Lesson 1
Introduction to Epidemiology

Epidemiology is considered the basic science of public health, and with good reason. Epidemiology is: a) a quantitative basic science built on a working knowledge of probability, statistics, and sound research methods; b) a method of causal reasoning based on developing and testing hypotheses pertaining to occurrence and prevention of morbidity and mortality; and c) a tool for public health action to promote and protect the public's health based on science, causal reasoning, and a dose of practical common sense (2).

As a public health discipline, epidemiology is instilled with the spirit that epidemiologic information should be used to promote and protect the public's health. Hence, epidemiology involves both science and public health practice. The term ***applied epidemiology*** *is sometimes used to describe the application or practice of epidemiology to address public health issues. Examples of applied epidemiology include the following:*

- *the monitoring of reports of communicable diseases in the community*
- *the study of whether a particular dietary component influences your risk of developing cancer*
- *evaluation of the effectiveness and impact of a cholesterol awareness program*
- *analysis of historical trends and current data to project future public health resource needs*

Objectives

After studying this lesson and answering the questions in the exercises, a student will be able to do the following:

- Define epidemiology
- Summarize the historical evolution of epidemiology
- Describe the elements of a case definition and state the effect of changing the value of any of the elements
- List the key features and uses of descriptive epidemiology
- List the key features and uses of analytic epidemiology
- List the three components of the epidemiologic triad
- List and describe primary applications of epidemiology in public health practice
- List and describe the different modes of transmission of communicable disease in a population

Introduction

The word **epidemiology** comes from the Greek words **epi**, meaning "on or upon," **demos**, meaning "people," and **logos**, meaning "the study of." Many definitions have been proposed, but the following definition captures the underlying principles and the public health spirit of epidemiology:

> "Epidemiology is the **study** of the **distribution** and **determinants of health-related states or events** in **specified populations**, and the **application** of this study to the control of health problems." (17)

This definition of epidemiology includes several terms which reflect some of the important principles of the discipline. As you study this definition, refer to the description of these terms below.

Study. Epidemiology is a scientific discipline, sometimes called "the basic science of public health." It has, at its foundation, sound methods of scientific inquiry.

Distribution. Epidemiology is concerned with the frequency and pattern of health events in a population. Frequency includes not only the number of such events in a population, but also the rate or risk of disease in the population. The rate (number of events divided by size of the population) is critical to epidemiologists because it allows valid comparisons across different populations.

Pattern refers to the occurrence of health-related events by time, place, and personal characteristics.

- Time characteristics include annual occurrence, seasonal occurrence, and daily or even hourly occurrence during an epidemic.
- Place characteristics include geographic variation, urban-rural differences, and location of worksites or schools.
- Personal characteristics include demographic factors such as age, race, sex, marital status, and socioeconomic status, as well as behaviors and environmental exposures.

This characterization of the distribution of health-related states or events is one broad aspect of epidemiology called **descriptive epidemiology**. Descriptive epidemiology provides the *What*, *Who*, *When*, and *Where* of health-related events. It is discussed in more detail beginning on page 16.

Determinants. Epidemiology is also used to search for causes and other factors that influence the occurrence of health-related events. **Analytic epidemiology** attempts to provide the *Why* and *How* of such events by comparing groups with different rates of disease occurrence and with differences in demographic characteristics, genetic or immunologic make-up, behaviors, environmental exposures, and other so-called potential risk factors. Under ideal circumstances, epidemiologic findings provide sufficient evidence to direct swift and effective public health control and prevention measures.

Health-related states or events. Originally, epidemiology was concerned with epidemics of communicable diseases. Then epidemiology was extended to endemic communicable diseases and noncommunicable infectious diseases. More recently, epidemiologic methods have been applied to chronic diseases, injuries, birth defects, maternal-child health, occupational health, and environmental health. Now, even behaviors related to health and well-being (amount of exercise, seat-belt use, etc.) are recognized as valid subjects for applying epidemiologic methods. In these lessons we use the term "disease" to refer to the range of health-related states or events.

Specified populations. Although epidemiologists and physicians in clinical practice are both concerned with disease and the control of disease, they differ greatly in how they view "the patient." **Clinicians are concerned with the health of an individual; epidemiologists are concerned with the collective health of the people in a community or other area.** When faced with a patient with diarrheal disease, for example, the clinician and the epidemiologist have different responsibilities. Although both are interested in establishing the correct diagnosis, the clinician usually focuses on treating and caring for the individual. The epidemiologist focuses on the exposure (action or source that caused the illness), the number of other persons who may have been similarly exposed, the potential for further spread in the community, and interventions to prevent additional cases or recurrences.

Application. Epidemiology is more than "the study of." As a discipline within public health, epidemiology provides data for directing public health action. However, using epidemiologic data is an art as well as a science. Consider again the medical model used above: To treat a patient, a clinician must call upon experience and creativity as well as scientific knowledge. Similarly, an epidemiologist uses the scientific methods of descriptive and analytic epidemiology in "diagnosing" the health of a community, but also must call upon experience and creativity when planning how to control and prevent disease in the community.

Evolution

Although epidemiologic thinking has been traced from Hippocrates (circa 400 B.C.) through Graunt (1662), Farr, Snow (both mid-1800's), and others, the discipline did not blossom until the end of the Second World War. The contributions of some of these early and more recent thinkers are described below.

Hippocrates (circa 400 B.C.) attempted to explain disease occurrence from a rational instead of a supernatural viewpoint. In his essay entitled "On Airs, Waters, and Places," Hippocrates suggested that environmental and host factors such as behaviors might influence the development of disease.

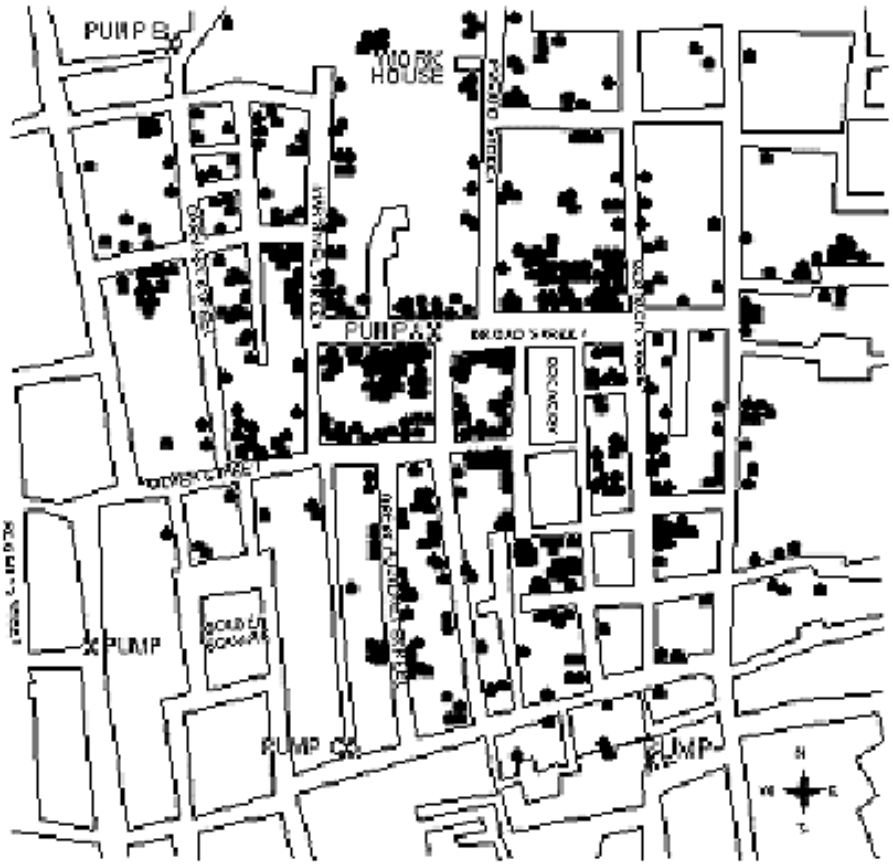
Another early contributor to epidemiology was John Graunt, a London haberdasher who published his landmark analysis of mortality data in 1662. He was the first to quantify patterns of birth, death, and disease occurrence, noting male-female disparities, high infant mortality, urban-rural differences, and seasonal variations. No one built upon Graunt's work until the mid-1800's, when William Farr began to systematically collect and analyze Britain's mortality statistics. Farr, considered the father of modern vital statistics and surveillance, developed many of the basic practices used today in vital statistics and disease classification. He extended the epidemiologic analysis of morbidity and mortality data, looking at the effects of marital status, occupation, and altitude. He also developed many epidemiologic concepts and techniques still in use today.

Meanwhile, an anesthesiologist named John Snow was conducting a series of investigations in London that later earned him the title "the father of field epidemiology." Twenty years before the development of the microscope, Snow conducted studies of cholera outbreaks both to discover the cause of disease and to prevent its recurrence. Because his work classically illustrates the sequence from descriptive epidemiology to hypothesis generation to hypothesis testing (analytic epidemiology) to application, we will consider two of his efforts in detail.

Snow conducted his classic study in 1854 when an epidemic of cholera developed in the Golden Square of London. He began his investigation by determining where in this area persons with cholera lived and worked. He then used this information to map the distribution of cases on what epidemiologists call a spot map. His map in shown in Figure 1.1.

Because Snow believed that water was a source of infection for cholera, he marked the location of water pumps on his spot map, and then looked for a relationship between the distribution of cholera case households and the location of pumps. He noticed that more case households clustered around Pump A, the Broad Street pump, than around Pump B or C, and he concluded that the Broad Street pump was the most likely source of infection. Questioning residents who lived near the other pumps, he found that they avoided Pump B because it was grossly contaminated, and that Pump C was located too inconveniently for most residents of the Golden Square area. From this information, it appeared to Snow that the Broad Street pump was probably the primary source of water for most persons with cholera in the Golden Square area. He realized, however, that it was too soon to draw that conclusion because the map showed no cholera cases in a two-block area to the east of the Broad Street pump. Perhaps no one lived in that area. Or perhaps the residents were somehow protected.

Figure 1.1
Distribution of cholera cases in the Golden Square area of London, August-September 1854



Upon investigating, Snow found that a brewery was located there and that it had a deep well on the premises where brewery workers, who also lived in the area, got their water. In addition, the brewery allotted workers a daily quota of malt liquor. Access to these uncontaminated rations could explain why none of the brewery's employees contracted cholera.

To confirm that the Broad Street pump was the source of the epidemic, Snow gathered information on where persons with cholera had obtained their water. Consumption of water from the Broad Street pump was the one common factor among the cholera patients. According to legend, Snow removed the handle of that pump and aborted the outbreak.

Figure 1.2
Water contaminated with deadly cholera flowed from the Broad Street pump

Figure not shown.

Snow's second major contribution involved another investigation of the same outbreak of cholera that occurred in London in 1854. In a London epidemic in 1849, Snow had noted that districts with the highest mortalities had water supplied by two companies: the Lambeth Company and the Southwark and Vauxhall Company. At that time, both companies obtained water from the Thames River, at intake points that were below London. In 1852, the Lambeth Company moved their water works to above London, thus obtaining water that was free of London sewage. When cholera returned to London in 1853, Snow realized the Lambeth Company's relocation of its intake point would allow him to compare districts that were supplied with water from above London with districts that received water from below London. Table 1.1 shows what Snow found when he made that comparison for cholera mortality over a 7-week period during the summer of 1854.

Table 1.1
Mortality from cholera in the districts of London supplied by the Southwark and Vauxhall and the Lambeth Companies, July 9-August 26, 1854

Districts with Water Supplied by	Population (1851 Census)	Deaths from Cholera	Cholera Death Rate per 1,000 Population
Southwark and Vauxhall Co. only	167,654	844	5.0
Lambeth Co. only	19,133	18	0.9
Both companies	300,149	652	2.2

Source: 27

The data in Table 1.1 show that the risk of death from cholera was more than 5 times higher in districts served only by the Southwark and Vauxhall Company than in those served only by the Lambeth Company. Interestingly, the mortality rate in districts supplied by both companies fell between the rates for districts served exclusively by either company. These data were consistent with the hypothesis that water obtained from the Thames below London was a source of cholera. Alternatively, the populations supplied by the two companies may have differed on a number of other factors which affected their risk of cholera.

To test his water supply hypothesis, Snow focused on the districts served by both companies, because the households within a district were generally comparable except for water supply company. In these districts, Snow identified the water supply company for every house in which a death from cholera had occurred during the 7-week period. Table 1.2 shows his findings.

This further study added support to Snow's hypothesis, and demonstrates the sequence of steps used today to investigate outbreaks of disease. Based on a characterization of the cases and population at risk by time, place, and person, Snow developed a testable hypothesis. He then tested this hypothesis with a more rigorously designed study, ensuring that the groups to be compared were comparable. After this study, efforts to control the epidemic were directed at changing the location of the water intake of the Southwark and Vauxhall Company to avoid sources of contamination. Thus, with no knowledge of the existence of microorganisms, Snow demonstrated through epidemiologic studies that water could serve as a vehicle for transmitting

Table 1.2
Mortality from cholera in London related to the water supply of individual houses in districts served by both the Southwark and Vauxhall Company and the Lambeth Company, July 9-August 26, 1854

Water Supply of Individual House	Population (1851 Census)	Deaths from Cholera	Death Rate per 1,000 Population
Southwark and Vauxhall Co.	98,862	419	4.2
Lambeth Co.	154,615	80	0.5

Source: 27

cholera and that epidemiologic information could be used to direct prompt and appropriate public health action.

In the mid- and late-1800's, many others in Europe and the United States began to apply epidemiologic methods to investigate disease occurrence. At that time, most investigators focused on acute infectious diseases. In the 1900's, epidemiologists extended their methods to noninfectious diseases. The period since the Second World War has seen an explosion in the development of research methods and the theoretical underpinnings of epidemiology, and in the application of epidemiology to the entire range of health-related outcomes, behaviors, and even knowledge and attitudes. The studies by Doll and Hill (13) linking smoking to lung cancer and the study of cardiovascular disease among residents of Framingham, Massachusetts (12), are two examples of how pioneering researchers have applied epidemiologic methods to chronic disease since World War II. Finally, during the 1960's and early 1970's health workers applied epidemiologic methods to eradicate smallpox worldwide. This was an achievement in applied epidemiology of unprecedented proportions.

Today, public health workers throughout the world accept and use epidemiology routinely. Epidemiology is often practiced or used by non-epidemiologists to characterize the health of their communities and to solve day-to-day problems. This landmark in the evolution of the discipline is less dramatic than the eradication of smallpox, but it is no less important in improving the health of people everywhere.

Uses

Epidemiology and the information generated by epidemiologic methods have many uses. These uses are categorized and described below.

Population or community health assessment. To set policy and plan programs, public health officials must assess the health of the population or community they serve and must determine whether health services are available, accessible, effective, and efficient. To do this, they must find answers to many questions: What are the actual and potential health problems in the community? Where are they? Who is at risk? Which problems are declining over time? Which ones are increasing or have the potential to increase? How do these patterns relate to the level and distribution of services available? The methods of descriptive and analytic epidemiology provide ways to answer these and other questions. With answers provided through the application of epidemiology, the officials can make informed decisions that will lead to improved health for the population they serve.

Individual decisions. People may not realize that they use epidemiologic information in their daily decisions. When they decide to stop smoking, take the stairs instead of the elevator, order a salad instead of a cheeseburger with French fries, or choose one method of contraception instead of another, they may be influenced, consciously or unconsciously, by epidemiologists' assessment of risk. Since World War II, epidemiologists have provided information related to all those decisions. In the 1950's, epidemiologists documented the increased risk of lung cancer among smokers; in the 1960's and 1970's, epidemiologists noted a variety of benefits and risks associated with different methods of birth control; in the mid-1980's, epidemiologists identified the increased risk of human immunodeficiency virus (HIV) infection associated with certain sexual and drug-related behaviors; and, more positively, epidemiologists continue to document the role of exercise and proper diet in reducing the risk of heart disease. These and hundreds of other epidemiologic findings are directly relevant to the choices that people make every day, choices that affect their health over a lifetime.

Completing the clinical picture. When studying a disease outbreak, epidemiologists depend on clinical physicians and laboratory scientists for the proper diagnosis of individual patients. But epidemiologists also contribute to physicians' understanding of the clinical picture and natural history of disease. For example, in late 1989 three patients in New Mexico were diagnosed as having myalgias (severe muscle pains in chest or abdomen) and unexplained eosinophilia (an increase in the number of one type of white blood cell). Their physician could not identify the cause of their symptoms, or put a name to the disorder. Epidemiologists began looking for other cases with similar symptoms, and within weeks had found enough additional cases of eosinophilia-myalgia syndrome to describe the illness, its complications, and its rate of mortality. Similarly, epidemiologists have documented the course of HIV infection, from the initial exposure to the development of a wide variety of clinical syndromes that include acquired immunodeficiency syndrome (AIDS). They have also documented the numerous conditions that are associated with cigarette smoking—from pulmonary and heart disease to lung and cervical cancer.

Search for causes. Much of epidemiologic research is devoted to a search for causes, factors which influence one's risk of disease. Sometimes this is an academic pursuit, but more often the goal is to identify a cause so that appropriate public health action might be taken. It has been said that epidemiology can never *prove* a causal relationship between an exposure and a disease. Nevertheless, epidemiology often provides enough information to support effective action. Examples include John Snow's removal of the pump handle and the withdrawal of a specific brand of tampon that was linked by epidemiologists to toxic shock syndrome. Just as often, epidemiology and laboratory science converge to provide the evidence needed to establish causation. For example, a team of epidemiologists were able to identify a variety of risk factors during an outbreak of a pneumonia among persons attending the American Legion Convention in Philadelphia in 1976. However, the outbreak was not "solved" until the Legionnaires' bacillus was identified in the laboratory almost 6 months later.

Exercise 1.1

In the early 1980's, epidemiologists recognized that AIDS occurred most frequently in men who had sex with men and in intravenous drug users.

Describe how this information might be used for each of the following:

a. Population or community health assessment

b. Individual decisions

c. Search for causes

Answers on page 62.

The Epidemiologic Approach

Like a newspaper reporter, an epidemiologist determines *What*, *When*, *Where*, *Who*, and *Why*. However, the epidemiologist is more likely to describe these concepts in slightly different terms: **case definition**, **time**, **place**, **person**, and **causes**.

Case Definition

A **case definition** is a set of standard criteria for deciding whether a person has a particular disease or other health-related condition. By using a standard case definition we ensure that every case is diagnosed in the same way, regardless of when or where it occurred, or who identified it. We can then compare the number of cases of the disease that occurred in one time or place with the number that occurred at another time or another place. For example, with a standard case definition, we can compare the number of cases of hepatitis A that occurred in New York City in 1991 with the number that occurred there in 1990. Or we can compare the number of cases that occurred in New York in 1991 with the number that occurred in San Francisco in 1991. With a standard case definition, when we find a difference in disease occurrence, we know it is likely to be a real difference rather than the result of differences in how cases were diagnosed.

Appendix C shows case definitions for several diseases of public health importance. A case definition consists of clinical criteria and, sometimes, limitations on time, place, and person. The clinical criteria usually include confirmatory laboratory tests, if available, or combinations of symptoms (subjective complaints), signs (objective physical findings), and other findings. For example, on page 13 see the case definition for rabies that has been excerpted from Appendix C; notice that it requires laboratory confirmation.

Compare this with the case definition for Kawasaki syndrome provided in Exercise 1.3 (page 15). Kawasaki syndrome is a childhood illness with fever and rash that has no known cause and no specifically distinctive laboratory findings. Notice that its case definition is based on the presence of fever, at least four of five specified clinical findings, and the lack of a more reasonable explanation.

A case definition may have several sets of criteria, depending on how certain the diagnosis is. For example, during an outbreak of measles, we might classify a person with a fever and rash as having a suspect, probable, or confirmed case of measles, depending on what additional evidence of measles was present. In other situations, we temporarily classify a case as suspect or probable until laboratory results are available. When we receive the laboratory report, we then reclassify the case as either confirmed or “not a case,” depending on the lab results. In the midst of a large outbreak of a disease caused by a known agent, we may permanently classify some cases as suspect or probable, because it is unnecessary and wasteful to run laboratory tests on every patient with a consistent clinical picture and a history of exposure (e.g., chickenpox). Case definitions should not rely on laboratory culture results alone, since organisms are sometimes present without causing disease.

Case definitions may also vary according to the purpose for classifying the occurrences of a disease. For example, health officials need to know as soon as possible if anyone has symptoms of plague or foodborne botulism so that they can begin planning what actions to take. For such rare but potentially severe communicable diseases, where it is important to identify every possible case, health officials use a **sensitive**, or "loose" case definition. On the other hand, investigators of the causes of a disease outbreak want to be certain that any person included in the investigation really had the disease. The investigator will prefer a **specific** or "strict" case definition. For instance, in an outbreak of *Salmonella agona*, the investigators would be more likely to identify the source of the infection if they included only persons who were confirmed to have been infected with that organism, rather than including anyone with acute diarrhea, because some persons may have had diarrhea from a different cause. In this setting, the only disadvantage of a strict case definition is an underestimate of the total number of cases.

Rabies, Human

Clinical description

Rabies is an acute encephalomyelitis that almost always progresses to coma or death within 10 days of the first symptom.

Laboratory criteria for diagnosis

- Detection by direct fluorescent antibody of viral antigens in a clinical specimen (preferably the brain or the nerves surrounding hair follicles in the nape of the neck), or
- Isolation (in cell culture or in a laboratory animal) of rabies virus from saliva, cerebrospinal fluid (CSF), or central nervous system tissue, or
- Identification of a rabies-neutralizing antibody titer greater than or equal to 5 (complete neutralization) in the serum or CSF of an unvaccinated person

Case classification

Confirmed: a clinically compatible illness that is laboratory confirmed

Comment

Laboratory confirmation by all of the above methods is strongly recommended.

Source: 3

Exercise 1.2

In the case definition for an apparent outbreak of trichinosis, investigators used the following classifications:

Clinical criteria

Confirmed case: signs and symptoms plus laboratory confirmation

Probable case: acute onset of at least three of the following four features: myalgia, fever, facial edema, or eosinophil count greater than 500/mm^3

Possible case: acute onset of two of the four features *plus* a physician diagnosis of trichinosis

Suspect case: unexplained eosinophilia

Not a case: failure to fulfill the criteria for a confirmed, probable, possible, or suspect case

Time

Onset after October 26, 1991

Place

Metropolitan Atlanta

Person

Any

Assign the appropriate classification to each of the persons included in the line listing below. (All were residents of Atlanta with acute onset of symptoms in November.)

ID #	Last name	myalgia	fever	facial edema	eosinophil count	Physician diagnosis	Lab confirm	Classification
1	Abels	yes	yes	no	495	trichinosis	yes	----------
2	Baker	yes	yes	yes	pending	trichinosis ?	pending	----------
3	Corey	yes	yes	no	1,100	trichinosis	pending	----------
4	Dale	yes	no	no	2,050	EMS ?	pending	----------
5	Ring	yes	no	no	600	trichinosis	not done	----------

Answers on page 62.

Exercise 1.3

The following is the official case definition for Kawasaki syndrome that is recommended by CDC:

Kawasaki Syndrome

Clinical case definition

A febrile illness of greater than or equal to 5 days' duration, with at least four of the five following physical findings and no other more reasonable explanation for the observed clinical findings:

- Bilateral conjunctival injection
- Oral changes (erythema of lips or oropharynx, strawberry tongue, or fissuring of the lips)
- Peripheral extremity changes (edema, erythema, or generalized or periungual desquamation)
- Rash
- Cervical lymphadenopathy (at least one lymph node greater than or equal to 1.5 cm in diameter)

Laboratory criteria for diagnosis

None

Case classification

Confirmed: a case that meets the clinical case definition

Comment

If fever disappears after intravenous gamma globulin therapy is started, fever may be of less than 5 days' duration, and the clinical case definition may still be met.

Source: 3

Discuss the pros and cons of this case definition for the purposes listed below. (For a brief description of Kawasaki syndrome, see Benenson's *Control of Communicable Diseases in Man*).

a. diagnosing and treating individual patients

b. tracking the occurrence of the disease for public health records

c. doing research to identify the cause of the disease

Answers on page 63.

Numbers and Rates

A basic task of a health department is counting cases in order to measure and describe morbidity. When physicians diagnose a case of a reportable disease they send a report of the case to their local health department. These reports are legally required to contain information on time (when the case occurred), place (where the patient lived), and person (the age, race, and sex of the patient). The health department combines the reports and summarizes the information by time, place, and person. From these summaries, the health department determines the extent and patterns of disease occurrence in the area, and identifies clusters or outbreaks of disease.

A simple count of cases, however, does not provide all the information a health department needs. To compare the occurrence of a disease at different locations or during different times, a health department converts the case counts into **rates**, which relate the number of cases to the size of the population where they occurred.

Rates are useful in many ways. With rates, the health department can identify groups in the community with an elevated risk of disease. These so-called **high-risk groups** can be further assessed and targeted for special intervention; the groups can be studied to identify **risk factors** that are related to the occurrence of disease. Individuals can use knowledge of these risk factors to guide their decisions about behaviors that influence health. (Lesson 2 discusses rates in more detail.)

Descriptive Epidemiology

In descriptive epidemiology, we organize and summarize data according to time, place, and person. These three characteristics are sometimes called the **epidemiologic variables**.

Compiling and analyzing data by time, place, and person is desirable for several reasons. First, the investigator becomes intimately familiar with the data and with the extent of the public health problem being investigated. Second, this provides a detailed description of the health of a population that is easily communicated. Third, such analysis identifies the populations that are at greatest risk of acquiring a particular disease. This information provides important clues to the causes of the disease, and these clues can be turned into testable hypotheses.

Time

Disease rates change over time. Some of these changes occur regularly and can be predicted. For example, the seasonal increase of influenza cases with the onset of cold weather is a pattern that is familiar to everyone. By knowing when flu outbreaks will occur, health departments can time their flu shot campaigns effectively. Other disease rates make unpredictable changes. By examining events that precede a disease rate increase or decrease, we may identify causes and appropriate actions to control or prevent further occurrence of the disease.

We usually show time data as a graph. We put the number or rate of cases or deaths on the vertical, *y-axis*; we put the time periods along the horizontal, *x-axis*. We often indicate on a graph when events occurred that we believe are related to the particular health problem described in the graph. For example, we may indicate the period of exposure or the date control measures were implemented. Such a graph provides a simple visual depiction of the relative size of a problem, its past trend and potential future course, as well as how other events may have affected the problem. Studying such a graph often gives us insights into what may have caused the problem.

Depending on what event we are describing, we may be interested in a period of years or decades, or we may limit the period to days, weeks, or months when the number of cases reported is greater than normal (an **epidemic period**). For some conditions—for many chronic diseases, for example—we are interested in long-term changes in the number of cases or rate of the condition. For other conditions, we may find it more revealing to look at the occurrence of the condition by season, month, day of the week, or even time of day. For a newly recognized problem, we need to assess the occurrence of the problem over time in a variety of ways until we discover the most appropriate and revealing time period to use. Some of the common types of time-related graphs are further described below.

Secular (long-term) trends. Graphing the annual cases or rate of a disease over a period of years shows long-term or **secular trends** in the occurrence of the disease. We commonly use these trends to suggest or predict the future incidence of a disease. We also use them in some instances to evaluate programs or policy decisions, or to suggest what caused an increase or decrease in the occurrence of a disease, particularly if the graph indicates when related events took place, as Figure 1.3 does. (NOTE: If you have difficulty understanding the graphs in this lesson, refer to Lesson 4 for information on Tables, Graphs, and Charts.)

Seasonality. By graphing the occurrence of a disease by week or month over the course of a year or more we can show its seasonal pattern, if any. Some diseases are known to have characteristic seasonal distributions; for example, as mentioned earlier, the number of reported cases of influenza typically increases in winter. Seasonal patterns may suggest hypotheses about how the infection is transmitted, what behavioral factors increase risk, and other possible contributors to the disease or condition. The seasonal pattern of farm tractor fatalities is shown in Figure 1.4. What factors might contribute to its seasonal pattern?

Notice that Figure 1.5 shows the occurrence of a disease event over the course of a year. Before reading further, examine the pattern of cases in this graph and decide whether you can conclude from this graph that the disease will have this same pattern every year.

From only the single year’s data in Figure 1.5, it is difficult to conclude whether the peak in June represents a characteristic seasonal pattern that would be repeated yearly, or whether it is simply an epidemic that occurred in the spring and summer of that particular year. You would need more than one year’s data before you could conclude that the pattern shown there represents the seasonal variation in this disease.

Figure 1.3
Malaria by year, United States, 1930-1990

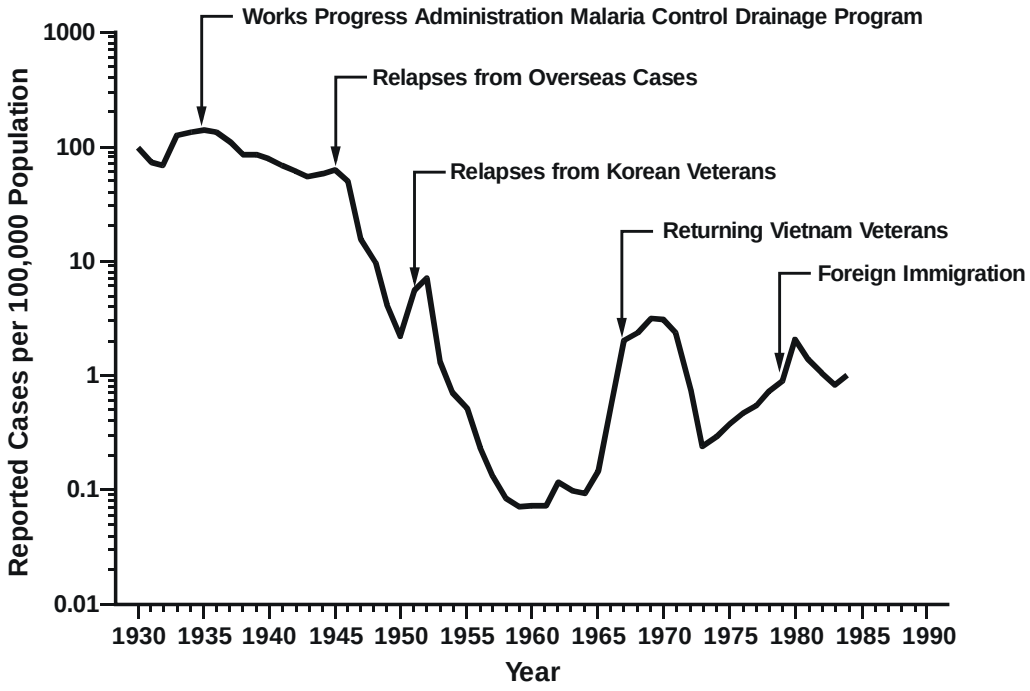


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Figure 1.4
Fatalities associated with farm tractor injuries by month of death, Georgia, 1971-1981

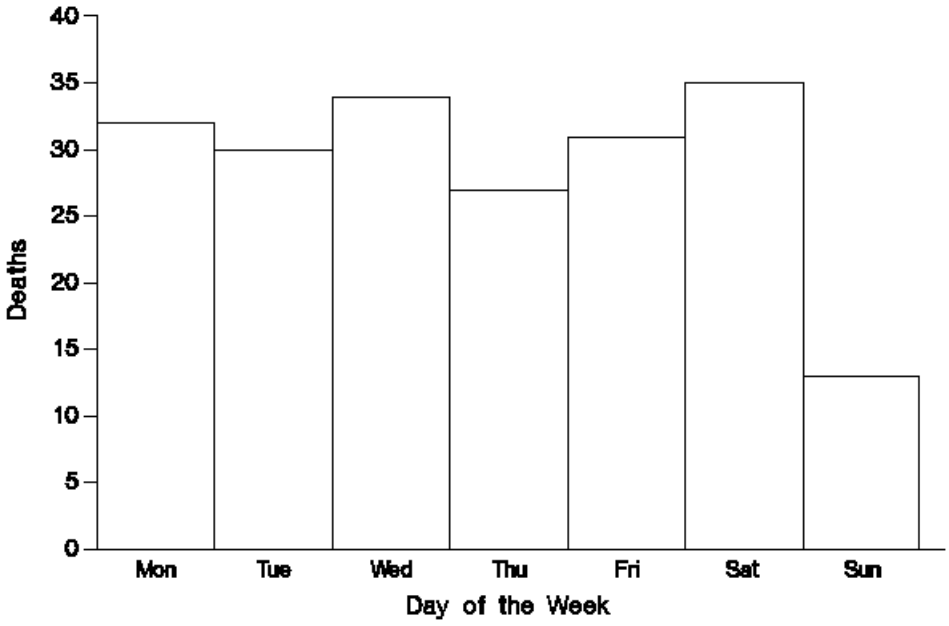

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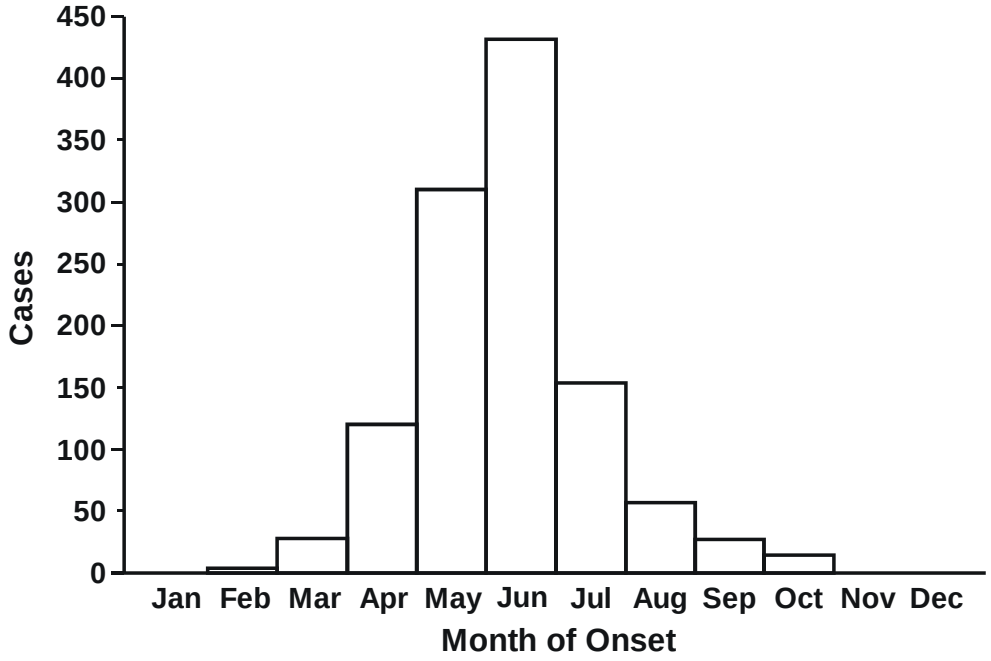
Figure 1.5
Cases of an unknown disease by month of onset



Source: 14

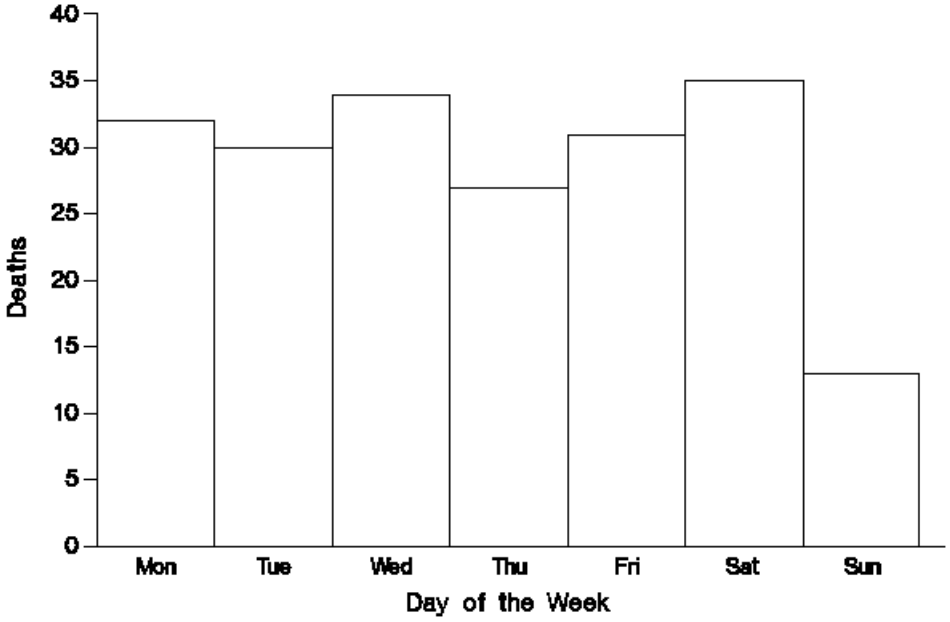
Day of week and time of day. Displaying data by days of the week or time of day may also be informative. Analysis at these shorter time periods is especially important for conditions that are potentially related to occupational or environmental exposures, which may occur at regularly scheduled intervals. In Figure 1.6, farm tractor fatalities are displayed by days of the week. Does this analysis at shorter time periods suggest any hypothesis?

In Figure 1.6 the number of farm tractor fatalities on Sundays is about half the number on the other days. We can only speculate why this is. One reasonable hypothesis is that farmers spend fewer hours on their tractors on Sundays than on the other days.

Examine the pattern of fatalities associated with farm tractor injuries by hour in Figure 1.7. How might you explain the morning peak at 11:00 AM, the dip at noon, and the afternoon peak at 4:00 PM?

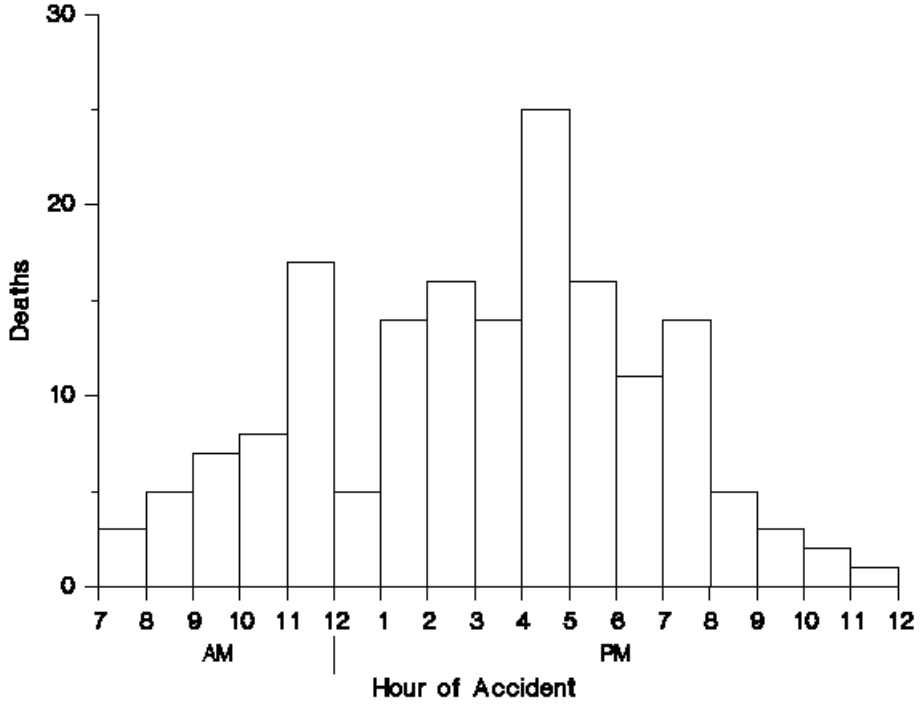
Epidemic period. To show the time course of a disease outbreak or epidemic, we use a specialized graph called an **epidemic curve**. As with the other graphs you have seen in this section, we place the number of cases on the vertical axis and time on the horizontal axis. For time, we use either the time of onset of symptoms or the date of diagnosis. For very acute diseases with short incubation periods (i.e., time period between exposure and onset of symptoms is short), we may show time as the hour of onset. For diseases with longer incubation periods, we might show time in 1-day, 2-day, 3-day, 1-week, or other appropriate intervals. Figure 1.8 shows an epidemic curve that uses a 3-day interval for a foodborne disease outbreak. Notice how the cases are stacked in adjoining columns. By convention, we use this format, called a **histogram**, for epidemic curves. The shape and other features of an epidemic curve can suggest hypotheses about the time and source of exposure, the mode of transmission, and the causative agent. Epidemic curves are discussed in more detail in Lessons 4 and 6.

Figure 1.6
Fatalities associated with farm tractor injuries
by day of death, Georgia, 1971-1981



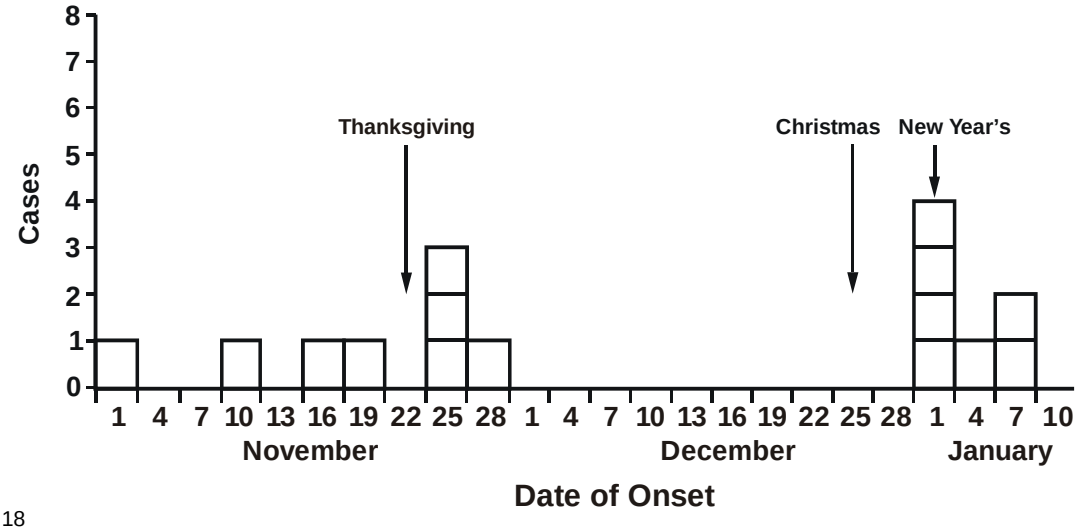
Source: 15

Figure 1.7
Fatalities associated with farm tractor injuries
by time of day, Georgia, 1971-1981



Source: 15

Figure 1.8
Date of onset of illness in patients with culture-confirmed *Yersinia enterocolitica* infections, Atlanta, November 1, 1988-January 10, 1989



Source: 18

Place

We describe a health event by place to gain insight into the geographical extent of the problem. For place, we may use place of residence, birthplace, place of employment, school district, hospital unit, etc., depending on which may be related to the occurrence of the health event. Similarly, we may use large or small geographic units: country, state, county, census tract, street address, map coordinates, or some other standard geographical designation. Sometimes, we may find it useful to analyze data according to place categories such as urban or rural, domestic or foreign, and institutional or noninstitutional.

Not all analyses by place will be equally informative. For example, examine the data shown in Table 1.3. Where were the malaria cases diagnosed? What "place" does the table break the data down by? Would it have been more or less useful to analyze the data according to the "state of residence" of the cases?

We believe that it provides more useful information to show the data in Table 1.3 by where the infection was acquired than it would have to show where the case-patients lived. By analyzing the malaria cases by place of acquisition, we can see where the risk of acquiring malaria is high.

By analyzing data by place, we can also get an idea of where the agent that causes a disease normally lives and multiplies, what may carry or transmit it, and how it spreads. When we find that the occurrence of a disease is associated with a place, we can infer that factors that increase the risk of the disease are present either in the persons living there (**host factors**) or in the environment, or both. For example, diseases that are passed from one person to another spread more rapidly in urban areas than in rural ones, mainly because the greater crowding in urban areas provides more opportunities for susceptible people to come into contact with someone who

Table 1.3
Malaria cases by distribution of Plasmodium species and area of acquisition, United States, 1989

	Species			
Area of Acquisition	**Vivax**	**Falciparum**	**Other**	**Total**
Africa	52	382	64	498
Asia	207	44	29	280
Central America & Caribbean	107	14	9	130
North America	131	3	13	147
(United States)	(5)	(0)	(0)	(5)
South America	10	1	2	13
Oceania	19	2	5	26
Unknown	6	2	0	8
Total	**532**	**448**	**122**	**1,102**

Source: 6

is infected. On the other hand, diseases that are passed from animals to humans often occur in greater numbers in rural and suburban areas because people in those areas are more likely to come into contact with disease-carrying animals, ticks, and the like. For example, perhaps Lyme disease has become more common because people have moved to wooded areas where they come into contact with infected deer ticks.

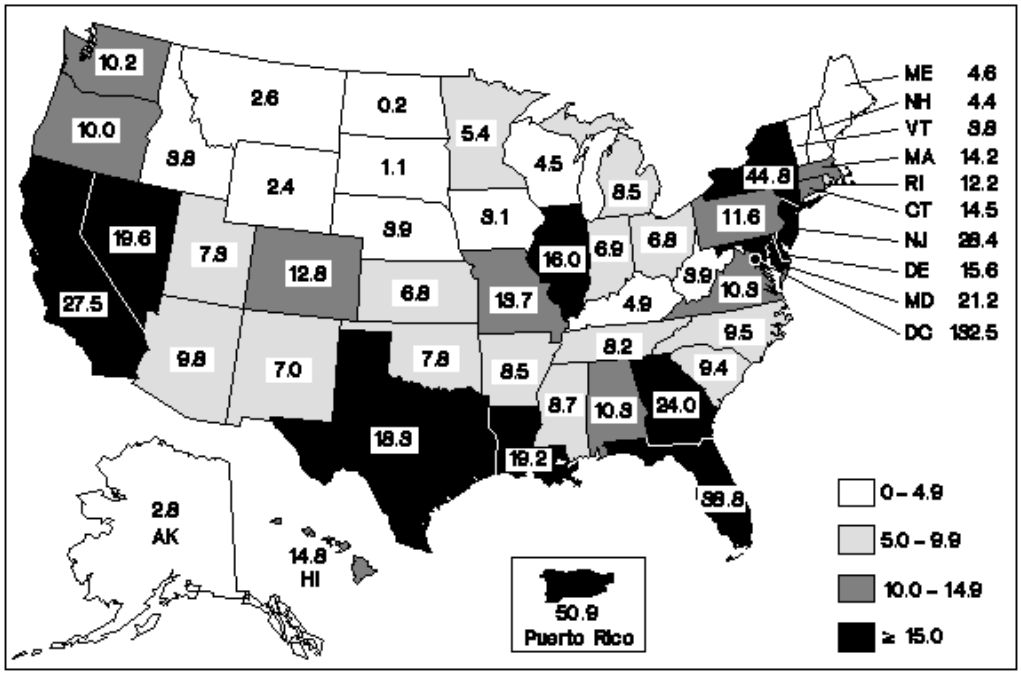
Although we can show data by place in a table—as Table 1.3 does—it is often better to show it pictorially in a map. On a map, we can use different shadings, color, or line patterns to indicate how a disease or health event has different numbers or rates of occurrence in different areas, as in Figure 1.9.

For a rare disease or outbreak, we often find it useful to prepare a **spot map**, like Snow's map of the Golden Square of London (Figure 1.1, page 5), in which we mark with a dot or an X the relation of each case to a place that is potentially relevant to the health event being investigated—such as where each case lived or worked. We may also label other sites on a spot map, such as where we believe cases may have been exposed, to show the orientation of cases within the area mapped.

Figure 1.10 is a spot map for an outbreak of mumps that occurred among employees of the Chicago futures exchanges. Study the location of each case in relation to other cases and to the trading pits. The four numbered areas delineated with heavy lines are the trading pits. Do the location of cases on the spot map lead you to any hypothesis about the source of infection?

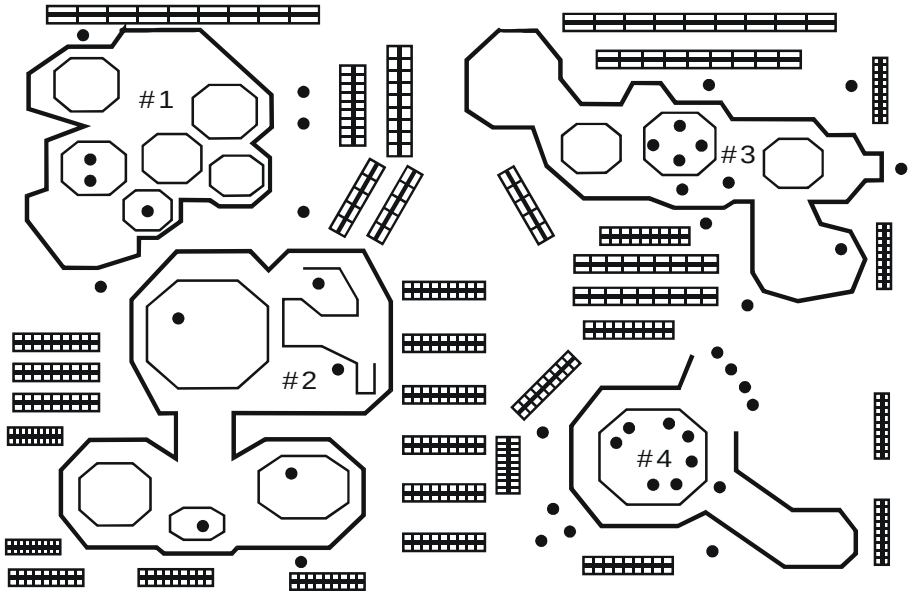
You probably observed that the cases occurred primarily among those working in trading pits #3 and #4. This clustering of illness within trading pits provides indirect evidence that the mumps was transmitted person-to person.

Figure 1.9
AIDS cases per 100,000 population,
United States, July 1991-June 1992



Source: 4

Figure 1.10
Mumps cases in trading pits of exchange A, Chicago, Illinois,
August 18-December 25, 1987



Pit areas are numbered and delineated by heavy lines.
Individual trading pits within pit areas are outlined by light lines.

Source: CDC, unpublished data, 1988

Person

In descriptive epidemiology, when we organize or analyze data by "person" there are several person categories available to us. We may use inherent characteristics of people (for example, age, race, sex), their acquired characteristics (immune or marital status), their activities (occupation, leisure activities, use of medications/tobacco/drugs), or the conditions under which they live (socioeconomic status, access to medical care). These categories determine to a large degree who is at greatest risk of experiencing some undesirable health condition, such as becoming infected with a particular disease organism. We may show person data in either tables or graphs.

In analyzing data by person, we often must try a number of different person categories before we find which are the most useful and enlightening. Age and sex are most critical; we almost always analyze data according to these. Depending on what health event we are studying, we may or may not break the data down by the other attributes. Often we analyze data into more than one category simultaneously; for example, we may look at age and sex simultaneously to see if the sexes differ in how they develop a condition that increases with age—as they do for heart disease.

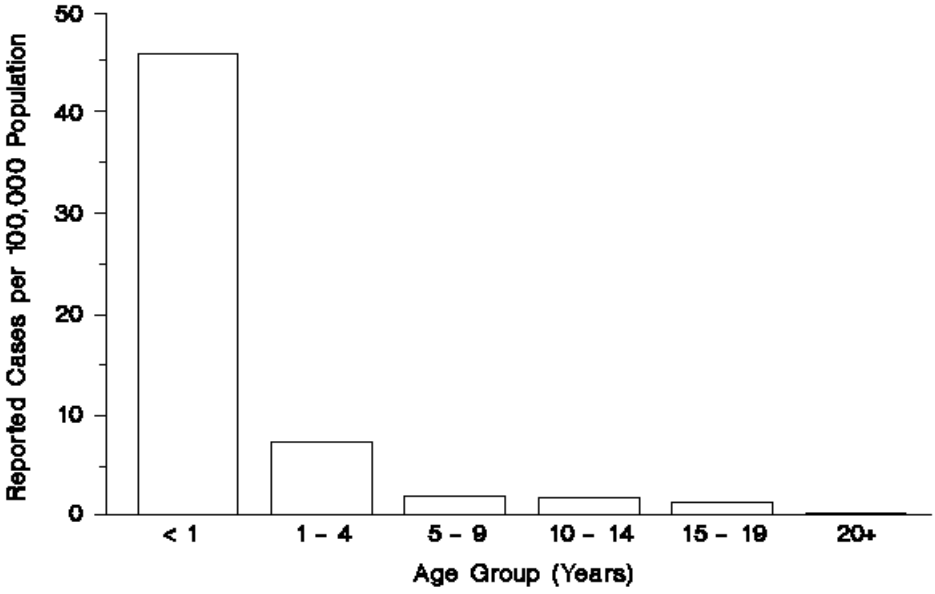
Age. Age is probably the single most important "person" attribute, because almost every health-related event or state varies with age. A number of factors that also vary with age are behind this association: susceptibility, opportunity for exposure, latency or incubation period of the disease, and physiologic response (which affects, among other things, disease development).

When we analyze data by age, we try to use age groups that are narrow enough to detect any age-related patterns that may be present in the data. In an initial breakdown by age, we commonly use 5-year age intervals: 0 to 4 years, 5 to 9, 10 to 14, and so on. Larger intervals, such as 0 to 19 years, 20 to 39, etc., can conceal variations related to age which we need to know to identify the true population at risk. Sometimes, even the commonly used 5-year age groups can hide important differences. Take time to examine Figure 1.11a, for example, before you read ahead. What does the information in this figure suggest health authorities should do to reduce the number of cases of whooping cough? Where should health authorities focus their efforts?

You probably said that health authorities should focus on immunizing infants against whooping cough during the first year of life. Now, examine Figure 1.11b. This figure shows the same data but they are presented in the usual 5-year intervals. Based on Figure 1.11b where would you have suggested that health authorities focus their efforts? Would this recommendation have been as effective and efficient in reducing cases of whooping cough?

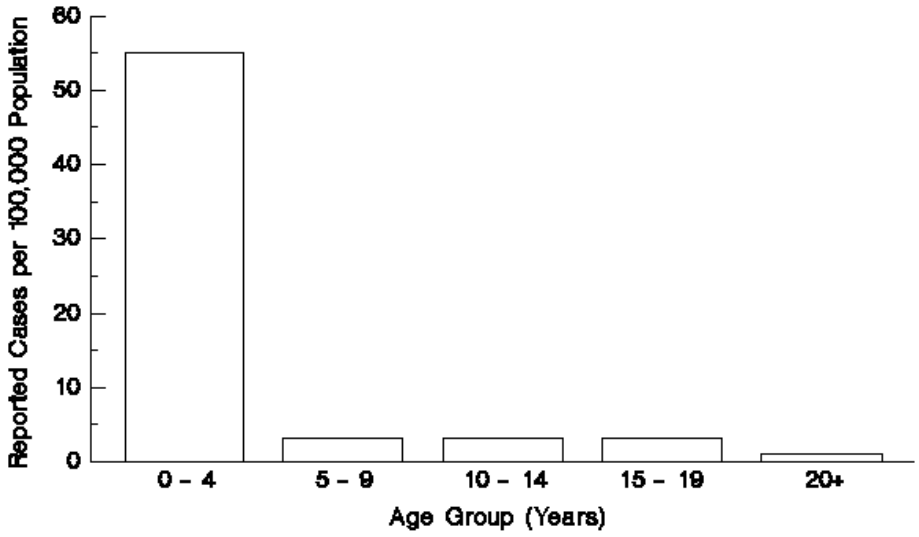
You probably said that health authorities should immunize infants and children before the age of 5. That recommendation would be effective, but it would not be efficient. You would be immunizing more children than actually necessary and wasting resources.

Figure 1.11a
Pertussis (whooping cough) incidence by age group, United States, 1989



Source: 9

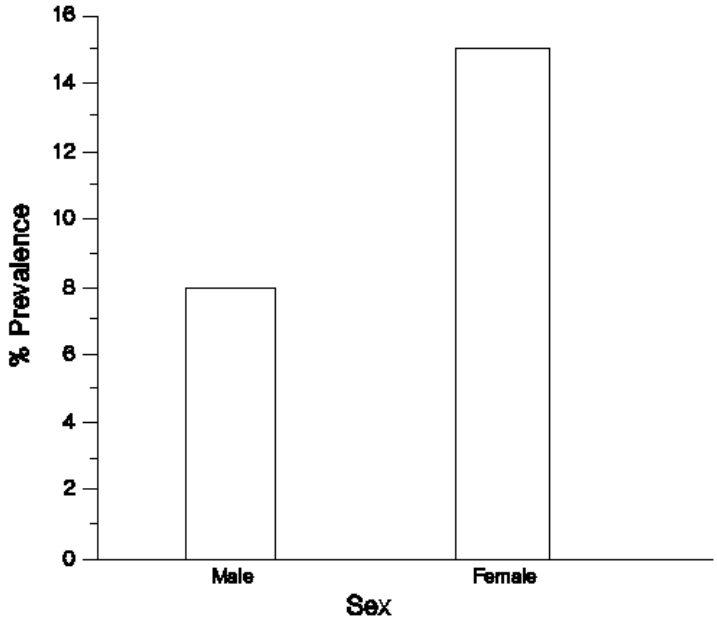
Figure 1.11b
Pertussis (whooping cough) incidence by age group, United States, 1989



Source: 9

Sex. In general, males have higher rates of illness and death than females do for a wide range of diseases. For some diseases, this sex-related difference is because of genetic, hormonal, anatomic, or other inherent differences between the sexes. These inherent differences affect their susceptibility or physiologic responses. For example, premenopausal women have a lower risk of heart disease than men of the same age. This difference is attributed to higher estrogen levels in women. On the other hand, the sex-related differences in the occurrence of many diseases reflect differences in opportunity or levels of exposure. For example, Figure 1.12 shows that hand/wrist disorders occur almost twice as often in females than in males. What are some sex-related differences that would cause a higher level of this disorder in females?

Figure 1.12
Prevalence of hand/wrist cumulative trauma disorder by sex, Newspaper Company A, 1990



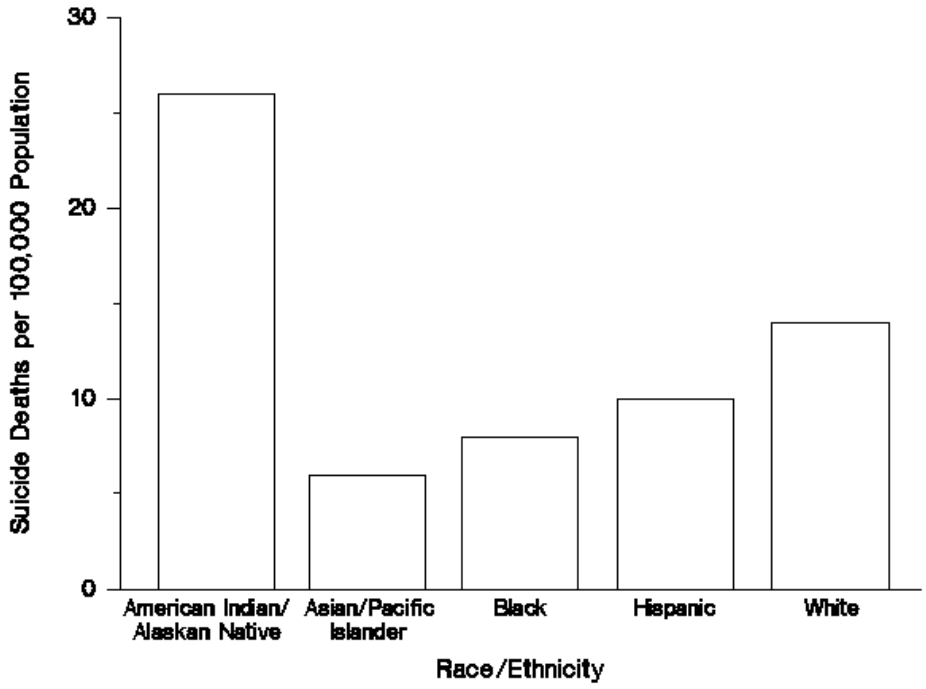
Source: NIOSH, unpublished data, 1991

You may have attributed the higher level of disorders in females to their higher level of exposure to occupational activities that require repetitive hand/wrist motion such as typing or keyboard entry. With occupationally-related illness, we usually find that sex differences reflect the number of workers in those occupations. You may also have attributed the higher level of disorders in females to anatomical differences; perhaps women's wrists are more susceptible to hand/wrist disorders.

Ethnic and racial groups. In examining epidemiologic data, we are interested in any group of people who have lived together long enough to acquire common characteristics, either biologically or socially. Several terms are commonly used to identify such groups: race, nationality, religion, or local reproductive or social groups, such as tribes and other geographically or socially isolated groups.

Differences that we observe in racial, ethnic, or other groups may reflect differences in their susceptibility or in their exposure, or they may reflect differences in other factors that bear more directly on the risk of disease, such as socioeconomic status and access to health care. In Figure 1.13, the rates of suicide for five groups of people are displayed.

Figure 1.13
Suicide death rates for persons 15 to 24 years of age according to race/ethnicity, United States, 1988



Source: 22

Clearly this graph displays a range of suicide death rates for the five groups of people. These data provide direction for prevention programs and for future studies to explain the differences.

Socioeconomic status. Socioeconomic status is difficult to quantify. It is made up of many variables such as occupation, family income, educational achievement, living conditions, and social standing. The variables that are easiest to measure may not reflect the overall concept. Nevertheless, we commonly use occupation, family income, and educational achievement, while recognizing that these do not measure socioeconomic status precisely.

The frequency of many adverse health conditions increases with decreasing socioeconomic status. For example, tuberculosis is more common among persons in lower socioeconomic strata. Infant mortality and time lost from work due to disability are both associated with lower income. These patterns may reflect more harmful exposures, lower resistance, and less access to health

care. Or they may in part reflect an interdependent relationship which is impossible to untangle—does low socioeconomic status contribute to disability or does disability contribute to lower socioeconomic status?

Some adverse health conditions are more frequent among persons of higher socioeconomic status. These conditions include breast cancer, Kawasaki syndrome, and tennis elbow. Again, differences in exposure account for at least some of the differences in the frequency of these conditions.

Exercise 1.4

The following series of tables show person information about cases of the unknown disease described in Figure 1.5. Look again at Figure 1.5 (page 19), study the information in the exercise tables, and then describe in words how the disease outbreak is distributed by time and person. Write your description below.

Answers on page 63.

Exercise 1.4 — continued

Exercise 1.4, Table 1
Incidence of the disease by age and sex
in 24 villages surveyed for one year

Age Group (years)	Males			Females		
	Population*	# Cases	Rate per 1,000	Population*	# Cases	Rate per 1,000
<1	327	0	0	365	0	0
1	233	2	8.6	205	1	4.9
2	408	30	73.5	365	16	43.8
3	368	26	70.7	331	28	84.6
4	348	33	94.8	321	32	99.7
5-9	1,574	193	122.6	1,531	174	113.7
10-14	1,329	131	98.6	1,276	95	74.5
15-19	1,212	4	3.3	1,510	17	11.3
20-24	1,055	1	.9	1,280	51	39.8
25-29	882	1	1.1	997	75	75.2
30-34	779	4	5.1	720	47	65.3
35-39	639	4	6.3	646	51	78.9
40-44	469	10	21.3	485	34	70.1
45-49	372	7	18.8	343	18	52.5
50-54	263	13	49.4	263	12	45.6
55-59	200	5	25.0	228	6	26.3
60-64	164	9	53.6	153	3	19.6
65-69	106	4	37.7	105	2	19.1
≥70	80	6	75.0	114	2	17.5
Total	**10,812**	**483**	**44.7**	**11,238**	**664**	**59.1**

*As enumerated between May 1 and July 15.

Exercise 1.4, Table 2
Incidence of the disease in women
by marital status and age

Age Group (years)	Married Women			Single Women		
	Population	#Cases	Rate per 1,000	Population	# Cases	Rate per 1,000
16-29	1,905	89	46.7	1,487	16	10.7
30-49	1,684	98	58.2	141	4	28.4
≥50	387	4	10.3	26	0	0
Total	**3,976**	**191**	**48.0**	**1,654**	**20**	**12.1**

Exercise 1.4 — continued

Exercise 1.4, Table 3
Incidence of the disease by occupation, age, and sex

Sex	Mill Worker?	Age Group	Ill	Well	Total	Percent Ill
Female	Yes	<10	0	0	0	—
		10-19	2	330	332	0.6
		20-29	4	194	198	2.0
		30-44	2	93	95	2.1
		45-54	0	9	9	0
		≥55	0	5	5	0
Female	No	<10	28	577	605	4.6
		10-19	5	200	205	2.4
		20-29	12	204	216	5.6
		30-44	16	220	236	6.8
		45-54	4	91	95	4.2
		≥55	1	92	93	1.1
Male	Yes	<10	0	0	0	—
		10-19	3	355	358	0.8
		20-29	1	361	362	0.3
		30-44	3	318	321	0.9
		45-54	0	93	93	0
		≥55	1	51	52	1.9
Male	No	<10	23	629	652	3.5
		10-19	4	161	165	2.4
		20-29	1	12	13	7.7
		30-44	0	10	10	0
		45-54	1	14	15	6.7
		≥55	4	26	30	13.3

Exercise 1.4, Table 4
Incidence of the disease by socioeconomic status in 24 villages* surveyed for one year

Family Socioeconomic Status	Cases	Population	Rate per 1,000
Stratum 1 (Lowest)	99	796	124.4
Stratum 2	240	2,888	83.1
Stratum 3	260	4,868	53.4
Stratum 4	177	5,035	35.2
Stratum 5	132	5,549	23.8
Stratum 6	23	1,832	12.6
Stratum 7 (Highest)	2	769	2.6
Total	**933**	**21,737**	**42.9**

*Restricted to cases developing after 30 day's residence.

Analytic Epidemiology

As you have seen, with descriptive epidemiology we can identify several characteristics of persons with disease, and we may question whether these features are really unusual, but descriptive epidemiology does not answer that question. Analytic epidemiology provides a way to find the answer: the comparison group. Comparison groups, which provide baseline data, are a key feature of analytic epidemiology.

For example, in one outbreak of hepatitis A, it was found that almost all of those infected ate pastries from a particular bakery and drank city water (26). However, without knowing the habits of persons without hepatitis, it was not possible to conclude that pastries, city water, or both were risk factors for hepatitis. Therefore, a comparison group of healthy persons from the same population were questioned. Among the comparison group without hepatitis, almost all drank city water but few were exposed to the pastries. This finding indicated that pastries from the particular bakery were a risk factor for hepatitis A.

When—as in the example above—we find that persons with a particular characteristic are more likely than those without the characteristic to develop a certain disease, then the characteristic is said to be **associated with** the disease. The characteristic may be a demographic factor such as age, race, or sex; a constitutional factor such as blood group or immune status; a behavior or act such as smoking or having eaten a specific food such as potato salad; or a circumstance such as living near a toxic waste site. Identifying factors that are associated with disease helps us identify populations at increased risk of disease; we can then target public health prevention and control activities. Identifying risk factors also provides clues to direct research activities into the causes of a disease.

Thus, analytic epidemiology is concerned with the search for causes and effects, or the *why* and the *how*. We use analytic epidemiology to quantify the association between exposures and outcomes and to test hypotheses about causal relationships. It is sometimes said that epidemiology can never *prove* that a particular exposure caused a particular outcome. Epidemiology may, however, provide sufficient evidence for us to take appropriate control and prevention measures.

Epidemiologic studies fall into two categories: **experimental** and **observational**. In an experimental study, we determine the exposure status for each individual (clinical trial) or community (community trial); we then follow the individuals or communities to detect the effects of the exposure. In an observational study, which is more common, we simply observe the exposure and outcome status of each study participant. The study of hepatitis A cases described above was an observational study.

Two types of observational studies are the **cohort study** and the **case-control study**. A **cohort** study is similar in concept to the experimental study. We categorize subjects on the basis of their exposure and then observe them to see if they develop the health conditions we are studying. This differs from an experimental study in that, in a cohort study, we observe the exposure status rather than determine it. After a period of time, we compare the disease rate in the exposed group with the disease rate in the unexposed group. The length of follow-up varies, ranging from a few days for acute diseases to several decades for cancer, cardiovascular disease, and other chronic diseases. The Framingham study is a well-known cohort study which has followed over 5,000 residents of Framingham, Massachusetts, since the early 1950's to establish the rates and risk factors for heart disease (12).

The **case-control** study—the other type of observational study—is more common than the **cohort** study. In a case-control study, we enroll a group of people with disease ("cases") and a group without disease ("controls") and compare their patterns of previous exposures. The study of hepatitis A described above is an example of a case-control study. The key in a case-control study is to identify an appropriate control, or comparison, group, because it provides our measure of the expected amount of exposure.

In summary, the purpose of an epidemiologic study is to quantify the relationship between an exposure and a health outcome. The hallmark of an epidemiologic study is the presence of at least two groups, one of which serves as a comparison group. In an experimental study, the investigator determines the exposure for the study subjects; in an observational study, the subjects determine their own exposure. In an observational cohort study, subjects first are enrolled on the basis of their exposure, then are followed to document occurrence of disease. In an observational case-control study, subjects first are enrolled according to whether they have the disease or not, then are questioned or tested to determine their prior exposure.

Exercise 1.5

Classify each of the following studies as experimental, observational/cohort, observational/case-control, or not an epidemiologic study.

_____ a. Vietnam Experience Study: Subjects were several thousand soldiers stationed in Vietnam from 1969-1971 and several thousand soldiers stationed in Europe from 1969-1971. In the mid-1980's, investigators determined and compared the death rate and prevalence of illness in both groups.

_____ b. Subjects were 59 patients with end-stage cancer. All were given a new treatment. The monthly survival was charted over 2 years.

_____ c. Subjects were persons with laboratory-confirmed trichinosis, and one healthy friend of each. All subjects were asked about their consumption of pork and other meat products.

_____ d. Subjects were children enrolled in a health maintenance organization. At 18 months, each child was randomly given one of two types of vaccine against *Haemophilus influenzae*. Parents were asked to record any side effects on a card, and mail it back after 2 weeks.

Answers on page 64.

Causation

Although we use analytic epidemiology to search for causes of disease, this is not a straightforward matter. First, not all associations between exposures and disease are causal relations. In addition, the accepted models of disease causation all require the precise interaction of factors and conditions before a disease will occur. Finally, the concept of cause itself continues to be debated as a philosophical matter in the scientific literature. Nonetheless, the following models and guidelines provide a framework for considering causation at a practical level.

For purposes of this course, we will define a **cause** of disease as a factor (characteristic, behavior, event, etc.) that influences the occurrence of disease. An increase in the factor leads to an increase in disease. Reduction in the factor leads to a reduction in disease. If disease does not develop without the factor being present, then we term the causative factor "**necessary**." If the disease always results from the factor, then we term the causative factor "**sufficient**." Exposure to *Mycobacterium tuberculosis* is necessary for tuberculosis to develop, but it is not sufficient, because not everyone infected develops disease. On the other hand, exposure to a large inoculum of rabies virus is a sufficient cause in a susceptible person, since clinical rabies and death will almost inevitably occur.

A variety of models of disease causation have been proposed. Models are purposely simplified representations. In this instance, the purpose of the model is to facilitate the understanding of nature, which is complex. Two of these models are discussed below.

The Epidemiologic Triad: Agent, Host, and Environment

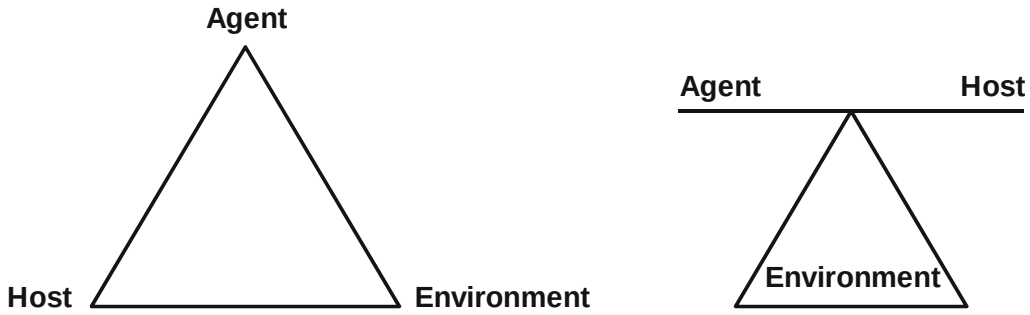
The **epidemiologic triangle** or **triad** is the traditional model of infectious disease causation. It has three components: an external agent, a susceptible host, and an environment that brings the host and agent together. In this model, the environment influences the agent, the host, and the route of transmission of the agent from a source to the host. Figure 1.14 shows two versions of this model in diagram form.

Agent factors

Agent originally referred to an infectious microorganism—virus, bacterium, parasite, or other microbe. Generally, these agents must be present for disease to occur. That is, they are necessary but not always sufficient to cause disease.

As epidemiology has been applied to noninfectious conditions, the concept of agent in this model has been broadened to include chemical and physical causes of disease. These include chemical contaminants, such as the l-tryptophan contaminant responsible for eosinophilia-myalgia syndrome, and physical forces, such as repetitive mechanical forces associated with carpal tunnel syndrome. This model does not work well for some noninfectious diseases, because it is not always clear whether a particular factor should be classified as an agent or as an environmental factor.

Figure 1.14
Epidemiologic triangle and triad (balance beam)



Host factors

Host factors are intrinsic factors that influence an individual's exposure, susceptibility, or response to a causative agent. Age, race, sex, socioeconomic status, and behaviors (smoking, drug abuse, lifestyle, sexual practices and contraception, eating habits) are just some of the many host factors which affect a person's likelihood of exposure. Age, genetic composition, nutritional and immunologic status, anatomic structure, presence of disease or medications, and psychological makeup are some of the host factors which affect a person's susceptibility and response to an agent.

Environmental factors

Environmental factors are extrinsic factors which affect the agent and the opportunity for exposure. Generally, environmental factors include physical factors such as geology, climate, and physical surroundings (e.g., a nursing home, hospital); biologic factors such as insects that transmit the agent; and socioeconomic factors such as crowding, sanitation, and the availability of health services.

Agent, host, and environmental factors interrelate in a variety of complex ways to produce disease in humans. Their balance and interactions are different for different diseases. When we search for causal relationships, we must look at all three components and analyze their interactions to find practical and effective prevention and control measures.

Component Causes and Causal Pies

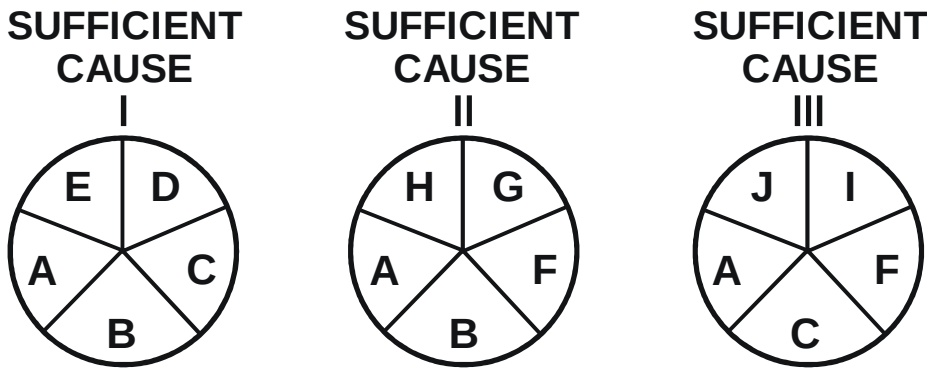
Because the agent-host-environment model does not work well for some noninfectious diseases, several other models have been proposed. One of the newer models is based on the multifactorial nature of causation in many diseases. This model is shown in Figure 1.15. It illustrates the factors that act to cause disease as pieces of a pie, the whole pie making up the sufficient cause for a disease. Notice that it shows that a disease may have more than one sufficient cause, with each sufficient cause being composed of several factors. What is the letter of the **necessary** cause shown for the hypothetical disease illustrated by this model?

The factors represented by the pieces of the pie in this model are called **component causes**. They include intrinsic host factors, as well as the agent and the environmental factors of the agent-host-environment model. A single component cause is rarely a sufficient cause by itself. For example, even exposure to a highly infectious agent such as measles virus does not invariably result in measles disease—the host must be susceptible; other host factors may also play a role.

At the other extreme, an agent which rarely causes disease in healthy persons may be pathogenic when other conditions are right. *Pneumocystis carinii* is one such organism, harmlessly colonizing some healthy persons but causing potentially lethal pneumonia in persons whose immune systems have been weakened by human immunodeficiency virus (HIV). Presence of *Pneumocystis carinii* organisms is therefore a necessary but not sufficient cause of pneumocystis pneumonia. In Figure 1.15 it would be represented by component A in each "pie."

If the three pies in the model represented all the sufficient causes for a particular disease, component A would be considered a necessary cause for the disease, as *P. carinii* is for pneumocystis pneumonia. Because component A is included in all sufficient causes for the disease, it would have to be present, usually with various combinations of other factors, for disease to occur. Infectious agents are likely to be represented by component A. Did you recognize earlier that "A" was the necessary cause for the hypothetical disease shown in each pie?

Figure 1.15
Rothman's causal pies: conceptual scheme for the causes of a hypothetical disease



Source: 25

As the model indicates, a particular disease may result from a variety of different sufficient causes. They are different pathways leading to the same end. For example, lung cancer may result from a sufficient cause which includes smoking as a component cause. Smoking is not a sufficient cause by itself, however, since not all smokers develop lung cancer. Neither is smoking a necessary cause, because lung cancer may occur in persons who never smoked. Thus smoking may be represented by component B, which is present in sufficient causes I and II but not in III. Asbestos exposure may be represented by component C, present in causes I and III but not in II. Indeed, since lung cancer may develop in persons with neither smoking or asbestos exposure, there would have to be at least one other sufficient cause pie that did not include components B and C.

To apply this model, we do not have to identify every component of a sufficient cause before we can take preventive action. We can prevent disease by blocking any single component of a sufficient cause, at least through that pathway. For example, eliminating smoking (component B) would prevent lung cancer from sufficient causes I and II, although some lung cancer would still occur through sufficient cause III.

Exercise 1.6

Use the two models (Agent-Host-Environment and Causal Pies) to describe the following:

a. Use the Agent-Host-Environment model to describe the role of the human immunodeficiency virus (HIV) in AIDS.

Agent:

Host:

Environment:

b. Some of the risk factors for heart disease are smoking, hypertension, obesity, diabetes, high cholesterol, inactivity, stress, and type A personality. Are these risk factors necessary causes, sufficient causes, or component causes?

Answers on page 64.

Epidemiology in Public Health Practice

Epidemiology is a tool that is essential for carrying out four fundamental functions: public health surveillance, disease investigation, analytic studies, and program evaluation. Although an active epidemiology unit will do other things as well, these are the key areas through which epidemiology contributes to the promotion of the public's health.

Public Health Surveillance

Through **public health surveillance**, a health department systematically collects, analyzes, interprets, and disseminates health data on an ongoing basis (28). Public health surveillance, which has been called "information for action" (23), is how a health department takes the pulse of its community. By knowing the ongoing pattern of disease occurrence and disease potential, a health department can effectively and efficiently investigate, prevent, and control disease in the community.

At the local level, the most common source of surveillance data is reports of disease cases received from health-care providers, who are required to report patients with certain "reportable" diseases, such as cholera or measles or syphilis. In addition, surveillance data may come from laboratory reports, surveys, disease registries, death certificates, and public health program data such as immunization coverage. It may also come from investigations by the health department of cases or clusters of cases reported to it.

Most health departments use simple surveillance systems. They monitor individual morbidity and mortality case reports, record a limited amount of information on each case, and look for patterns by time, place, and person. Unfortunately, with some reportable diseases, a health department may receive reports of only 10% to 25% of the cases that actually occur (20). Nevertheless, health departments have found that even a simple surveillance system can be invaluable in detecting problems and guiding public health action. The principal epidemiologist of a large county health department has said that "surveillance is the practicing epidemiologist's primary occupation; it pervades and keynotes all his activities" (24). We will discuss surveillance in more detail in Lesson 5.

Disease Investigation

As noted above, surveillance is considered information for action. The first action of a health department when it receives a report of a case or a cluster of cases of a disease is to investigate. The investigation may be as limited as a telephone call to the health-care provider to confirm or clarify the circumstances of the reported case, or it may be as extensive as a field investigation coordinating the efforts of dozens of people to determine the extent and cause of a large outbreak.

The objectives of such investigations vary. With a communicable disease, one objective may be to identify additional unreported or unrecognized cases in order to control spread of the disease. For example, one of the hallmarks of sexually transmitted disease investigations is the identification of sexual contacts of cases. When these contacts are interviewed and tested they are often found to have asymptomatic infections. By providing treatment that these contacts had not realized they needed, the health department prevents them from spreading the disease further.

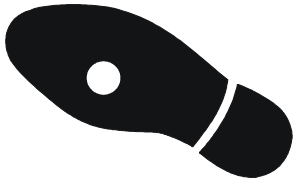
For other diseases, the objective of an investigation may be to identify a source or vehicle of infection which can be controlled or eliminated. For example, the investigation of a case of botulism usually focuses on trying to identify the vehicle contaminated with botulinum toxin, such as a food that was improperly canned. Once they have identified the vehicle, the investigators can establish how many other people may have been exposed and how many continue to be at risk, and take action to prevent their exposure. In Taiwan, investigators of a cluster of botulism cases implicated consumption of canned peanuts prepared by a single manufacturer (10). They then initiated a nationwide recall of that product from warehouses, stores, and homes to reduce the risk of exposure for others.

For some diseases, the objective of an investigation may be simply to learn more about the disease itself—its natural history, clinical spectrum, descriptive epidemiology, and risk factors. In the nationwide outbreak of toxic shock syndrome in 1980, early investigations focused on establishing a case definition based on the clinical symptoms, and on describing the populations at risk by time, place, and person. From the descriptive epidemiology, investigators were able to develop hypotheses which they could test with analytic studies. They conducted a series of increasingly specific studies which narrowed specific risk factors down from menstruating women to tampon users to users of a specific brand of tampon. This information prompted the withdrawal of that brand from the market, and subsequent research to identify what factors in the composition and use of the tampon were necessary for the syndrome to develop (8).

Field investigations of the type described above are sometimes referred to as “shoe-leather epidemiology,” conjuring images of dedicated if haggard epidemiologists beating the pavement in search of additional cases to interview and clues to identify the source and mode of transmission. This approach is commemorated in the symbol of the Epidemic Intelligence Service, CDC’s cadre of disease detectives—a shoe with a hole in the sole.

We will discuss disease investigation in more detail in Lesson 6.

Figure 1.16
Epidemic Intelligence Service (EIS) shoe



Analytic Studies

Surveillance and case investigation sometimes are sufficient to identify causes, modes of transmission, and appropriate control and prevention measures. Sometimes they provide clues or hypotheses which must be assessed with appropriate analytic techniques.

Investigators initially use descriptive epidemiology to examine clusters of cases or outbreaks of disease. They examine incidence of the disease and its distribution by time, place, and person. They calculate rates and identify parts of the population that are at higher risk than others. When they find a strong association between exposure and disease, the investigators may implement control measures immediately. More often, investigators find that descriptive studies, like case investigations, generate hypotheses which they can then test with analytic studies.

Epidemiologists must be familiar with all aspects of the analytic study, including its design, conduct, analysis, and interpretation. In addition, the epidemiologist must be able to communicate the findings as well.

- Study **design** includes determining the appropriate study design, writing justifications and protocols, calculating sample sizes, deciding on criteria for subject selection (e.g., choosing controls), designing questionnaires, and numerous other tasks that are part of the study plan.
- To **conduct** a study requires securing appropriate clearances and approvals, abstracting records, tracking down and interviewing subjects, collecting and handling specimens, and managing the data.
- **Analysis** begins with describing the characteristics of the subjects and progresses to calculating rates, creating comparative tables (e.g., two-by-two tables), and computing measures of association (e.g., risk ratios and odds ratios), tests of statistical significance (e.g., chi-square), confidence intervals, and the like. These techniques will be discussed in Lessons 2 and 6. Many epidemiologic studies require more advanced analytic techniques such as stratified analysis, regression, and modeling.
- Finally, **interpretation** involves putting the findings of the study into perspective and making appropriate recommendations.

Evaluation

Evaluation of control and prevention measures is another responsibility of epidemiologists. Evaluation often addresses both **effectiveness** and **efficiency**. **Effectiveness** refers to the ability of a program to produce the intended or expected results in the field. Effectiveness differs from **efficacy**, which is the ability to produce results under *ideal* conditions. Finally, **efficiency** refers to the ability of the program to produce the intended results with a minimum expenditure of time and resources. Evaluation of an immunization program, for example, might compare the stated efficacy with the field effectiveness of the program, and might assess the efficiency with which the acceptable results are achieved.

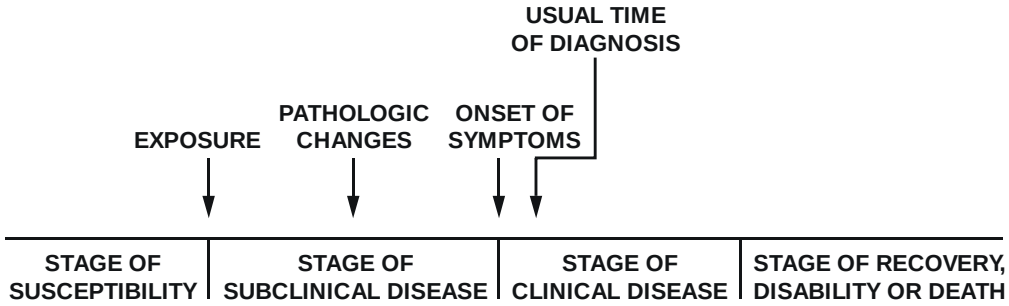
Selected Topics in Epidemiology and Disease

Although epidemiologic approaches can be applied to all types of disease, injury, and health conditions, the chain of infection for infectious diseases is better understood. In addition, infectious diseases remain an important focus of state and local public health department activities. Therefore, a description of some of the key concepts of infectious disease epidemiology are presented below. These concepts are rooted in infectious disease, but are also relevant to noninfectious diseases.

Natural History and Spectrum of Disease

Natural history of disease refers to the progress of a disease process in an individual over time, in the absence of intervention. The process begins with exposure to or accumulation of factors capable of causing disease. Without medical intervention, the process ends with recovery, disability, or death. The stages in the natural history of disease are shown in Figure 1.17. Most diseases have a characteristic natural history (which is poorly understood for many diseases), although the time frame and specific manifestations of disease may vary from individual to individual. With a particular individual, the usual course of a disease may be halted at any point in the progression by preventive and therapeutic measures, host factors, and other influences.

Figure 1.17
Natural history of disease



As shown in Figure 1.17, the natural history begins with the appropriate exposure to or accumulation of factors sufficient to begin the disease process in a susceptible host. For infectious disease, the exposure usually is a microorganism. For cancers, the critical factors may require both **cancer initiators**, such as asbestos fibers or components in tobacco smoke (for lung cancer), and **cancer promoters**, such as estrogens (for endometrial cancer).

Usually, a period of subclinical or inapparent pathologic changes follows exposure, ending with the onset of symptoms. For infectious diseases, this period is usually called the **incubation period**; for chronic diseases, this period is usually called the **latency period**. This period may be as brief as seconds for hypersensitivity and toxic reactions to as long as decades for certain chronic diseases. Even for a single disease, the characteristic incubation period has a range. For example, for hepatitis A, this range is about 2 to 6 weeks. For leukemia associated with exposure to the atomic bomb blast in Hiroshima, the range was 2 to 12 years with a peak at 6 to 7 years

(11). Although disease is inapparent during the incubation period, some pathologic changes may be detectable with laboratory, radiographic, or other screening methods. Most screening programs attempt to identify the disease process during this phase of its natural history, since early intervention may be more effective than treatment at a later stage of disease progression.

The onset of symptoms marks the transition from subclinical to clinical disease. Most diagnoses are made during the stage of clinical disease. In some people, however, the disease process may never progress to clinically apparent illness. In others, the disease process may result in a wide spectrum of clinical illness, ranging from mild to severe or fatal.

Three terms are used to describe an infectious disease according to the various outcomes that may occur after exposure to its causative agent.

- **Infectivity** refers to the proportion of exposed persons who become infected.
- **Pathogenicity** refers to the proportion of infected persons who develop clinical disease.
- **Virulence** refers to the proportion of persons with clinical disease who become severely ill or die.

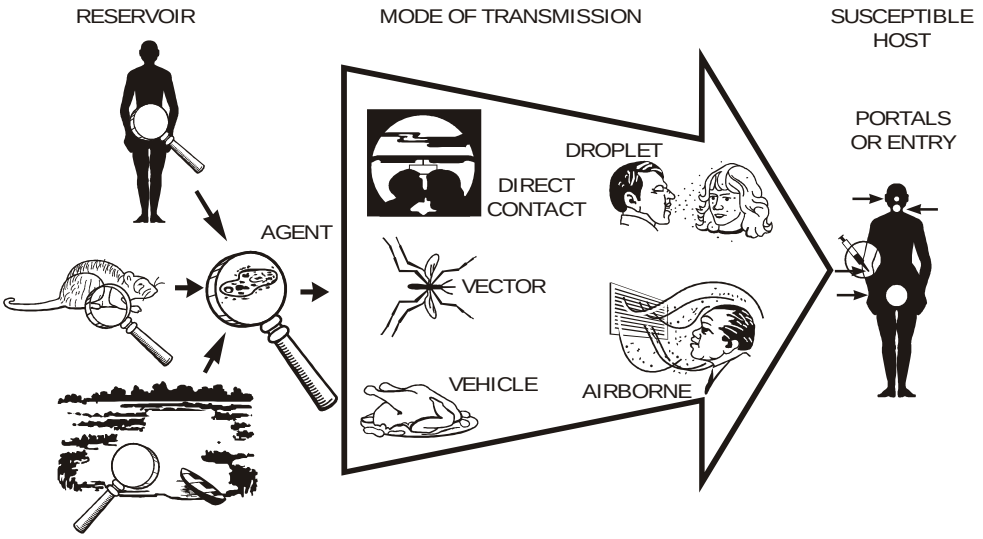
For example, hepatitis A virus in children has low pathogenicity and low virulence, since many infected children remain asymptomatic and few develop severe illness. In persons with good nutrition and health, measles virus has high pathogenicity but low virulence, since almost all infected persons develop the characteristic rash illness but few develop the life-threatening presentations of measles, pneumonia, or encephalitis. In persons with poorer nutrition and health, measles is a more virulent disease, with mortality as high as 5-10%. Finally, rabies virus is both highly pathogenic and virulent, since virtually 100% of all infected persons (who do not receive treatment) progress to clinical disease and death.

The natural history and spectrum of disease presents challenges to the clinician and to the public health worker. Because of the clinical spectrum, cases of illness diagnosed by clinicians in the community often represent only the “tip of the iceberg.” Many additional cases may be too early to diagnose or may remain asymptomatic. For the public health worker, the challenge is that persons with inapparent or undiagnosed infections may nonetheless be able to transmit them to others. Such persons who are infectious but have subclinical disease are called **carriers**. Frequently, carriers are persons with incubating disease or inapparent infection. Persons with measles, hepatitis A, and several other diseases become infectious a few days before the onset of symptoms. On the other hand, carriers may also be persons who appear to have recovered from their clinical illness, such as chronic carriers of hepatitis B virus.

Chain of Infection

As described on page 35 of this lesson, the traditional model (epi triad) illustrates that infectious diseases result from the interaction of agent, host, and environment. More specifically, transmission occurs when the **agent** leaves its **reservoir** or host through a **portal of exit**, and is conveyed by some **mode of transmission**, and enters through an appropriate **portal of entry** to infect a susceptible **host**. This is sometimes called the chain of infection and is illustrated in Figure 1.18.

Figure 1.18
Chain of infection



Reservoir

The **reservoir** of an agent is the habitat in which an infectious agent normally lives, grows, and multiplies. Reservoirs include humans, animals, and the environment. The reservoir may or may not be the source from which an agent is transferred to a host. For example, the reservoir of *Clostridium botulinum* is soil, but the source of most botulism infections is improperly canned food containing *C. botulinum* spores.

Human reservoirs. Many of the common infectious diseases have human reservoirs. Diseases which are transmitted from person to person without intermediaries include the sexually transmitted diseases, measles, mumps, streptococcal infection, most respiratory pathogens, and many others. Smallpox was eradicated after the last human case was identified and isolated because humans were the only reservoir for the smallpox virus. Two types of human reservoir exist:

- persons with symptomatic illness
- carriers

A **carrier** is a person without apparent disease who is nonetheless capable of transmitting the agent to others. Carriers may be **asymptomatic carriers**, who never show symptoms during the time they are infected, or may be **incubatory** or **convalescent carriers**, who are capable of transmission before or after they are clinically ill. A **chronic carrier** is one who continues to harbor an agent (such as hepatitis B virus or *Salmonella typhi*—the agent of typhoid fever) for an extended time (months or years) following the initial infection. Carriers commonly transmit disease because they do not recognize they are infected and consequently take no special precautions to prevent transmission. Symptomatic persons, on the other hand, are usually less likely to transmit infection widely because their symptoms increase their likelihood of being diagnosed and treated, thereby reducing their opportunity for contact with others.

Animal reservoirs. Infectious diseases that are transmissible under normal conditions from animals to humans are called **zoonoses** (ZOH-uh-NOH-seez). In general, these diseases are transmitted from animal to animal, with humans as incidental hosts. Such diseases include brucellosis (cows and pigs), anthrax (sheep), plague (rodents), trichinosis (swine), and rabies (bats, raccoons, dogs, and other mammals).

Another group of diseases with animal reservoirs are those caused by viruses transmitted by insects and caused by parasites that have complex life cycles, with different reservoirs at different stages of development. Such diseases include St. Louis encephalitis and malaria (both requiring mosquitos) and schistosomiasis (requiring fresh water snails). Lyme disease is a zoonotic disease of deer incidentally transmitted to humans by the deer tick.

Environmental reservoirs. Plants, soil, and water in the environment are also reservoirs for some infectious agents. Many fungal agents, such as those causing histoplasmosis, live and multiply in the soil. The primary reservoir of Legionnaires' bacillus appears to be pools of water, including those produced by cooling towers and evaporative condensers.

Portal of exit

Portal of exit is the path by which an agent leaves the source host. The portal of exit usually corresponds to the site at which the agent is localized. Thus, tubercle bacilli and influenza viruses exit the respiratory tract, schistosomes through urine, cholera vibrios in feces, *Sarcoptes scabiei* in scabies skin lesions, and enterovirus 70, an agent of hemorrhagic conjunctivitis, in conjunctival secretions. Some bloodborne agents can exit by crossing the placenta (rubella, syphilis, toxoplasmosis), while others exit by way of the skin (percutaneously) through cuts or needles (hepatitis B) or blood-sucking arthropods (malaria).

Modes of transmission

After an agent exits its natural reservoir, it may be transmitted to a susceptible host in numerous ways. These modes of transmission are classified as:

- Direct
  - — Direct contact
  - — Droplet spread
- Indirect
  - — Airborne
  - — Vehicleborne
  - — Vectorborne
    - Mechanical
    - Biologic

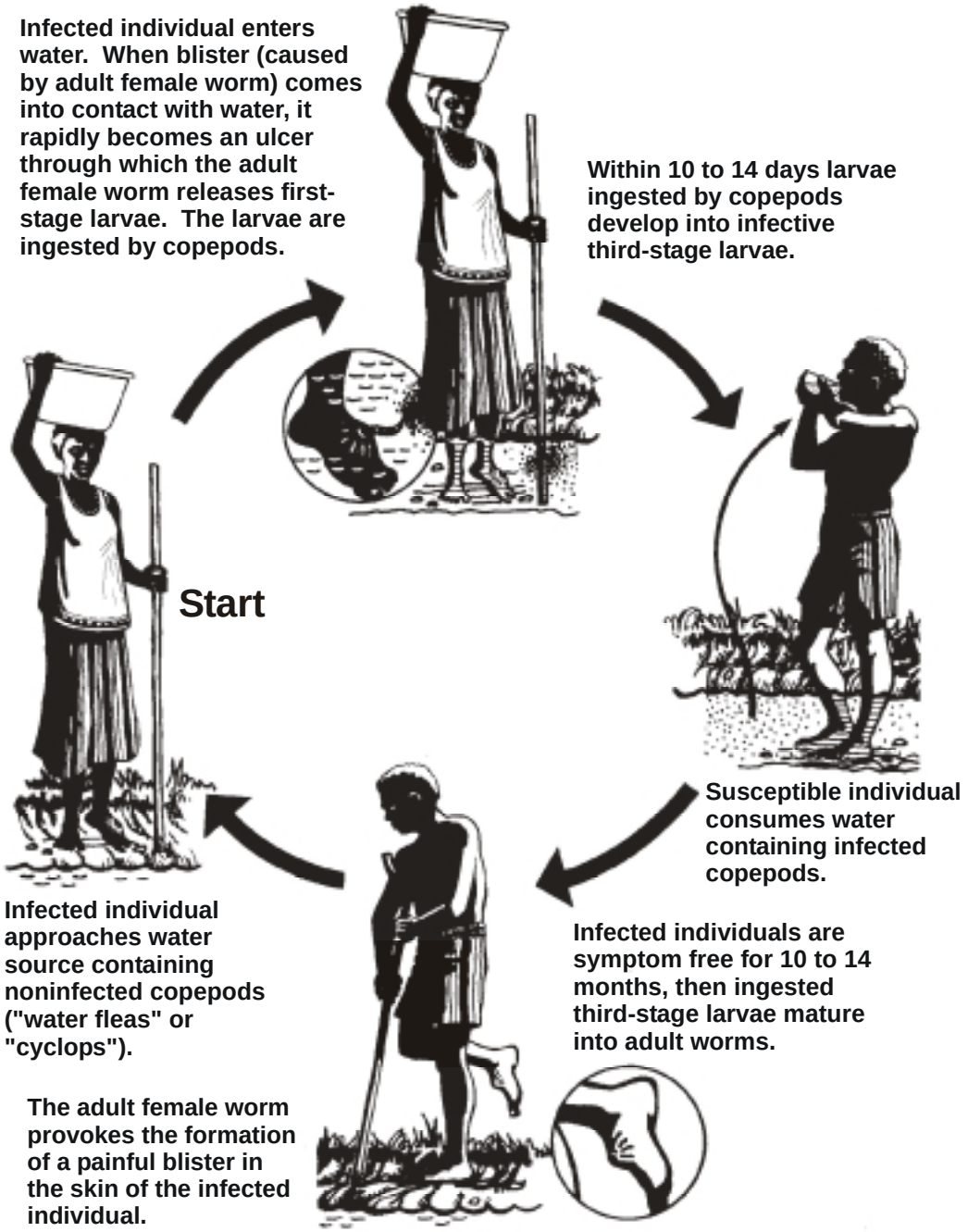
In **direct transmission**, there is essentially immediate transfer of the agent from a reservoir to a susceptible host by direct contact or droplet spread. **Direct contact** occurs through kissing, skin-to-skin contact, and sexual intercourse. Direct contact refers also to contact with soil or vegetation harboring infectious organisms. Thus, infectious mononucleosis ("kissing disease") and gonorrhea are spread from person-to-person by direct contact. Hookworm is spread by direct contact with contaminated soil. Droplet spread refers to spray with relatively large, short-range aerosols produced by sneezing, coughing, or even talking. **Droplet spread** is classified as direct because transmission is by direct spray over a few feet, before the droplets fall to the ground.

In **indirect transmission**, an agent is carried from a reservoir to a susceptible host by suspended air particles or by animate (**vector**) or inanimate (**vehicle**) intermediaries. Most **vectors** are arthropods such as mosquitoes, fleas, and ticks. These may carry the agent through purely mechanical means. For example, flies carry *Shigella* on appendages; fleas carry *Yersinia pestis* (agent that causes plague) in the gut and deposit the agent on the skin of a new host. In mechanical transmission, the agent does not multiply or undergo physiologic changes in the vector. This is in contrast to instances in which an agent undergoes part of its life cycle inside a vector before being transmitted to a new host. When the agent undergoes changes within the vector, the vector is serving as both an intermediate host and a mode of transmission. This type of indirect transmission is a **biologic transmission**.

Guinea worm disease and many other vectorborne diseases have complex life cycles which require an intermediate host. Follow the life cycle of *Dracunculus medinensis* (Guinea worm) illustrated in Figure 1.19 on page 48. What type of transmission does this illustrate?

Since the agent undergoes part of its life cycle in the intermediate host, the agent cannot be transmitted by the intermediate host until the agent has completed that part of its life cycle. Therefore, this is an indirect, vectorborne, biologic transmission.

Figure 1.19
The complex life cycle of *Dracunculus medinensis* (Guinea worm)



The agent, *Dracunculus*, develops in the intermediate host (fresh water copepod). Man acquires the infection by ingesting infected copepods in drinking water.

Vehicles that may indirectly transmit an agent include food, water, biologic products (blood), and fomites (inanimate objects such as handkerchiefs, bedding, or surgical scalpels). As with vectors, vehicles may passively carry an agent—as food or water may carry hepatitis A virus—or may provide an environment in which the agent grows, multiplies, or produces toxin—as improperly canned foods may provide an environment in which *C. botulinum* produces toxin.

Airborne transmission is by particles that are suspended in air. There are two types of these particles: **dust** and **droplet nuclei**. Airborne **dust** includes infectious particles blown from the soil by the wind as well as material that has settled on surfaces and become resuspended by air currents. **Droplet nuclei** are the residue of dried droplets. The nuclei are less than 5 μ (microns) in size and may remain suspended in the air for long periods, may be blown over great distances, and are easily inhaled into the lungs and exhaled. This makes them an important means of transmission for some diseases. Tuberculosis, for example, is believed to be transmitted more often indirectly, through droplet nuclei, than directly, through droplet spread. Legionnaires' disease and histoplasmosis are also spread through airborne transmission.

Portal of entry

An agent enters a susceptible host through a portal of entry. The portal of entry must provide access to tissues in which the agent can multiply or a toxin can act. Often, organisms use the same portal to enter a new host that they use to exit the source host. For example, influenza virus must exit the respiratory tract of the source host and enter the respiratory tract of the new host. The route of transmission of many enteric (intestinal) pathogenic agents is described as "fecal-oral" because the organisms are shed in feces, carried on inadequately washed hands, and then transferred through a vehicle (such as food, water, or cooking utensil) to the mouth of a new host. Other portals of entry include the skin (hookworm), mucous membranes (syphilis, trachoma), and blood (hepatitis B).

Host

The final link in the chain of infection is a susceptible host. Susceptibility of a host depends on genetic factors, specified acquired immunity, and other general factors which alter an individual's ability to resist infection or to limit pathogenicity. An individual's genetic makeup may either increase or decrease susceptibility. General factors which defend against infection include the skin, mucous membranes, gastric acidity, cilia in the respiratory tract, the cough reflex, and nonspecific immune response. General factors that may increase susceptibility are malnutrition, alcoholism, and disease or therapy which impairs the nonspecific immune response. Specific acquired immunity refers to protective antibodies that are directed against a specific agent. Individuals gain protective antibodies in two ways: 1) They develop antibodies in response to infection, vaccine, or toxoid; immunity developed in these ways is called **active immunity**. 2) They acquire their mothers' antibodies before birth through the placenta or they receive injections of antitoxins or immune globulin; immunity that is acquired in these ways is called **passive immunity**.

Note that the chain of infection may be interrupted when an agent does not find a susceptible host. This may occur if a high proportion of individuals in a population is resistant to an agent. These persons limit spread to the relatively few who are susceptible by reducing the probability of contact between infected and susceptible persons. This concept is called **herd immunity**. The degree of herd immunity necessary to prevent or abort an outbreak varies by disease. In theory, herd immunity means that not everyone in a community needs to be resistant (immune) to prevent disease spread and occurrence of an outbreak. In practice, herd immunity has not prevented outbreaks of measles and rubella in populations with immunity levels as high as 85 to 90%. One problem is that, in highly immunized populations, the relatively few susceptible persons are often clustered in population subgroups, usually defined by socioeconomic or cultural factors. If the agent is introduced into one of these subgroups, an outbreak may occur.

Implications for public health

By knowing how an agent exits and enters a host, and what its modes of transmission are, we can determine appropriate control measures. In general, we should direct control measures against the link in the infection chain that is most susceptible to interference, unless practical issues dictate otherwise.

For some diseases, the most appropriate intervention may be directed at controlling or eliminating the agent at its source. In the hospital setting, patients may be treated and/or isolated, with appropriate “enteric precautions,” “respiratory precautions,” “universal precautions,” and the like for different exit pathways. In the community, soil may be decontaminated or covered to prevent escape of the agent.

Sometimes, we direct interventions at the mode of transmission. For direct transmission, we may provide treatment to the source host or educate the source host to avoid the specific type of contact associated with transmission. In the hospital setting, since most infections are transmitted by direct contact, handwashing is the single most important way to prevent diseases from spreading. For vehicleborne transmission, we may decontaminate or eliminate the vehicle. For fecal-oral transmission, we may also try to reduce the risk of contamination in the future by rearranging the environment and educating the persons involved in better personal hygiene. For airborne transmission, we may modify ventilation or air pressure, and filter or treat the air. For vectorborne transmission, we usually attempt to control (i.e., reduce or eradicate) the vector population.

Finally, we may apply measures that protect portals of entry of a susceptible potential host or reduce the susceptibility of the potential host. For example, a dentist’s mask and gloves are intended to protect the dentist from a patient’s blood, secretions, and droplets, as well to protect the patient from the dentist. Prophylactic antibiotics and vaccination are strategies to improve a potential host’s defenses.

Exercise 1.7

Information describing viral hepatitis A and yellow fever is provided on the following pages. After you study this information, outline the chain of infection of each disease by identifying the reservoirs, portals of exit, modes of transmission, portals of entry, and factors in host susceptibility.

Yellow Fever

Reservoirs:

Portals of exit:

Modes of transmission:

Portals of entry:

Factors in host susceptibility:

Answers on page 65.

Viral Hepatitis A

Reservoirs:

Portals of exit:

Modes of transmission:

Portals of entry:

Factors in host susceptibility:

Answers on page 65.

YELLOW FEVER[1] ICD-9 060

1. Identification — An acute infectious viral disease of short duration and varying severity. The mildest cases are clinically indeterminate; typical attacks are characterized by a dengue-like illness, i.e., sudden onset, fever, chills, headache, backache, generalized muscle pain, prostration, nausea and vomiting. As the disease progresses, the pulse slows and weakens, even though the temperature may be elevated (Faget's sign); albuminuria (sometimes pronounced) and anuria may occur. A saddle-back fever curve is common. Leukopenia appears early and is most pronounced about the fifth day. Common hemorrhagic symptoms include epistaxis, buccal bleeding, hematemesis (coffee-ground or black), and melena. Jaundice is moderate early in the disease and is intensified later. The case fatality rate among indigenous populations of endemic regions is <5%, but may exceed 50% among nonindigenous groups and in epidemics.

Laboratory diagnosis is made by isolation of virus from blood by inoculation of suckling mice, mosquitoes or cell cultures (especially those of mosquito cells); by demonstration of viral antigen in the blood or liver tissue by ELISA or FA and in tissues by use of labeled specific antibodies; and by demonstration of viral genome in liver tissue by hybridization probes. Serologic diagnosis is made by demonstrating specific IgM in early sera or a rise in titer of specific antibodies in paired acute-phase and convalescent sera. Serologic cross-reactions occur with other flaviviruses and vaccine-derived antibodies cannot be distinguished from natural immunity. The diagnosis is suggested but not proven by demonstration of typical lesions in the liver.

2. Infectious agent — The virus of yellow fever, a flavivirus.

* * *

4. Reservoir — In urban areas, man and *Aedes aegypti* mosquitoes; in forest areas, vertebrates other than man, mainly monkeys and possibly marsupials, and forest mosquitoes. Transovarian transmission in mosquitoes may contribute to maintenance of infection. Man has no essential role in transmission of jungle yellow fever or in maintaining the virus.

5. Mode of transmission — In urban and certain rural areas, by the bite of infective *Aedes aegypti* mosquitoes. In forests of S America, by the bite of several species of forest mosquitoes of the genus *Haemagogus*. In East Africa, *Ae. africanus* is the vector in the monkey population, while semidomestic *Ae. bromeliae* and *Ae. simpsoni*, and probably other *Aedes species*, transmit the virus from monkey to man. In large epidemics in Ethiopia, good epidemiologic evidence incriminated *Ae. simpsoni* as a person-to-person vector. In West Africa, *Ae. furcifer-taylori*, *Ae. luteocephalus* and other species are responsible for spread between monkey and man. *Ae. albopictus* has been introduced into Brazil and the USA from Asia and has the potential for bridging the sylvatic and urban cycles of yellow fever in the Western Hemisphere. However, no instance of involvement of this species in transmission of yellow fever has been documented.

* * *

8. Susceptibility and resistance — Recovery from yellow fever is followed by lasting immunity; second attacks are unknown. Mild inapparent infections are common in endemic areas. Transient passive immunity in infants born to immune mothers may persist for up to 6 months. In natural infections, antibodies appear in the blood within the first week.

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[1]This material is from *Control of Communicable Diseases in Man*, Fifteenth Edition, Abram S. Benenson (ed), 1990. Reprinted by permission of American Public Health Association.

I. VIRAL HEPATITIS A[2] ICD-9 070.1

(Infectious hepatitis, Epidemic hepatitis, Epidemic jaundice, Catarrhal jaundice, Type A hepatitis, HA)

1. Identification — Onset is usually abrupt with fever, malaise, anorexia, nausea and abdominal discomfort, followed within a few days by jaundice. The disease varies in clinical severity from a mild illness lasting 1-2 weeks, to a severely disabling disease lasting several months (rare). Convalescence often is prolonged. In general, severity increases with age, but complete recovery without sequelae or recurrences is the rule. Many infections are asymptomatic; many are mild and without jaundice, especially in children, and recognizable only by liver function tests. The case fatality rate is low (about 0.6%); the rare death usually occurs in an older patient in whom the disease has a fulminant course.

Diagnosis is established by the demonstration of IgM antibodies against hepatitis A virus in the serum of acutely or recently ill patients; IgM may remain detectable for 4-6 months after onset. Diagnosis may also be made by a fourfold or greater rise in specific antibodies in paired sera; virus and antibody can be detected by RIA or ELISA. (Assay kits for the detection of IgM and total antibodies to the virus are available commercially.) If laboratory tests are not available, epidemiologic evidence can provide support for the diagnosis. However, HA cannot be distinguished epidemiologically from hepatitis E, in areas where the latter is endemic.

2. Infectious agent — Hepatitis A virus (HAV), a 27-nm picornavirus (i.e., a positive-strand RNA virus). It has been classified as *Enterovirus* type 72, a member of the family Picornaviridae.

* * *

4. Reservoir — Man, and rarely captive chimpanzees; less frequently, certain other nonhuman primates. An enzootic focus has been identified in Malaysia, but there is no suggestion of transmission to man.

5. Mode of transmission — Person-to-person by the fecal-oral route. The infectious agent is found in feces, reaching peak levels the week or two before onset of symptoms, and diminishing rapidly after liver dysfunction or symptoms appear, which is concurrent with the appearance of circulating antibodies to HAV. Direct transmission occurs among male homosexuals. Common-source outbreaks have been related to contaminated water; food contaminated by infected foodhandlers, including sandwiches and salads which are not cooked or are handled after cooking; and raw or undercooked molluscs harvested from contaminated waters. Although rare, instances have been reported of transmission by transfusion of blood from a donor during the incubation period.

* * *

8. Susceptibility and resistance — Susceptibility is general. Low incidence of manifest disease in infants and preschool children suggests that mild and anicteric infections are common. Homologous immunity after attack probably lasts for life.

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[2]This material is from *Control of Communicable Diseases in Man*, Fifteenth Edition, Abram S. Beneson (ed), 1990. Reprinted by permission of American Public Health Association.

Epidemic Disease Occurrence

Level of disease

The amount of a particular disease that is usually present in a community is the baseline level of the disease. This level is not necessarily the preferred level, which should in fact be zero; rather it is the observed level. Theoretically, if no intervention occurred and if the level is low enough not to deplete the pool of susceptible persons, the disease occurrence should continue at the baseline level indefinitely. Thus, the baseline level is often considered the **expected** level of the disease. For example, over the past 4 years the number of reported cases of poliomyelitis has ranged from 5 to 9. Therefore, assuming there is no change in population, we would expect to see approximately 7 reported cases next year.

Different diseases, in different communities, show different patterns of expected occurrence: 1) a persistent level of occurrence with a low to moderate disease level is referred to as an **endemic** level; 2) a persistently high level of occurrence is called a **hyperendemic** level; 3) an irregular pattern of occurrence, with occasional cases occurring at irregular intervals is called **sporadic**.

Occasionally, the level of disease rises above the expected level. When the occurrence of a disease within an area is clearly in excess of the expected level for a given time period, it is called an **epidemic**. Public health officials often use the term **outbreak**, which means the same thing, because it is less provocative to the public. When an epidemic spreads over several countries or continents, affecting a large number of people, it is called a **pandemic**.

Epidemics occur when an agent and susceptible hosts are present in adequate numbers, and the agent can effectively be conveyed from a source to the susceptible hosts. More specifically, an epidemic may result from the following:

- a recent increase in amount or virulence of the agent
- the recent introduction of the agent into a setting where it has not been before
- an enhanced mode of transmission so that more susceptibles are exposed
- some change in the susceptibility of the host response to the agent
- factors that increase host exposure or involve introduction through new portals of entry (16)

Epidemic patterns

We sometimes classify epidemics by how they spread through a population, as shown below:

- Common source
  — Point
  — Intermittent
  — Continuous
- Propagated
- Mixed
- Other

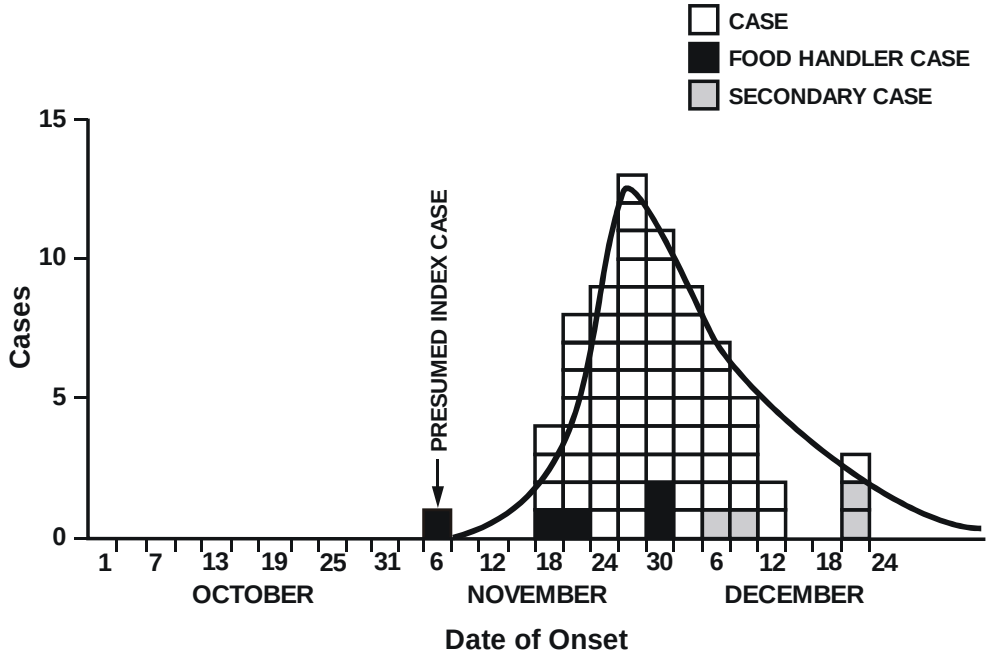
A **common source outbreak** is one in which a group of persons is exposed to a common noxious influence, such as an infectious agent or a toxin. If the group is exposed over a relatively brief period, so that everyone who becomes ill develops disease at the end of one incubation period, then the common source outbreak is further classified as a **point source outbreak**. The epidemic of leukemia cases in Hiroshima following the atomic bomb blast and the epidemic of hepatitis A among college football players who unknowingly drank contaminated water after practice one day each had a point source of exposure (11, 21). When the number of cases in a point source epidemic is plotted over time, the resulting epidemic curve classically has a steep upslope and a more gradual downslope (a so-called "log-normal distribution"). Figure 1.20 is an example of the typical log-normal distribution of a point source outbreak.

In some common source outbreaks, cases may be exposed over a period of days, weeks, or longer, with the exposure being either **intermittent** or **continuous**. Figure 1.21 is an epidemic curve of a common source outbreak with continuous exposure. When we plot the cases of a continuous common source outbreak over time, the range of exposures and range of incubation periods tend to dampen and widen the peaks of the epidemic curve. Similarly, when we plot an intermittent common source outbreak we often find an irregular pattern that reflects the intermittent nature of the exposure.

An outbreak that does not have a common source, but instead spreads gradually from person to person—usually growing as it spreads—is called a **propagated** outbreak. Usually transmission is by direct person-to-person contact, as with syphilis. Transmission may also be vehicleborne, as the transmission of hepatitis B or HIV by sharing needles, or vectorborne, as the transmission of yellow fever by mosquitoes.

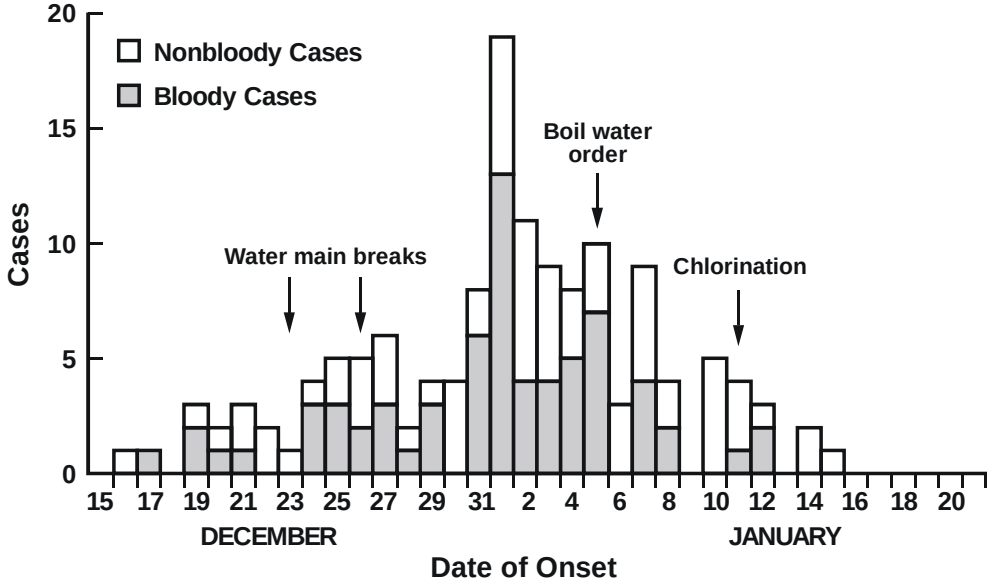
In a propagated epidemic, cases occur over more than one incubation period. In theory, the epidemic curve of a propagated epidemic would have a successive series of peaks reflecting increasing numbers of cases in each generation. The epidemic usually wanes after a few generations, either because the number of susceptibles falls below some critical level, or because intervention measures become effective. Figure 1.22 shows such an epidemic curve.

Figure 1.20
Example of common source outbreak with point source exposure: Hepatitis A cases by date of onset, Fayetteville, Arkansas, November-December 1978, with log-normal curve superimposed



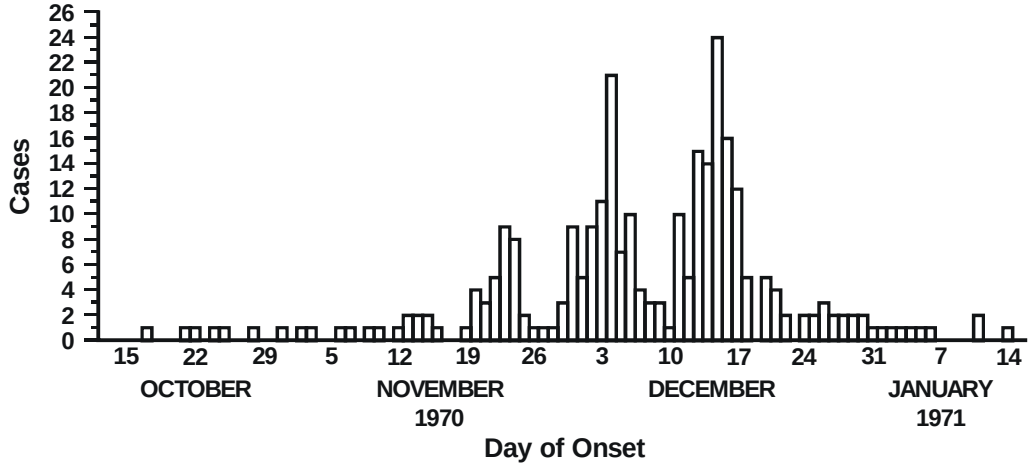
Source: CDC, unpublished data, 1979

Figure 1.21
Example of common source outbreak with continuous exposure: Diarrheal illness in city residents by date of onset and character of stool, Cabool, Missouri, December 1989-January 1990



Source: CDC, unpublished data, 1990

Figure 1.22
Example of the classic epidemic curve of a propagated epidemic: Measles cases by date of onset, Aberdeen, South Dakota, October 15, 1970-January 16, 1971



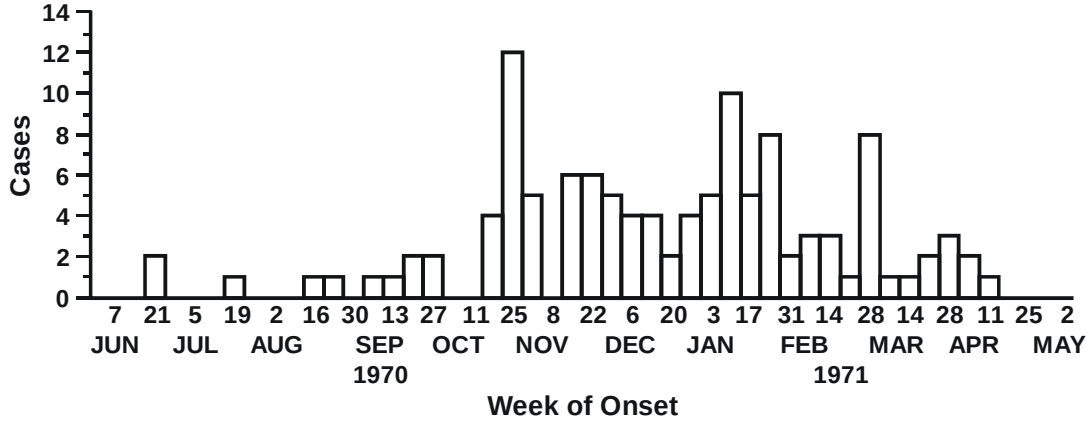
Source: 7

In reality, few propagated outbreaks provide as classic a pattern as that shown in Figure 1.22. For many diseases, the variability of time of exposure and range of incubation periods tend to smooth out the peaks and valleys, as shown in Figure 1.23. For influenza, the incubation period is so short and transmission is so effective that its epidemic curve can look like that of a point source epidemic.

Some epidemics may have features of both common source epidemics and propagated epidemics. The pattern of a common source outbreak followed by secondary person-to-person spread is not uncommon. These are called **mixed** epidemics. For example, Figure 1.24 illustrates a common source epidemic of shigellosis that occurred among a group of 3,000 women attending a national music festival. Many developed symptoms after returning home. Over the next few weeks, several state health departments detected subsequent generations of shigella cases spread by person-to-person transmission from festival attendees (19).

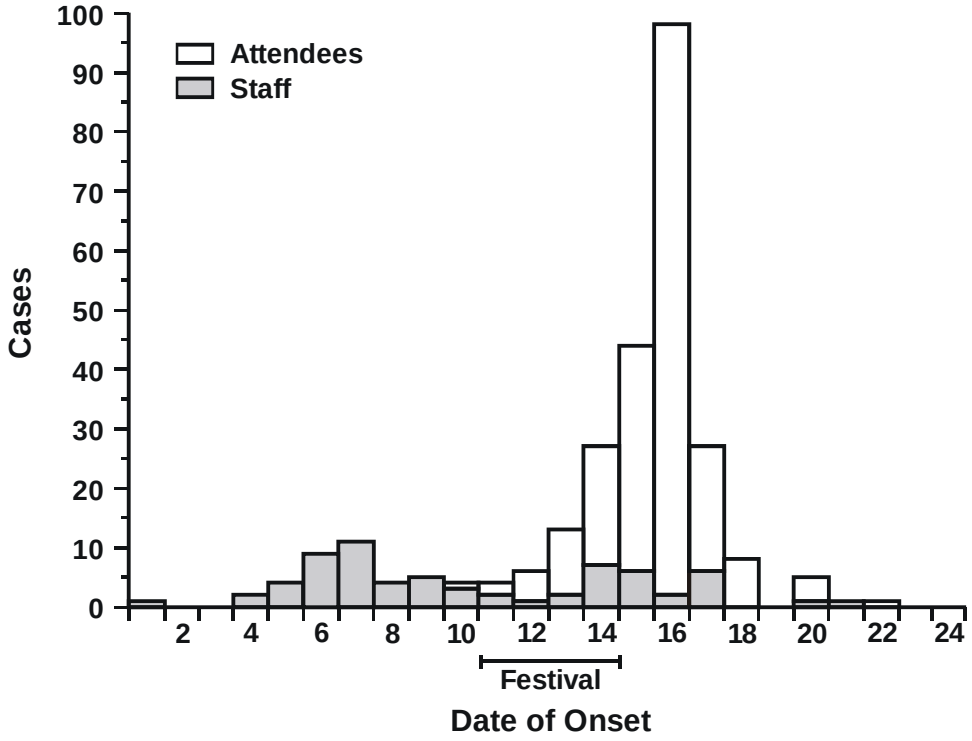
Finally, some epidemics are neither common source in its usual sense nor propagated from person-to-person. Outbreaks of zoonotic or vectorborne disease may result from sufficient prevalence of infection in host species, sufficient presence of vectors, and sufficient human-vector interaction. Examples include the epidemic of Lyme disease which affected several states in the northeastern United States in the late 1980's and the large epidemic of St. Louis encephalitis in Florida in 1990.

Figure 1.23
Example of a propagated epidemic that does not show the classic pattern: Infectious hepatitis cases by week of onset, Barren County, Kentucky, June 1970-April 1971



Source: 5

Figure 1.24
Example of a mixed epidemic: Shigella cases at a music festival by day of onset, Michigan, August 1988



Source: 19

Exercise 1.8

You have just studied about three epidemic patterns:

1) point source, 2) intermittent or continuous, and 3) propagated. For each of the following outbreak settings, choose the most likely epidemic pattern.

Pattern **Outbreak Setting**

_____ a. Outbreak of salmonellosis traced to turkey cooked and held at an improper temperature and served at a pot-luck supper.

_____ b. Outbreak of influenza among nursing home residents, new cases occurring over a 3-week period (Hint: incubation period for influenza is less than 5 days.)

_____ c. Episodic cases of Legionnaires' disease in hospitalized patients traced to showers and the hospital's water supply.

Answers on page 72.

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