attended with a violent cough. When it was once settled about the mouth of the stomach, a retching, and vomiting of bilious stuff, in as great a variety as ever was known among physicians, succeeded, but not without the greatest anxiety imaginable. Many were seized with a hiccup, that brought up nothing, but occasioned a violent convulsion, which in some went off presently, but in others continued much longer. The body outwardly was neither very hot to the touch, nor pale, but reddish, livid, and flowered (as it were) all over with little pimply eruptions, and ulcers; but inwardly the heat was so exceedingly great, that they could not endure the slightest covering, or the finest linen, or any thing short of absolute nakedness. It was also an infinite pleasure to them to plunge into cold water; and many of those who were not well attended did so, running to the wells, to quench their insatiable thirst: not that it signified whether they drank much or little; a great uneasiness and restlessness attending them, together with a continual watching. While the distemper was

> advancing to the height, the body did not fall away, but resisted the vehemence of it beyond expectation; so that many of them died the ninth and the seventh day of the inward burning, some strength yet remaining; or, if they held out longer, many of them afterwards died of weakness; the distemper descending into the belly, and there producing violent ulcerations, and fluxes of the simple or unmixed kind.[28]

Hippocrates, in *On Airs, Waters, and Places*,[29] gave birth in about 400 BC to the idea that disease might be associated with the physical environment; his thinking represented a movement away from supernatural explanations of disease causation to a rational account of the origin of humankind's illnesses. Note in the following passage his reference to climate and physical environment:

> Whoever wishes to investigate medicine properly should proceed thus: in the first place to consider the seasons of the year, and what effects each of them produces (for they are not at all alike, but differ much from themselves in regard to their changes). Then the winds, the hot and the cold, especially such as are common to all countries, and then such as are peculiar to each locality. We must also consider the qualities of the waters, for as they differ from one another in taste and weight, so also do they differ much in their qualities. In the same manner, when one comes into a city to which he is a stranger, he ought to consider its situation, how it lies as to the winds and the rising of the sun; for its influence is not the same whether it lies to the north or the south, to the rising or to the setting sun. These things one ought to consider most attentively, and concerning the waters which the inhabitants use, whether they be marshy and soft, or hard, and running from elevated and rocky situations, and then if saltish and unfit for cooking; and the ground, whether it be naked and deficient in water, or wooded and well watered, and whether it lies in a hollow, confined situation, or is elevated and cold; and the mode in which the inhabitants live, and what are their pursuits, whether they are fond of drinking and eating to excess, and given to indolence, or are fond of exercise and labor, and not given to excess in eating and drinking.[29(pp 156–157)]

The Black Death

Occurring between 1346 and 1352, the Black Death is a dramatic example of a pandemic of great historical significance to epidemiology.[30] The Black Death is noteworthy because of the scope of human mortality that it produced as well as for its impact upon medieval civilization. Estimates suggest that the Black Death claimed about one-quarter to one-third of the population of Europe. Northern Africa and the near Middle East also were affected severely; at the inception of the outbreak, the population of this region including Europe numbered about 100 million people; 20–30 million people are believed to have died in Europe.

Historians attribute the Black Death to bubonic plague, which is the most common of the three forms of plague.[30,31] The bacterium *Yersinia pestis* produces swelling of the lymph nodes in the groin and other sites of the body.

These painful swellings, called buboes, are followed in several days by high fever and the appearance of black splotches on the skin. The reservoir for *Y. pestis* is various types of rodents, including rats. Plague can be transmitted when fleas that feed on rodents bite a human host. At the time of the Black Death, no method for treatment of plague existed. Most victims died within a few days after the occurrence of buboes. Currently, plague is treatable with antibiotics. In addition, improvement in sanitary conditions has led to the decline in plague cases; 2,118 cases were reported worldwide in 2003.[31] From 1,000 to 2,000 plague cases are reported annually to the World Health Organization (according to data available in 2012).[32]

Use of Mortality Counts

In 1662, John Graunt published *Natural and Political Observations Mentioned in a Following Index, and Made Upon the Bills of Mortality*.[33] This work recorded descriptive characteristics of birth and death data, including seasonal variations, infant mortality, and excess male over female differences in mortality. Graunt's work made a fundamental contribution by discovering regularities in medical and social phenomena. He is said to be the first to employ quantitative methods in describing population vital statistics by organizing mortality data in a mortality table and has been referred to as the Columbus of statistics. Graunt's procedures allowed the discovery of trends in births and deaths due to specific causes. Although his conclusions were sometimes erroneous, his development of statistical methods was highly important.[34]

Concerning sex differences in death rates, Graunt wrote:

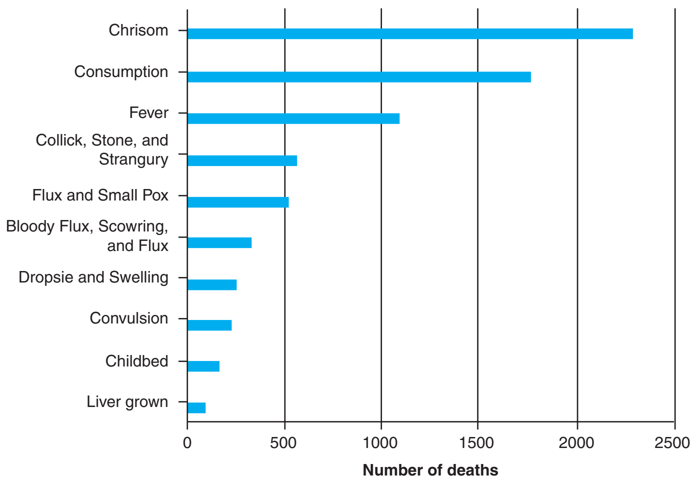
> *Of the difference between the numbers of Males and Females*. The next Observation is, That there be more Males than Females . . . There have been Buried from the year 1628, to the year 1662, exclusive, 209436 Males, and but 190474 Females: but it will be objected, That in London it may be indeed so, though otherwise elsewhere; because London is the great Stage and Shop of business, wherein the Masculine Sex bears the greatest part. But we Answer, That there have been also Christened within the same time 139782 Males, and but 130866 Females, and that the Country-Accounts are consonant enough to those of London upon this matter.[33(p 44)]

Figure 1–8 shows the 10 leading causes of mortality from the Yearly Mortality Bill for 1632. A legend at bottom of the figure defines the archaic terms used in Graunt's time.

Edward Jenner and Smallpox Vaccination

The term *vaccination* derives from the Latin word for cow (*vacca*), the source of the cowpox virus that was used to create a vaccine against smallpox. A precursor of smallpox vaccination was variolation, which referred to an early Asian method of conferring immunity to smallpox by introducing dried scabs from smallpox patients into the noses of potential victims who wished to be protected from this disease.[35] Variolation often produced a milder case of disease with a much lower fatality rate than that caused by community-acquired smallpox. The method gained popularity in Europe during the early 1700s, when the procedure was modified by injecting infectious material under the skin; variolation was first tested among abandoned children and prisoners. When it was declared safe, members of the English royal family were inoculated.

Edward Jenner (**Figure 1–9**) is credited with the development of the smallpox vaccination, a lower-risk method for conferring immunity against smallpox than



Glossary of Terms Used in Chart

Bloody flux	Dysentery
Chrisom	Death of a child within one month of baptism
Consumption	Tuberculosis
Dropsie	Dropsy—edema
Flox	Hemorrhagic smallpox
Flux	Excessive flow or discharge from the boby
Liver grown	Having an enlarged liver
Scowring	Scouring—purging of the bowels; probably referring to diarrhea
Small pox	Smallpox
Stone	Calculus, e.g., gallstone
Strangury	Slow and painful discharge of urine

FIGURE 1–8 Yearly Mortality Bill for 1632: The 10 leading causes of mortality in Graunt's Time. *Source:* Data from Graunt J. Natural and Political Observations, Mentioned in a Following Index, and Made upon the Bills of Mortality, 2nd ed. London: Tho. Roycroft; 1662: p. 8.

FIGURE 1–9 Edward Jenner vaccinating a child. *Source:* Images from the History of Medicine, National Library of Medicine.

variolation.[36] He was fascinated by folk wisdom, which suggested that dairymaids who had contracted cowpox seemed to be immune to smallpox. Infection with the cowpox virus produced a much less severe form of disease than smallpox. Jenner conducted an experiment in which he used scabs from the cowpox lesions on the arm of a dairymaid, Sarah Nelmes (**Figure 1–10**), to create a smallpox vaccine. He then used the material to vaccinate an 8-year-old boy, James Phipps. Following the vaccination, Phipps appeared to develop immunity to the smallpox virus to which he was reexposed several times subsequently.

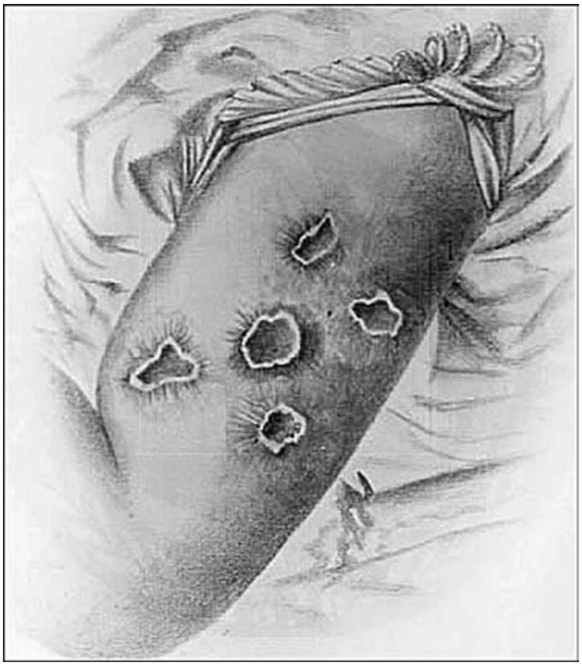


FIGURE 1–10 Arm of Sarah Nelmes with lesions of cowpox. *Source:* Reproduced from the National Library of Medicine. Smallpox: A great and terrible scourge: Vaccination. Available at: http://www.nlm.nih.gov/exhibition/smallpox/sp_vaccination.html. Accessed July 19, 2012.

Later, Jenner vaccinated his own son and several other children, obtaining similar positive findings, which were published in 1798. (In 1978 smallpox was finally eliminated worldwide. Since 1972, routine vaccination of the nonmilitary population of the United States has been discontinued.)[37]

Use of Natural Experiments

A *natural experiment* refers to "[n]aturally occurring circumstances in which subsets of the population have different levels of exposure to a supposed causal factor in a situation resembling an actual experiment, where human subjects would be randomly allocated to groups. The presence of persons in a particular group is typically nonrandom;"[6] the following section is an account of John Snow's natural experiment.

During the 19th century, water from the highly polluted Thames River was London's primary source of drinking water. **Figure 1–11** expresses concerns about the cleanliness of Thames River water during this time period. In this context John Snow conducted a famous natural experiment.

Snow investigated a cholera epidemic that occurred during the mid-19th century in Broad Street, Golden Square, London. Snow's work, a classic study that linked the cholera epidemic to contaminated water supplies, is noteworthy because it utilized many of the features of epidemiologic inquiry: a spot map of cases and tabulation of fatal attacks and deaths. Through the application of his keen powers of observation and inference, he developed the hypothesis that contaminated water might be associated with outbreaks of cholera. He made several observations that others had not previously made. One observation was that cholera was associated with water from one of two water supplies that served the Golden Square district of London.[38] Broad Street was served by two separate water companies, the Lambeth Company and the Southwark and Vauxhall Company. Lilienfeld and Lilienfeld[39] wrote:

> In London, several water companies were responsible for supplying water to different parts of the city. In 1849, Snow noted that the cholera rates were particularly

FIGURE 1–11 George Cruickshank, 1792–1878, artist. Salus Populi Suprema Lex Source of the South Warwick Water Works. *Source:* Images from the History of Medicine, National Library of Medicine.

high in those areas of London that were supplied by the Lambeth Company and the Southwark and Vauxhall Company, both of whom obtained their water from the Thames River at a point heavily polluted with sewage.[39(p 36)]

Snow's account of the outbreak of 1849 is found in **Exhibit 1–2**.

Between 1849 and 1854 the Lambeth Company had its source of water relocated to a less contaminated part of the Thames. In 1854, another epidemic of

EXHIBIT 1–2

Snow on Cholera

The most terrible outbreak of cholera which ever occurred in this kingdom, is probably that which took place in Broad Street, Golden Square, and the adjoining streets, a few weeks ago. Within two hundred and fifty yards of the spot where Cambridge Street joins Broad Street, there were upwards of five hundred fatal attacks of cholera in ten days. The mortality in this limited area probably equals any that was ever caused in this country, even by the plague; and it was much more sudden, as the greater number of cases terminated in a few hours. The mortality would undoubtedly have been much greater had it not been for the flight of the population. Persons in furnished lodgings left first, then other lodgers went away, leaving their furniture to be sent for when they could meet with a place to put it in. Many houses were closed altogether, owing to the death of the proprietors; and, in a great number of instances, the tradesmen who remained had sent away their families: so that in less than six days from the commencement of the outbreak, the most afflicted streets were deserted by more than three-quarters of their inhabitants.

There were a few cases of cholera in the neighbourhood of Broad Street, Golden Square, in the latter part of August; and the so-called outbreak, which commenced in the night between the 31st August and the 1st September, was, as in all similar instances, only a violent increase of the malady. As soon as I became acquainted with the situation and extent of this irruption of cholera, I suspected some contamination of the water of the much-frequented street-pump in Broad Street, near the end of Cambridge Street; but on examining the water, on the evening of the 3rd September, I found so little impurity in it of an organic nature, that I hesitated to come to a conclusion. Further inquiry, however, showed me that

continues

EXHIBIT 1–2 *continued*

there was no other circumstance or agent common to the circumscribed locality in which this sudden increase of cholera occurred, and not extending beyond it, except the water of the above mentioned pump. I found, moreover, that the water varied, during the next two days, in the amount of organic impurity, visible to the naked eye, on close inspection, in the form of small white, flocculent particles; and I concluded that, at the commencement of the outbreak, it might possibly have been still more impure.

The deaths which occurred during this fatal outbreak of cholera are indicated in the accompanying map (**Figure 1–12**), as far as I could ascertain them . . . The dotted line on the map surrounds the sub-districts of Golden Square, St. James's, and Berwick Street, St. James's, together with the adjoining portion of the sub-district of St. Anne, Soho, extending from Wardour Street to Dean Street, and a small part of the sub-district of St. James's Square enclosed by Marylebone Street, Titchfield Street, Great Windmill Street, and Brewer Street. All the deaths from cholera which were registered in the six weeks from 19th August to 30th September within this locality, as well as those of persons removed into Middlesex Hospital, are shown in the map by a black line in the situation of the house in which it occurred, or in which the fatal attack was contracted . . . The pump in Broad Street is indicated on the map, as well as all the surrounding pumps to which the public had access at the time. It requires to be stated that the water of the pump in Marlborough Street, at the end of Carnaby Street, was so impure that many people avoided using it. And I found that the persons who died near this pump in the beginning of September, had water from the Broad Street pump. With regard to the pump in Rupert Street, it will be noticed that some streets which are near to it on the map, are in fact a good way removed, on account of the circuitous road to it. These circumstances being taken into account, it will be observed that the deaths either very much diminished, or ceased altogether at every point where it becomes decidedly nearer to send to another pump than to the one in Broad Street. It may also be noticed that the deaths are most numerous near to the pump where the water could be more readily obtained . . . The greatest number of attacks in any one day occurred on the 1st of September, immediately after the outbreak commenced. The following

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EXHIBIT 1–2 *continued*

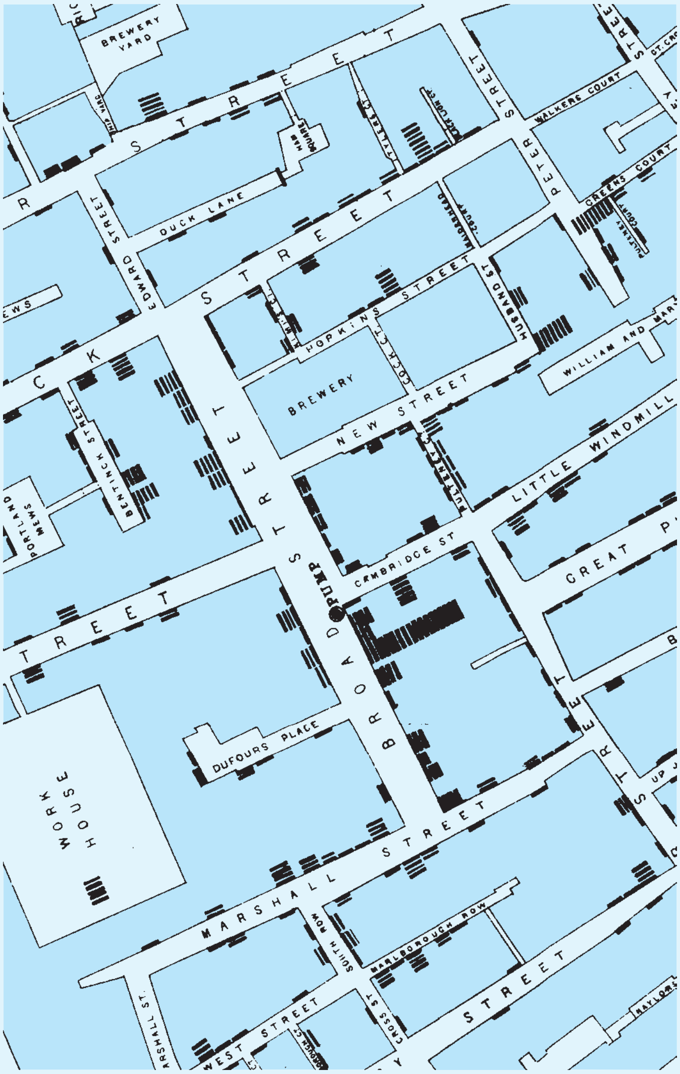

FIGURE 1–12 Cholera deaths in the neighborhood of Broad Street, August 19 to September 30, 1849. *Source:* Reproduced from John Snow's dot map of the Broad Street and Golden Square area of London, in *Snow on Cholera* by John Snow, Commonwealth Fund: New York, 1936.

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EXHIBIT 1–2 *continued*

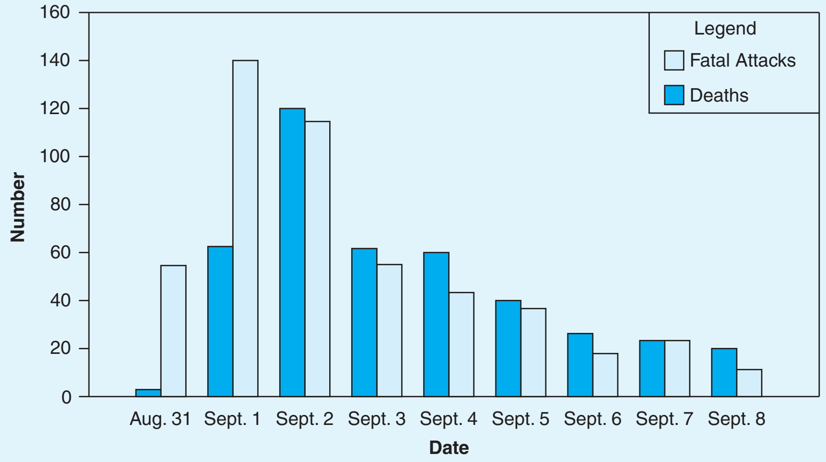

FIGURE 1–13 The 1849 cholera outbreak in Golden Square district, London. Fatal attacks and deaths, August 31–September 8. *Source:* Data from Table I, Snow J. *Snow on Cholera*, p. 49, Harvard University Press, © 1965.

day the attacks fell from one hundred and forty-three to one hundred and sixteen, and the day afterwards to fifty-four . . . The fresh attacks continued to become less numerous every day. On September the 8th—the day when the handle of the pump was removed—there were twelve attacks; on the 9th, eleven; on the 10th, five; on the 11th, five; on the 12th, only one; and after this time, there were never more than four attacks on one day. During the decline of the epidemic the deaths were more numerous than the attacks, owing to the decrease of many persons who had lingered for several days in consecutive fever (**Figure 1–13**).

Source: Reprinted from Snow J. *Snow on Cholera.* Cambridge, MA: Harvard University Press: 1965:38–51.

cholera occurred. This epidemic was in an area that consisted of two-thirds of London's resident population south of the Thames and was being served by both companies. In this area, the two companies had their water mains laid out in an interpenetrating manner, so that houses on the same street were receiving their water from different sources.[39]

This was a naturally occurring situation, a "natural experiment," if you will, because in 1849 all residents received contaminated water from the two water companies. After 1849, the Lambeth Company used less contaminated water by relocating its water supply. Snow demonstrated that a disproportionate number of residents who contracted cholera in the 1854 outbreak used water from one water company, which used polluted water, in comparison with the other company, which used relatively unpolluted water.

Snow's methodology maintains contemporary relevance. His methods utilized logical organization of observations, a natural experiment, and a quantitative approach.[39] All these methods are hallmarks of present-day epidemiologic inquiry. Note that it is possible to visit the site of the pump that figured so prominently in Snow's investigation of cholera; a London public house on the original site of the pump has been named in Snow's honor. A replica of the pump is located nearby. Refer to **Exhibit 1–3** for pictures of the site and the pump with a reproduction of the text on the base of the replica.

Another study, occurring during the mid-19th century, also used nascent epidemiologic methods. Ignaz Semmelweis,[40] in his position as a clinical assistant in obstetrics and gynecology at a Vienna hospital, observed that women in the maternity wards were dying at high rates from puerperal fever. In 1840, when the medical education system changed, he found a much higher mortality rate among the women on the teaching wards for medical students

EXHIBIT 1–3

A Visit to the Broad Street Pump and the Sir John Snow Public House, Located at 39 Broadwick Street, London, England W1F9QJ

Figure 1–14 shows John Snow, **Figure 1–15** displays a replica of the Broad Street pump. Broad Street has been renamed Broadwick Street. **Figure 1–16** shows a plaque titled "The Soho Chloera Epidemic" at the base of the pump. **Figure 1–17** presents a picture of the John Snow Pub.

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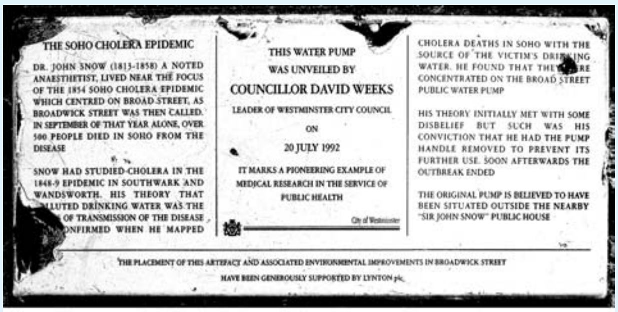
EXHIBIT 1–3 *continued*

FIGURE 1–14 Photograph of John Snow. *Source:* © National Library of Medicine.

FIGURE 1–15 Replica of Broad Street pump near its approximate original location.



The Soho Cholera Epidemic

Dr. John Snow (1813–1858), a noted anaesthesiologist, lived near the focus of the 1854 Soho cholera epidemic which centred on Broad Street, as Broadwick Street was then called. In September of that year alone, over 500 people died in Soho from the disease. Snow had studied cholera in the 1848–49 epidemic in Southwark and Wandsworth. His theory that polluted drinking water was the [source] of transmission of the disease [was] confirmed when he mapped cholera deaths in Soho with the source of the victim's drinking water. He found that they were concentrated on the Broad Street public water pump. His theory initially met with some disbelief but such was his conviction that he had the pump handle removed to prevent its further use. Soon afterwards the outbreak ended. The original pump is believed to have been situated outside the nearby "Sir John Snow" Public House.

FIGURE 1–16 Plaque commemorating the Soho cholera epidemic, 1854.

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EXHIBIT 1–3 *continued*

FIGURE 1–17 The John Snow Pub named in honor of the British Anesthesiologist.

and physicians than on the teaching wards for midwives. He postulated that medical students and physicians had contaminated their hands during autopsies. As a result, they transmitted infections while attending women in the maternity wards.[41] When the practice of hand washing with chlorinated solutions was introduced, the death rate for puerperal fever in the wards for medical students and physicians dropped to a rate equal to that in the wards for midwives.

William Farr

A contemporary of John Snow, William Farr assumed the post of "Compiler of Abstracts" at the General Register Office (located in England) in 1839 and held this position for 40 years. Among Farr's contributions to public health and epidemiology was the development of a more sophisticated system for codifying medical conditions than was previously in use. Farr's classification scheme, which departed from a narrow medical view, provided the foundation for the International Classification of Diseases in use today. Also noteworthy is the fact that Farr used data such as census reports to study occupational mortality in England. In addition, he explored the possible linkage between mortality rates and population density, showing that both the average number of deaths and births per 1,000 living persons increased with population density (defined as number of persons per square mile). Because of the excess of births over deaths in all except the most crowded areas, the population tended to increase in the less crowded areas. With respect to deaths in high mortality districts, such as Liverpool, which had a mortality rate more than 22 per 1,000 greater than that experienced in healthier districts, he attributed mortality to factors such as ". . . impurities of water, pernicious dirts, floating dusts, zynotic contagions, [and] crowdings in lodgings . . ."[42(p 90)] The healthier districts had ". . . a salubrious soil, and supply the inhabitants with water generally free from organic impurities."[42(pp 90–91)]

Identification of Specific Agents of Disease

In the late 1800s, Robert Koch verified that a human disease was caused by a specific living organism. His epoch-making study, *Die Aetiologie der Tuberkulose*, was published in 1882. This breakthrough made possible greater refinement of the classification of disease by specific causal organisms.[43] Previously, the grouping together of diseases according to grosser classifications had hampered their epidemiologic study.

King[44] noted that Koch's postulates are usually formatted as follows:

1. The microorganism must be observed in every case of the disease.
2. It must be isolated and grown in pure culture.
3. The pure culture must, when inoculated into a susceptible animal, reproduce the disease.
4. The microorganism must be observed in, and recovered from, the experimentally diseased animal.[44]

King noted, "What Koch accomplished, in brief, was to demonstrate for the first time in any human disease a strict relation between a micro-organism and a disease."[44(p 351)] This specification of the causal disease organism provided a definite criterion for the identification of a disease, rather than the vague standards Koch's predecessors and contemporaries had employed.

Increasing awareness of the role of microbial agents in the causation of human illness—the germ theory of disease—eventually reached the public health community. One method to limit the spread of infectious disease was through the use of cartoons published in the popular media. **Figure 1–18** suggested that skirts that trail on the ground (in fashion around the turn of the 20th century) could bring deadly germs into the household.[45]

FIGURE 1–18 Samuel D. Erhart, Communicable diseases spread by household and street dust. *Source:* Images from the History of Medicine, National Library of Medicine.

The 1918 Influenza Pandemic

So great was its impact, this outbreak has been referred to as "the Mother of All Pandemics."[46] Also known as the Spanish Flu, the pandemic that occurred during the period of 1918–1919 killed from 50 to 100 million persons worldwide. Estimates suggest that one-third of the world's population of 1.5 billion at the time was infected and developed clinically observable illness. This very severe form of influenza had case-fatality rates of approximately 2.5% compared with the 0.1% or lower rates observed in other influenza pandemics. Differentiating this form of influenza from other outbreaks was its impact on healthy young adults; persons aged 20–40 accounted for nearly half of the mortality toll in this pandemic, whereas influenza deaths normally are more frequent among the very young and the very old.[47,48] The pandemic spread in three distinct waves during a one-year period throughout Europe, Asia, and North America; the first wave began in spring 1918, with two subsequent waves occurring during the fall and winter of 1918–1919. In the United States, the flu's impact was so great that healthcare facilities were taxed to the limit. As a result of large numbers of deaths, the bodies of victims accumulated in morgues awaiting burial, which was delayed because of a shortage of coffins and morticians.

A repeat of the 1918 pandemic is within the realm of possibility, as suggested by the 2009 H1N1 influenza pandemic. This event raised questions about how modern society would cope with a global outbreak of influenza or other highly communicable disease. Will healthcare facilities have adequate "surge" capacity to deal with a sudden and large increase in the number of patients? Will it be necessary to enforce "social distancing" to reduce the spread of epidemic diseases? How will essential services be maintained? These are examples of issues for which the public health community will need to be prepared.

Other Significant Historical Developments

Alexander Fleming, Alexander Langmuir, Wade Hampton Frost, and Joseph Goldberger made several other historically significant contributions. Scottish researcher Fleming is credited with discovering the antimicrobial properties of the mold *Pencillium notatum* in 1928. This discovery led to development of the antibiotic penicillin, which became available toward the end of World War II. Langmuir, regarded as the father of infectious disease epidemiology, in 1949 established the epidemiology section of the federal agency presently called the Centers for Disease Control and Prevention. This section later came to be known as the Epidemic Intelligence Service (EIS), which celebrated its 60th anniversary in 2011. Frost, who held the first professorship of epidemiology in the United States beginning in 1930 at Johns Hopkins University, advocated the use of quantitative methods (e.g., a procedure known as cohort analysis) to illuminate public health problems, although his concept of epidemiology tended to be restricted narrowly to the study of infectious diseases. Finally, Goldberger's discovery of the cure for pellagra, a nutritional deficiency disease characterized by the so-called three Ds (dermatitis, diarrhea, and dementia), led to reductions in the occurrence of the disease, which had gained attention in the early 1900s.

Recent Applications of Epidemiology

Epidemiologic activity has exploded during the past several decades.[49] For example, the ongoing Framingham Heart Study, begun in 1948, is one of the pioneering research investigations of risk factors for coronary heart disease. Refer to the classic article by Kannell and Abbott for a description of the study.[50] Another development, occurring after World War II, was research on the association between smoking and lung cancer.[51] An example is the historically significant work of Doll and Peto,[52] based on a fascinating study of British physicians.

The computer and powerful statistical software have aided the proliferation of epidemiologic research studies. Popular interest in epidemiologic findings is also intense. Almost every day now, one encounters media reports of epidemiologic research into such diverse health concerns as acquired immune deficiency syndrome, chemical spills, breast cancer screening, and the health effects of secondhand cigarette smoke. Table 1–1 reports triumphs in epidemiology; these are examples in which epidemiologists have identified risk factors for cancer, heart disease, infectious diseases, and many other conditions. One triumph in Table 1–1 is how epidemiology helped to uncover the association between the human papillomavirus and cervical cancer. On June 8, 2006, the FDA announced the licensing of the first vaccine (Gardisil®) to prevent cervical cancer caused by four types of human papillomavirus and approved its use in females aged 9–26 years. Returning to **Table 1–1**, the reader should note that although many of the terms used in the table have not yet been discussed in this book, later sections of the text will cover some of them. Additional examples of applications of epidemiology are provided in the following sections.

Infectious Diseases in the Community

Infectious disease epidemiology, one of the most familiar types of epidemiology, investigates the occurrence of epidemics of infectious and communicable diseases. Examples are studying diseases caused by bacteria, viruses, and microbiologic agents; tracking down the cause of foodborne illness; and investigating

Table 1–1 Triumphs in Epidemiology

Risk Factor Categories	Disease	Risk Factors	Direction
Alcohol	Esophageal cancer	alcohol (interaction with smoking)	IR
Viruses	Liver cancer	hepatitis B virus	IR
	Burkitt lymphoma	Epstein Barr virus	IR
	Kaposi sarcoma	Herpes simplex virus type B	IR
	Cervical cancer	"something transmitted sexually" (human papilloma virus)	IR
	Nasopharyngeal carcinoma	Epstein Barr virus	IR
	Yellow fever	"something transmitted by mosquitos" (Flavivirus)	IR
	New variant (nv) Creutzfeldt-Jacob disease	prions (interaction with genotype)	IR
Bacteria	Cholera	"something in water" (Vibrio cholera)	IR
	Peptic ulcer	*Helicobactor pylori*	IR
	Puerperal fever	"something on doctor's hands" (group B Streptococcus)	IR
Nutrition	Pellagra	"something in bread" (niacin)	P
	Neural tube defects	folic acid, folate	P
	Oral clefts	folic acid	P
Occupation	Lung cancer	asbestos (interaction with smoking)	IR
	Bladder cancer	aniline dye	IR
	Mesothelioma	asbestos	IR
	Angiosarcoma	vinyl chloride	IR
	Infertility (male)	DBCP	IR
	Nasal cancer	nickel smelting	IR
	Lung cancer	"something in uranium mines" (interaction with smoking)	IR
Environment	Dental caries	fluoride [deficiency]	P
	Cancer	arsenic	IR
Drugs/ Devices	Myocardial infarction	aspirin	P
	Micoagthnia	iso-retinene during pregnancy	IR
	Pelvic inflammatory disease	Dalkon Shield IUD	IR
	Septic abortion	Dalkon Shield IUD	IR

continues

Table 1–1 *continued*

Risk Factor Categories	Disease	Risk Factors	Direction
Hormones	Clear cell adenocarcinoma of the vagina	diethylstilbestrol prenatally	IR
	Venous thromboembolism	combined estrogen/progestin (oral contraceptives)	IR
	Venous thromboembolism	postmenopausal estrogen	IR
	Ovarian cancer	oral contraceptives	P
	Endometrial cancer	combined estrogen/progestin	P
	Endometrial cancer	oral contraceptives: postmenopausal estrogen	IR
	Iron deficiency anemia	oral contraceptives	P
	Benign breast disease	oral contraceptives	P
	Myocardial infarction	oral contraceptives (interaction with smoking)	IR
	Ischemic stroke	oral contraceptives (interaction with hypertension; modified by dose)	IR
Genetics	Breast cancer	"something genetic" (BRCA1, BRCA2 mutations)	IR
	Ovarian cancer	"something genetic" (BRCA2 mutations)	IR
	Colon cancer	"something genetic" (APC1 mutations)	IR
Miscellaneous	Toxic shock syndrome	super absorbent tampons	IR
	SIDS	prone sleep position	IR
	Reyes syndrome	aspirin (interaction with infection)	IR
Smoking	Lung cancer	smoking	IR
	Coronary disease	smoking	IR
	Hemorrhagic stroke	smoking	IR
	Ischemic stroke	smoking	IR
	Abdominal aortic aneurism	smoking	IR
	Peripheral vascular disease	smoking	IR
	Parkinson's disease	smoking	P
	Ulcerative colitis	smoking	P
	Laryngeal cancer	smoking	IR
	Intrauterine growth retardation	smoking during pregnancy	IR
	Toxemia/pre-eclampsia	smoking during pregnancy	P

Abbreviations: IR, increased risk; P, protective (see Chapters 3, 6, and 7).

Source: Compiled by Diane Petitti. Adapted with permission from *The Epidemiology Monitor*. October 2001; 6.

new diseases such as SARS, pandemic influenza 2009 H1N1 (Exhibit 1–1), and avian influenza (**Exhibit 1–4**). An illustration is the use of epidemiologic methods to attempt to eradicate, when possible, polio, measles, smallpox, and other communicable diseases. Another example is outbreaks of infectious diseases in hospitals (nosocomial infections). The role of the Epidemic Intelligence Service in investigating disease outbreaks is defined as follows:

> The Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia tracks disease outbreaks that occur in the United States and throughout the world. As one facet of this process, the CDC supports a training program for personnel who

EXHIBIT 1–4

Highly Pathogenic Avian Influenza (HPAI) Avian Influenza (H5N1)

Investigations into an outbreak of highly pathogenic avian influenza (HPAI) demonstrate the role of epidemiology in containing outbreaks of infectious diseases that threaten the health of the population. The arrival of avian influenza (caused by the H5N1 virus) that began in the late 1990s is an example of the occurrence of an infectious disease with potential to impact a specific community as well as the entire world. This highly fatal condition worried public health authorities who were concerned that avian influenza could create a worldwide pandemic, mirroring the 1918 pandemic and lesser influenza epidemics that occurred later in the 20th century. The emergence of a pandemic might be the consequence of mutation of the virus into a version that could be communicated rapidly on a person-to-person basis.

Beginning in 1997, avian influenza appeared in Hong Kong, with an initial 18 human cases, of which 6 were fatal.[54] These human cases coincided with outbreaks among poultry on farms and in markets that sold live poultry. Authorities destroyed the entire chicken population in Hong Kong; subsequently, no additional human cases linked to the source in Hong Kong were reported. Two additional human cases were reported in Hong Kong in 2003 and were associated with travel to mainland China.

The epidemic did not end in Hong Kong: Additional cases began appearing in Southeast Asia during late 2003. Virus outbreaks involving animals and humans were limited primarily to Vietnam and some other areas of Southeast Asia (e.g., Thailand). One case of probable person-to-person spread of H5N1 virus is believed to have occurred in Thailand. Then, in 2005, the virus manifested itself in central Asia, spreading to Europe, Africa, and the Middle East. From December 1, 2003 to April 30, 2006, nine countries reported a total of 205 laboratory-verified cases to

continues

EXHIBIT 1–4 *continued*

the World Health Organization, with 113 of these illnesses being fatal. At about the same time, infection with the virus was reported among flocks of domestic and wild birds in 50 countries.

Officials were concerned that migrating flocks of wild birds, which cover vast geographical areas, could spread H5N1 to domestic poultry in many parts of the world (**Figure 1–19**).[55] Humans who come into contact with these domestic birds would be at risk of contracting the highly pathogenic virus.

As of 2012, the following conclusions have been reached about HPAI (H5N1):

- Since November 2003 more than 600 human cases (with about a 60% case fatality rate) have been reported worldwide from 15 countries. Nations with the greatest number of cases are Indonesia, Vietnam, and Egypt.
- The virus can cause severe infections (e.g., severe respiratory illness and death) in humans.
- Human contact with infected poultry has been associated with most cases.
- The virus does not show evidence of efficient person-to-person transmission. ■

FIGURE 1–19 Pathogenic avian influenza (H5N1) can appear in wild and domestic avian flocks.

respond to requests for assistance in investigating diseases and offer other forms of epidemiologic expertise. Known as the Epidemic Intelligence Service (EIS), this two-year program provides educational opportunities in applied epidemiology. Since 1951, more than 3,000 EIS officers have applied their training to tackle complex health problems. Selected EIS candidates are physicians, nurses, and individuals who have had public health training. Examples of EIS activities include investigating outbreaks of foodborne illnesses such as salmonellosis and listeriosis, potential transmission of hepatitis, and occurrence of Legionnaires' disease. A classic example of EIS detective work is the investigation of a 1987 cholera outbreak in an inland village in Guinea-Bissau, Africa. The EIS linked this episode, which killed 11 people, to the body of a dockworker smuggled from the coast to an inland village for burial. More than half of the participants at a funeral feast for the deceased later developed cholera. Traditional practices such as washing bodies of the dead and preparation of funeral feasts (in an unsanitary environment) might have contributed to the cholera outbreak in the village.[53]

Health and the Environment

Toxic chemicals used in industry, air pollutants, contaminants in drinking water, unsafe homes and vehicles, and other environmental factors agents may affect human health. Both occupational and environmental epidemiology address the occurrence and distribution of adverse health outcomes such as dust-associated conditions, occupational dermatoses, and diseases linked to harmful physical energy (e.g., ionizing radiation from X-ray machines and other sources). Many of the diseases studied by environmental epidemiologists have agents and manifestations similar to those in occupational epidemiology, for example, the role of pesticides in causing environmentally associated illness. Injury control epidemiology studies risk factors associated with unintentional injuries (e.g., motor vehicle crashes, bicycle injuries, falls, and occupational injuries). Findings may suggest preventive measures including environmental modifications, safer design of vehicles, and safety laws to prevent injuries. Reproductive and perinatal epidemiology investigates environmental and occupational exposures and birth outcomes. Related topics are sudden infant death syndrome, epidemiology of neonatal brain hemorrhage, early pregnancy, and methodological issues in drug epidemiology.

Chronic Disease, Lifestyle, and Health Promotion

An example of this category is the role of *lifestyle* (e.g., exercise, diet, smoking, and alcohol consumption) in physical health outcomes such as obesity, coronary heart disease, arthritis, diabetes, and cancer. Hypothesized risk factors studied include antecedent variables within the person's physical and psychosocial environment that may be associated with health and disease. To illustrate, epidemiologic research has explored the relationship between obesity and the tendency of the built environment to dissuade people from walking. Also, poor dietary choices, smoking, substance abuse, and excessive alcohol consumption are linked to many chronic illnesses. Regarding the psychosocial environment, cultural practices affect behaviors that are linked to health and disease. Epidemiologic studies are central to the identification of the causes and methods for addressing health disparities in society.

Psychological and Social Factors in Health

Stress, social support, and socioeconomic status affect the occurrence and outcomes of mental and physical health. Research has examined the relationship between the psychological and dimensions and illnesses such as arthritis, some gastrointestinal conditions, and essential hypertension. A related topic involves epidemiologic studies of personality factors and disease, exemplified by the type A personality (coronary prone) and its potential link to heart disease. Psychiatric epidemiology is concerned with the distribution and determinants of mental disorders. Examples are the definition and measurement of mental disorders, social factors related to them, and urban and rural differences in their frequency. Major research programs conducted in the community have investigated the epidemiology of depressive symptomatology.

Also studied as psychosocial determinants are factors that affect the distribution of disabilities (e.g., impaired cognition in children, genetic syndromes, autism). Social, cultural, and demographic factors (socioeconomic status, gender, employment, marital status, and race) are demonstrated correlates of mental and physical health status. An important aspect of this branch of epidemiology is the role of such determinants in health disparities.

Molecular and Genetic Epidemiology

Numerous advances in molecular and genetic epidemiology have taken place during the genomics age. The field of *molecular epidemiology* applies the techniques of molecular biology to epidemiologic studies. An illustration is using genetic and molecular markers (e.g., deoxyribonucleic acid (DNA) typing) to examine behavioral outcomes and host susceptibility to disease. *Genetic epidemiology* studies the distribution of genetically associated diseases among the population. For example, research has demonstrated inherited susceptibility to severe breast and ovarian cancer as well as to alcohol use disorders (AUDs). Refer to the National Cancer Institute website for more information on cancer genetics.[56] With respect to alcohol use disorders, researchers have examined the contribution of specific genes to the increased mortality found in individuals with AUDs.[57]

A landmark of the genomics age was the completion of the Human Genome Project. Two excellent overview articles discuss how epidemiology interacts with genomics,[58] and how the genomics revolution has transformed epidemiology.[59] Khoury et al. write that, "[e]pidemiology is essential to fulfill the promise of genomics for clinical and public health practice. . . . Genomics can enhance potential for epidemiology to contribute to multidisciplinary scientific research."[58(p 936)]

Conclusion

Epidemiology is concerned with the occurrence, distribution, and determinants of health-related states or events (e.g., health and diseases, morbidity, injuries, disability, and mortality in populations). Epidemiologic studies are applied to the control of health problems in populations. As a result, sometimes the discipline is called population medicine. Several examples demonstrated that the etiologic bases of disease and health conditions in the population are often unknown. Epidemiology is used as a tool to suggest factors associated with occurrence of disease and introduce methods to stop the spread of infectious and communicable disease.

Three aspects characterize the epidemiologic approach. The first is quantification, which is counting of cases of disease and construction of tables that show variation of disease by time, place, and person. The second is use of special vocabulary, for example, epidemic and epidemic frequency of disease. The third is interdisciplinary composition, which draws from microbiology, biostatistics, social and behavioral sciences, and clinical medicine.

The historical antecedents of epidemiology began with Hippocrates, who implicated the environment as a factor in disease causation. Second, Graunt, one of the biostatistics pioneers, compiled vital statistics in the mid-1600s. Third, Snow used natural experiments to track a cholera outbreak in Golden Square, London. Finally, Koch's postulates advanced the theory of specific disease agents. At present, epidemiology is relevant to many kinds of health problems found in the community.

Study Questions and Exercises

1. Using your own words, give a definition of epidemiology. Before you read Chapter 1, what were your impressions regarding the scope of epidemiology? Based on the material presented in this chapter, what topics are covered by epidemiology? That is, to what extent does epidemiology focus exclusively upon the study of infectious diseases or upon other types of diseases and conditions?
2. How would the clinical and epidemiologic descriptions of a disease differ, and how would they be similar?
3. To what extent does epidemiology rely on medical disciplines for its content, and to what extent does it draw upon other disciplines? Explain the statement that epidemiology is interdisciplinary.
4. Describe the significance for epidemiology of the following historical developments:
   a. associating the environment with disease causality
   b. use of vital statistics
   c. use of natural experiments
   d. identification of specific agents of disease
5. Explain what is meant by the following components of the definition of epidemiology:
   a. determinants
   b. distribution
   c. morbidity and mortality
6. The following questions pertain to the term epidemic.
   a. What is meant by an epidemic? Give a definition in your own words.
   b. Describe a scenario in which only one or two cases of disease may represent an epidemic.
   c. What is the purpose of surveillance?
   d. Give an example of a disease that has cyclic patterns.
   e. What is the epidemic threshold for a disease? In what sense is it possible to conceive of the epidemic threshold as a statistical concept?
7. Epidemiologic research and findings often receive dramatic media coverage. Find an article in a media source (e.g., *The New York Times*) on a topic related to epidemiology. In a one-page essay, summarize the findings and discuss how the article illustrates the approach of epidemiology to the study of diseases (health conditions) in populations. You may search online for an appropriate article.

8. During the next week, read and review health-related articles available on the Internet or in your local or national newspaper. Try to find the following terms used in newspaper articles; keep a record of them and describe how they are used:
   a. epidemiology
   b. epidemiologist
   c. infectious disease
   d. chronic disease
   e. clinical trial
   f. increased risk of mortality associated with a new medication
9. What is the definition of a natural experiment? Identify any recent examples of natural experiments. To what extent might changes in legislation to limit smoking in public places or to increase the speed limit on highways be considered natural experiments?
10. Review Exhibit 1–2, Snow on Cholera. What do you believe was the purpose of each of the following observations by Snow?
    a. "small white, flocculent particles" in the water from the Broad Street pump
    b. the location of cholera deaths as shown in Figure 1–12
    c. people who died avoided the pump in Marlborough Street and instead had the water from the Broad Street pump
    d. "the greatest number of attacks in any one day occurred on the 1st of September, . . ."
    e. "On September 8th—the day when the handle of the pump was removed . . ." To what extent do you think removing the pump handle was effective in stopping the disease outbreak?
11. How does quantification support the accomplishment of the four aims of epidemiology?
12. How did Koch's postulates contribute to the advancement of epidemiology? To what extent is identification of specific agent factors a prerequisite for tracking down the causes of disease outbreaks?
13. What are the characteristics that distinguish pandemic disease from epidemic disease? Name some examples of notorious pandemics that occurred in history. Why did the "Spanish Flu" of 1918 qualify as a pandemic? In giving your answer, be sure to distinguish among the terms epidemic, pandemic, and endemic.
14. Identify some infectious diseases that could reach pandemic occurrence during the 21st century. What conditions do you believe exist at present

that could incite the occurrence of pandemics? Why have public health officials been concerned about the emergence of new diseases such as "bird flu"? Speculate about what might happen to organized society and the healthcare system should an outbreak of pandemic influenza occur.

15. The Black Death that occurred during the Middle Ages eradicated a large proportion of the world population at that time. Estimate how likely it would be for a similar epidemic of plague to develop during the current decade.
16. In developed countries, many safeguards exist for the prevention of foodborne illness. Discuss how it would be possible for a foodborne illness outbreak such as the one caused by *E. coli* to erupt in a developed country.

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