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CHAPTER

2

Historic Developments in Epidemiology

OBJECTIVES

After completing this chapter, you will be able to:

- Describe important historic events in the field of epidemiology.
- List and describe the contribution made by several key individuals to the field of epidemiology.
- Recognize the development and use of certain study designs in the advancement of epidemiology.

The history of epidemiology has involved many key players who sought to understand and explain illness, injury, and death from an observational scientific perspective. These individuals also sought to provide information for the prevention and control of health-related states and events. They advanced the study of disease from a supernatural viewpoint to a viewpoint based on a scientific foundation; from no approach for assessment to systematic methods for summarizing and describing public health problems; from no clear understanding of the natural course of disease to a knowledge of the probable causes, modes of transmission, and health outcomes; and from no means for preventing and controlling disease to effective approaches for solving public health problems.

Initially, epidemiologic knowledge advanced slowly, with large segments in time where little or no advancement in the field occurred. The time from Hippocrates (460–377 BC), who attempted to explain disease occurrence from a rational viewpoint, to John Graunt (1620–1674 AD), who described disease occurrence and death with the use of systematic methods and who developed and calculated life tables and life expectancy, and Thomas Sydenham (1624–1689), who approached the study of disease from an observational angle

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rather than a theoretical one, was 2,000 years. Approximately 200 years later, William Farr (1807–1883) advanced John Graunt's work in order to better describe epidemiologic problems . In the 19th century, John Snow, Ignaz Semmelweis, Louis Pasteur, Robert Koch, Florence Nightingale, and others also made important contributions to the field of epidemiology. Since then, the science of epidemiology has rapidly progressed. Although it is impossible to identify all of the contributors to the field of epidemiology in this chapter, several of these individuals and their contributions are considered here.

HIPPOCRATES, THE FIRST EPIDEMIOLOGIST

Hippocrates was a physician who became known as the father of medicine and the first epidemiologist (**Figure 2-1**). His three books entitled *Epidemic I*, *Epidemic III*, and *On Airs, Waters and Places* attempted to describe disease from a rational perspective, rather than a supernatural basis. He observed that different diseases occurred in different locations. He noted that malaria and yellow fever most commonly occurred in swampy areas. It was not known, however, that the mosquito was responsible for such diseases until in 1900, when Walter Reed, MD, a U.S. Army physician working in the tropics, made the connection. Hippocrates also introduced terms like epidemic and endemic.[1–4]

Hippocrates gave advice to persons wishing to pursue the science of medicine and provided insights on the effects of the seasons of the year and hot and cold winds on health. He believed the properties of water should be examined and advised that the source of water should be considered.[1–4] He asked questions such as, "Is the water from a marshy soft-ground source, or is the water from the rocky heights? Is the water brackish and harsh?" Hippocrates also made some noteworthy observations on the behavior of the populace. He believed the effective physician should be observant of peoples' behavior, such as eating, drinking, and other activities. Did they eat lunch, eat too much, or drink too little? Were they industrious?

For traveling physicians, Hippocrates suggested they become familiar with local diseases and with the nature of those prevailing diseases. He believed that as time passed the physician should be able to tell what epidemic diseases might attack and in what season and that this could be determined by the settings of the stars. Sources of water, smells, and how water sets or flows were always considered in his study of disease states.[1–4]

Hippocrates identified hot and cold diseases and, consequently, hot and cold treatments. **Hot diseases** were treated with cold treatments, and **cold diseases** required hot treatments. The process of deciding whether a disease was hot or cold was complex. An example is diarrhea, which was considered a hot disease and was believed to be cured with a cold treatment such as eating fruit.[1–4]

Hippocrates also ascribed to and incorporated into his theory what is now considered the **atomic theory**—that is, the belief that everything is made of tiny particles. He theorized that there were four types of atoms: earth atoms (solid and cold), air atoms (dry), fire atoms (hot), and water atoms (wet). Additionally, Hippocrates believed that the body was composed of four humors: phlegm (earth and water atoms), yellow bile (fire and air atoms), blood (fire and water atoms), and black bile (earth and air atoms). Sickness was thought to be caused by an imbalance of these humors, and fever was thought to be caused by too much blood. The treatment for fever was to reduce the amount of blood in the body through bloodletting or the application of bloodsuckers (leeches). Imbalances were ascribed to a change in the body's "constitution." Climate, moisture, stars, meteorites, winds, vapors, and diet were thought to cause imbalances and contribute to disease. Diet was both a cause and cure of disease. Cures for illness and protection from disease came from maintaining a balance and avoiding imbalance in the constitution.

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FIGURE 2-1 Hippocrates. *Source:* United States National Library of Medicine, National Institutes of Health, History of Medicine. Available at: http://www.ihm.nlm.nih.gov/ihm/images/B/14/553.jpg. Accessed December 29, 2008.

The essentials of epidemiology noted by Hippocrates included observations on how diseases affected populations and how disease spread. He further addressed issues of diseases in relation to time and seasons, place, environmental conditions, and disease control, especially as it related to water and the seasons. The broader contribution to epidemiology made by Hippocrates was that of epidemiologic observation. His teachings about how to observe any and all contributing or causal factors of a disease are still sound epidemiologic concepts.[1–4]

DISEASE OBSERVATIONS OF SYDENHAM

Thomas Sydenham (1624–1689), although a graduate of Oxford Medical School, did not at first practice medicine but served in the military and as a college administrator. While at All Souls College, Oxford, he became acquainted with Robert Boyle, a colleague who sparked Sydenham's interest in diseases and epidemics. Sydenham went on to get his medical license, and he spoke out for strong empirical approaches to medicine and close observations of disease. Sydenham wrote the details of what he observed about diseases without letting various traditional theories of disease and medical treatment influence his work and observations. From this close observation process, he was able to identify and recognize different diseases. Sydenham published his observations in a book in 1676 titled *Observationes Medicae*.[4]

One of the major works of Sydenham was the classification of fevers plaguing London in the 1660s and 1670s. Sydenham came up with three levels or classes of fevers: continued fevers, intermittent fevers, and smallpox. Some of Sydenham's theories were embraced, whereas others were criticized, mostly because his ideas and observations went against the usual Hippocratic approaches. He treated smallpox with bed rest and normal bed covers. The treatment of the time, based on the Hippocratic theory, was to use heat and extensive bed coverings. He was met with good results but was erroneous in identifying the cause of the disease.[4]

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Sydenham was persecuted by his colleagues, who at one time threatened to take away his medical license for irregular practice that did not follow the theories of the time; however, he gained a good reputation with the public, and some young open-minded physicians agreed with his empirical principles. Sydenham described and distinguished different diseases, including some psychological maladies. He also advanced useful treatments and remedies, including exercise, fresh air, and a healthy diet, which other physicians rejected at the time.[4]

THE EPIDEMIOLOGY OF SCURVY

In the 1700s, it was observed that armies lost more men to disease than to the sword. James Lind (1716–1794), a Scottish naval surgeon, focused on illnesses in these populations. He observed the effect of time, place, weather, and diet on the spread of disease. His 1754 book *A Treatise on Scurvy* identified the symptoms of scurvy and the fact that the disease became common in sailors after as little as a month at sea.[3,4]

Lind noticed that while on long ocean voyages, sailors would become sick from scurvy, a disease marked by spongy and bleeding gums, bleeding under the skin, and extreme weakness. He saw that scurvy began to occur after 4–6 weeks at sea. Lind noted that even though the water was good and the provisions were not tainted, the sailors still fell sick. Lind pointed out that the months most common to scurvy were April, May, and June. He also observed that cold, rainy, foggy, and thick weather were often present. Influenced by the Hippocratic theory of medicine, Lind kept looking to the air as the source of disease. Dampness of the air, damp living arrangements, and life at sea were the main focus of his observations as he searched for an explanation of the cause of disease and, most of all, the cause of scurvy.[5] Although not correct about the link with weather and climate at sea, Lind looked at all sides of the issue and considered what was happening to the sick. He then compared their experience with the experiences of those who were healthy.

When Lind began to look at the diet of the mariners, he observed that the sea diet was extremely gross and hard on digestion. Concerned with the extent of sickness in large numbers of sailors, Lind set up some experiments with mariners. In 1747, while serving on the HMS Salisbury, he conducted an experimental study on scurvy. He took 12 ill patients who had all of the classic symptoms of scurvy. They all seemed to have a similar level of the illness. He described their symptoms as putrid gums, spots, and lassitude, with weakness in their knees. He put the sailors in six groups of two and, in addition to a common diet of foods like water-gruel sweetened with sugar, fresh mutton broth, puddings, boiled biscuit with sugar, barley and raisins, rice and currants, and sago and wine, each of the groups received an additional dietary intervention. Two men received a quart of cider a day on an empty stomach. Two men took two spoonfuls of vinegar three times a day on an empty stomach. Two men were given a half-pint of sea water every day. Two men were given lemons and oranges to eat on an empty stomach. Two men received an elixir recommended by a hospital surgeon, and two men were fed a combination of garlic, mustard seed, and horseradish. Lind says that the men given the lemons and oranges ate them with "greediness." The most sudden and visible good effects were seen in those who ate lemons and oranges. In 6 days, the two men eating citrus were fit for duty. All of the others had putrid gums, spots, lassitude, and weakness of the knees. Free of symptoms, the two citrus-eating sailors were asked to nurse the others who were still sick. Thus, Lind observed that oranges and lemons were the most effective remedies for scurvy at sea.[5] As a consequence of Lind's epidemiologic work, since 1895, the British navy has required that

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limes or lime juice be included in the diet of seamen, resulting in the nickname of British seamen of "limeys."

The epidemiologic contributions of Lind were many. He was concerned with the occurrence of disease in large groups of people. Lind not only participated in the identification of the effect of diet on disease, but he made clinical observations, used experimental design, asked classic epidemiologic questions, observed population changes and their effect on disease, and considered sources of disease, including place, time, and season.

EPIDEMIOLOGY OF COWPOX AND SMALLPOX

In England, Benjamin Jesty, a farmer/dairyman in the mid 1700s, noticed his milkmaids never got **smallpox**, a disease characterized by chills, fever, headache, and backache, with eruption of pimples that blister and form pockmarks; however, the milkmaids did develop cowpox from the cows. Jesty believed there was a link between acquiring cowpox and not getting smallpox. In 1774, Jesty exposed his wife and children to cowpox to protect them from smallpox. It worked. The exposed family members developed immunity to smallpox. Unfortunately, little was publicized about Jesty's experiment and observations.[4]

The experiment of Jesty and similar reported experiences in Turkey, the Orient, America, and Hungary were known to Edward Jenner (1749–1823), an English rural physician. He personally observed that dairymen's servants and milkmaids got cowpox and did not get smallpox. For many centuries, the Chinese had made observations about weaker and stronger strains of smallpox. They learned that it was wise to catch a weaker strain of the disease. If one had a weak strain of the disease, one would not get the full disease later on. This was termed **variolation**.[3,4]

In the late 1700s, servants were often the ones who milked the cows. Servants were also required to tend to the sores on the heels of horses affected with cowpox. The pus and infectious fluids from these sores were referred to as "the grease" of the disease. Left unwashed because of a lack of concern about sanitation and cleanliness, the servants' grease-covered hands would then spread the disease to the cows during milking. The cowpox in turn was transmitted to the dairymaids. Jenner observed that when a person had cowpox this same person would not get smallpox if exposed to it. Jenner attempted to give a dairymaid, exposed to a mild case of cowpox in her youth, a case of smallpox by cutting her arm and rubbing some of the infectious "grease" into the wound. She did not become ill. Cowpox was thus found to shield against smallpox.[3,4] Jenner invented a vaccination for smallpox with this knowledge. The vaccine was used to protect populations from this disease.[3,4,6]

The Worldwide Global Smallpox Eradication Campaign of the late 1960s and early 1970s encouraged vaccination against smallpox and was effective at eliminating this disease. As part of the effort to eradicate smallpox, a photograph was widely distributed in 1975 of a small child who had been stricken with the disease (**Figure 2-2**). On October 26, 1977, World Health Organization workers supposedly tracked down the world's last case of naturally occurring smallpox. The patient was 23-year-old Ali Maow Maalin, a hospital cook in Merka, Somalia. Two cases of smallpox occurred in 1978 as a result of a laboratory accident. Because it is believed that smallpox has been eradicated from the earth, vaccinations have been halted; however, some public-health and healthcare professionals are skeptical and fear that such acts may set the stage for an unexpected future epidemic of smallpox because the pathogen still exists in military and government labs. As unvaccinated persons proliferate, so does the risk of future smallpox epidemics.

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FIGURE 2-2 Picture of a boy taken by Dr. Stan Foster, EIS, Officer, class of 1962. Pictures courtesy of Centers for Disease Control and Prevention, Atlanta, Georgia.

EPIDEMIOLOGY OF CHILDBED FEVER IN A LYING-IN HOSPITAL

Historically, epidemiology was centered on the study of the great epidemics: cholera, bubonic plague, smallpox, and typhus. As the diseases were identified and differentiated, the focus of epidemiology changed. Such a change in focus came through the work of another physician–epidemiologist, Ignaz Semmelweis, in the early to mid 1800s.[7]

In the 1840s, one of the greatest fears a pregnant mother had was dying of **childbed fever** (a uterine infection, usually of the placental site, after childbirth). Babies were born to mothers with the usual risks that warranted obstetric assistance, and this often resulted in an uneventful birth; however, after the birth of the child, the mother would get an infection and die of childbed fever, a streptococcal disease. Many times the child would become infected and die as well. After many years of observing the course of the disease and the symptoms associated with childbed fever, Semmelweis began a series of investigations.[7]

The Viennese Maternity Hospital (called a lying-in hospital), of which Semmelweis was clinical director, was divided into two clinics. The first clinic consistently had greater numbers of maternal deaths than the second clinic. In 1846, the maternal mortality rate of this clinic was five times greater than that of the second clinic, and over a 6-year period, it was three times as great. Semmelweis observed that the mothers became ill either immediately during birth or within 24–36 hours after delivery. The mothers died quickly of rapidly developing childbed fever. Often the children would soon die as well. This was not the case in the second clinic.[7]

Semmelweis observed it was not the actual labor that was the problem but that the examination of the patients seemed to be connected to the onset of the disease. Through clinical observation, retrospective study, collection and analysis of data on maternal deaths and infant deaths, and clinically controlled experimentation, he was able to ascertain that the communication of childbed fever was through germs passed from patient to patient by the physician in the process of doing pelvic examinations. Semmelweis discovered that, unlike the second clinic, the medical students would come directly from

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the death house after performing autopsies of infected and decaying dead bodies and then would conduct pelvic exams on the mothers ready to give birth. Hand washing or any form of infection control was not a common practice. Unclean hands with putrefied cadaver material on student doctors' hands were used to conduct the routine daily pelvic exams, and the practice was never questioned. There was no reason to be concerned about clean hands because the theory of medicine that was accepted at the time relied on the Hippocratic theory of medicine and the idea that disease developed spontaneously. Semmelweis observed that a whole row of patients became ill while patients in the adjacent row stayed healthy.[7]

Semmelweis discovered that any infected or putrefied tissue, whether from a living patient or a cadaver, could cause disease to spread. In order to destroy the cadaverous or putrefied matter on the hands, it was necessary that every person, physician or midwife, performing an examination, would wash their hands in chlorinated lime upon entering the labor ward in clinic 1. At first, Semmelweis said it was only necessary to wash during entry to the labor ward; however, a cancerous womb was discovered to also cause the spread of the disease, and thus, Semmelweis required washing with chlorinated lime between each examination. When strict adherence to hand washing was required of all medical personnel who examined patients in the maternity hospital, mortality rates fell at unbelievable rates. In 1842, the percentage of deaths was 12.1% (730 of 6,024) compared with 1.3% (91 of 7,095) in 1848.[7]

At this time in the history of public health, the causes of disease were unknown, yet suspected. It was known that hand washing with chlorinated lime between each examination reduced the illness and deaths from childbed fever, but even with the evidence of this success, Semmelweis's discovery was discounted by most of his colleagues.[7] Today, it is known that hand washing is still one of the best sanitation practices for medical and lay people alike. What Ignaz Semmelweis discovered is still one of the easiest disease- and infection-control methods known.

JOHN SNOW'S EPIDEMIOLOGIC INVESTIGATIONS OF CHOLERA

In the 1850s, John Snow (1813–1858) was a respected physician and the anesthesiologist of Queen Victoria of England (**Figure 2-3**). He is noted for his medical work with the royal family, including the administration of chloroform to the queen at the birth of her children; however, Snow is most famous for his pioneering work in epidemiology. Among epidemiologists, Snow is considered one of the most important contributors to the field. Many of the approaches, concepts, and methods used by Snow in his epidemiologic work are still useful and valuable in epidemiologic work today.[8–10]

Throughout his medical career, Snow studied cholera. Cholera is a disease characterized by watery diarrhea, loss of fluid and electrolytes, dehydration, and collapse. From his studies, he established sound and useful epidemiologic methods. He observed and recorded important factors related to the course of disease. In the later part of his career, Snow conducted two major investigative studies of cholera. The first involved a descriptive epidemiologic investigation of a cholera outbreak in the Soho district of London in the Broad Street area. The second involved an analytic epidemiologic investigation of a cholera epidemic in which he compared death rates from the disease to where the sufferers got their water, either the Lambeth Water Company or the Southwark and Vauxhall Water Company.[8–10]

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In the mid 1840s, in the Soho and Golden Square districts of London, a major outbreak of cholera occurred. Within 250 yards of the intersection of Cambridge Street and Broad Street, about 500 fatal attacks of cholera occurred in 10 days. Many more deaths were averted because of the flight of most of the population. Snow was able to identify incubation times, the length of time from infection until death, modes of transmission of the disease, and the importance of the flight of the population from the dangerous areas. He also plotted statistics based on dates and mortality rates. He studied sources of contamination of the water, causation and infection, and the flow of the water in the underground aquifer by assessing water from wells and pumps. He found that nearly all deaths had taken place within a short distance of the Broad Street pump.

Snow observed that in the Soho district there were two separate populations of persons not so heavily affected by the cholera epidemic, such that death rates were not equal to those of the surrounding populations. A brewery with its own wells and a workhouse, also with its own water source, were the protected populations. Snow used a spot map (sometimes called a dot map) to identify the locations of all deaths. He plotted data on the progress of the course of the epidemic and the occurrence of new cases as well as when the epidemic started, peaked, and subsided. Snow examined the water, movement of people, sources of exposure, transmission of the disease between and among close and distant people, and possible causation. Toward the end of the epidemic, as a control measure, protection from any reoccurrence, and a political statement to the community, Snow removed the handle from the Broad Street pump.[8–10]

In his early days as a practicing physician before the Broad Street outbreak, Snow recorded detailed scenarios of several cases of cholera, many of which he witnessed firsthand. Many of the details he chose to record were epidemiologic in nature, such as various modes of transmission of cholera, incubation times, cause–effect association, clinical observations and clinical manifestations of the disease, scientific observations on water and the different sources (including observations made with a microscope), temperature, climate, diet, differences between those who got the disease and those who did not, and immigration and emigration differences.[8–10]

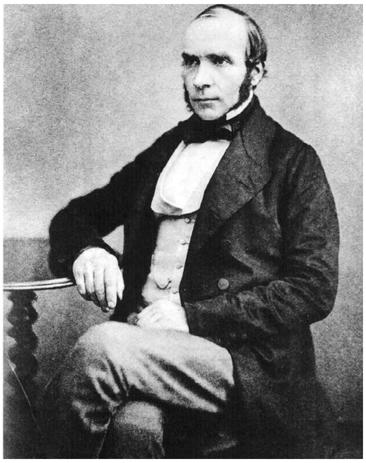

FIGURE 2-3 John Snow.

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In 1853, a larger cholera outbreak occurred in London. London had not had a cholera outbreak for about 5 years. During this period, the Lambeth Water Company moved their intake source of water upriver on the Thames, from opposite Hungerford Market to a source above the city, Thames Ditton. By moving the source of water upriver to a place above the sewage outlets, Lambeth was able to draw water free from London's sewage, contamination, and pollution. The Southwark and Vauxhall Water Company, however, did not relocate its source of water. Throughout the south district of the city, both water companies had pipes down every street. The citizens were free to pick and choose which water company they wanted for their household water. Thus, by mere coincidence, Snow encountered a populace using water randomly selected throughout the south district. Snow could not have arranged better sampling techniques than those which had occurred by chance.[8–10]

The registrar general in London published a "Weekly Return of Births and Deaths." On November 26, 1853, the Registrar General observed from a table of mortality that mortality rates were fairly consistent across the districts supplied with the water from the Hungerford market area. The old supply system of Lambeth and the regular supply of the Southwark and Vauxhall Company were separate systems but drew water from the same area in the river. The registrar general also published a mortality list from cholera. Snow developed comparison tables on death by source of water by subdistricts. Snow was able to conclude that the water drawn upriver solely by Lambeth Water Company caused no deaths. The water drawn downstream, in areas that were below the sewage inlets, mostly by Southwark and Vauxhall Water Company, was associated with very high death rates.[8–10]

Gaining cooperation and permission from the registrar general, Snow was supplied with addresses of persons who had died from cholera. He went into the subdistrict of Kennington One and Kennington Two and found that 38 of 44 deaths in this subdistrict received their water from Southwark and Vauxhall Company. Each house had randomly selected different water companies, and many households did not know from which one they received water. Snow developed a test that used chloride of silver to identify which water source each household had by sampling water from within the houses of those he contacted. Snow was eventually able to tell the source of water by appearance and smell.[8–10]

Vital statistics data and death rates compared according to water supplier presented conclusive evidence as to the source of contamination. A report to Parliament showed that in the 30,046 households that were supplied water by the Southwark and Vauxhall Company, 286 persons died of cholera. Of the 26,107 houses supplied by Lambeth, only 14 died of cholera. The death rate was 71 per 10,000 in Southwark and Vauxhall households and 5 per 10,000 for Lambeth households. The mortality at the height of the epidemic in households supplied with water by Southwark and Vauxhall was eight to nine times greater than in those supplied by Lambeth. Snow was finally able to prove his hypothesis that contaminated water passing down the sewers into the river, then being drawn from the river and distributed through miles of pipes into peoples' homes, produced cholera throughout the community. Snow showed that cholera was a **waterborne** disease that traveled in both surface and groundwater supplies[8–10] (see News File).

Snow laid the groundwork for descriptive and analytic epidemiologic approaches found useful in epidemiology today. He identified various modes of transmission and incubation times and, in his second study, employed a comparison group to establish more definitively a cause–effect association. It was not until Koch's work in 1883 in Egypt, when he isolated and cultivated Vibrio cholerae, that the accuracy and correctness of Snow's work was proved and accepted.[3,4,8–10] Because of the contributions made by John Snow, he has been referred to by many as the Father of Epidemiology.

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EPIDEMIOLOGIC WORK OF PASTEUR AND KOCH

In the 1870s, on journeys into the countryside of Europe, it was not uncommon to see dead sheep lying in the fields. These sheep had died from anthrax, which most commonly occurs in animals but can also occur in humans. Anthrax was a major epidemic that plagued the farmers and destroyed them economically.[3,4]

By this time, Louis Pasteur (1822–1895), a French chemist, had been accepted into France's Academy of Medicine for his work in microbiology. Pasteur had distinguished himself as a scientist and a respected contributor to the field of medicine and public health (even though it was not recognized as a separate field at the time). Pasteur had already identified the cause of rabies and many other devastating diseases. Because of his many past successes in microbiology, Pasteur had confidence in his ability to take on the challenge of conquering anthrax.[3,4]

Pasteur was convinced that it was the bacteria identified as anthrax that caused the disease, because anthrax bacteria were always present on necropsy (autopsy) of sheep that died from anthrax. It was unclear, however, why the course of the disease occurred the way it did. The cause–effect association seemed to have some loopholes in it. How did the sheep get anthrax? How were the sheep disposed of? Why did the anthrax occur in some areas and not in others? How was the disease transmitted? How did the disease survive? All were questions that Louis Pasteur sought to answer.

Pasteur observed that the dead sheep were buried. The key and insightful discovery was that anthrax spores and/or bacteria were brought back to the surface by earthworms. Koch had previously shown that the anthrax bacteria existed in silkworms and that anthrax was an intestinal disease. Pasteur made the earthworm connection.

Pasteur and his assistants had worked on a vaccine for anthrax for months, and in 1881, an anthrax vaccine was discovered. After a presentation at the Academy of Sciences in Paris, Pasteur was challenged to prove that his vaccine was effective. He put his career and reputation at stake to prove that his vaccine would work, that disease was caused by microorganisms, and that a cause–effect association exists between a particular microbe and a certain disease.

Pasteur agreed to the challenge with a public demonstration to prove his vaccination process could prevent sheep from getting anthrax. He went to a farm in rural France where 60 sheep were provided for the experiment. He was to vaccinate 25 of the sheep with his new vaccine. After the proper waiting time, Pasteur was then to inoculate 50 of the sheep with a virulent injection of anthrax. Ten sheep were to receive no treatment and were used to compare with the survivors of the experiment (a control group). Pasteur was successful. The inoculated sheep lived. The unvaccinated sheep died, and the control group had no changes. Pasteur successfully demonstrated that his method was sound, that vaccinations were effective approaches in disease control, and that bacteria were indeed causes of disease.

Historically many scientists have contributed to the method used in epidemiology. Robert Koch (1843–1910) lived in Wollstein, a small town near Breslau, in rural Germany (Prussia). Koch was a private practice physician and district medical officer. Because of his compelling desire to study disease experimentally, he set up a laboratory in his home and purchased equipment, including photography equipment, out of his meager earnings. Robert Koch became a key medical research scientist in Germany in the period of the explosion of knowledge in medicine and public health, and he used photography to take the first pictures of microbes in order to show the world that microorganisms do in fact exist and that they are what cause disease.[3,4,11]

In the 1870s, Koch showed that anthrax was transmissible and reproducible in experimental animals (mice). He identified the spore stage of the growth cycle of microorganisms.

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The epidemiologic significance that Koch demonstrated was that the anthrax bacillus was the only organism that caused anthrax in a susceptible animal.

In 1882, Koch discovered the tubercle bacillus with the use of special culturing and staining methods. Koch and his assistant also perfected the concept of steam sterilization. In Egypt and India, he and his assistants discovered the cholera bacterium and proved that it was transmitted by drinking water, food, and clothing. Incidental to the cholera investigations, Koch also found the microorganisms that cause infectious conjunctivitis. One of his major contributions to epidemiology was a paper on waterborne epidemics and how they can be largely prevented by proper water filtration.[3,4,11]

Koch, who began as a country family physician, pioneered the identification of microorganisms and many different bacteria that caused different diseases as well as pure culturing techniques for growing microorganisms in laboratory conditions. Some of the major public health contributions that Koch made were the identification of the tuberculosis and cholera microorganisms and the establishment of the importance of water purification in disease prevention. He was the recipient of many honors throughout his lifetime, including the Nobel Prize in 1905 for his work in microbiology.[3,4,11,12]

Both Pasteur and Koch were successful in putting to rest a major misguided notion of medicine at the time: that the diseases were a result of "spontaneous generation"—that is, organisms would simply appear out of other organisms, and a fly would spontaneously appear out of garbage, and so forth.[8]

THE INVENTION OF THE MICROSCOPE

The important findings of Koch, Pasteur, Snow, and many others in this era of sanitation and microbe discovery would have been impossible without the use of the microscope. Koch's camera would not have been invented if the microscope had not been developed and its lenses adapted to picture taking.

The microscope first found scientific use in the 1600s through the work of Cornelius Drebbel (1572–1633), the Janssen brothers of the Netherlands (1590s), and Antoni Van Leeuwenhoek (1632–1723). The microscope was used for medical and scientific purposes by Athanasius Kircher of Fulda (1602–1680). In 1658 in Rome, he wrote his publication *Scrutinium Pestis*. He conducted experiments on the nature of putrefaction and showed how microscopic living organisms and maggots develop in decaying matter. He also discovered that the blood of plague patients was filled with countless "worms" not visible to the human eye.

Most of the credit goes to Leeuwenhoek for the advancement, development, and perfection of the use of the microscope. He was the first to effectively apply the microscope in the study of disease and medicine, even though he was not a physician. Because of a driving interest in the microscope, Leeuwenhoek was able to devote much time to microscopy, owning over 247 microscopes and over 400 lenses (many of which he ground himself). He was the first to describe the structure of the crystalline lens.

Leeuwenhoek made contributions to epidemiology. He did a morphologic study of red corpuscles in the blood. He saw the connection of arterial circulation to venous circulation in the human body through the microscopic study of capillary networks. With his microscope, Leeuwenhoek contributed indirectly to epidemiology through microbiology by discovering "animalcules" (microscopic organisms, later called microbes, bacteria, and microorganisms).

In addition to epidemiology and microbiology, chemistry and histology were also developed because of the advent of the microscope, which influenced advances in the study and control of diseases.[4,13]

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JOHN GRAUNT AND VITAL STATISTICS

Another major contributor to epidemiology, but in a different manner, was John Graunt (1620–1674). In 1603 in London, a systematic recording of deaths commenced and was called the "bills of mortality." It is summarized in **Table 2-1**. This was the first major contribution to record-keeping on a population and was the beginning of the vital statistics aspect of epidemiology. When Graunt took over the work, he systematically recorded ages,

TABLE 2-1 Selections from *Natural and Political Observations Made Upon the Bills of Mortality* by John Graunt (First Edition 1662)

The Diseases and Casualties This Year Being 1632

Abortive and Stillborn	445	Jaundies	43
Afrighted	1	Jawfain	8
Aged	628	Impostume	74
Ague	43	Kil'd by Several Accident	46
Apoplex, and Meagrom	17	King's Evil	38
Bit with a mad dog	1	Lethargie	2
Bloody flux, Scowring, and Flux	348	Lunatique	5
Brused, Issues, Sores, and Ulcers	28	Made away themselves	15
Burnt and Scalded	5	Measles	80
Burst, and Rupture	9	Murthered	7
Cancer, and Wolf	10	Over-laid/starved at nurse	7
Canker	1	Palsie	25
Childbed	171	Piles	8
Chrisomes, and Infants	2,268	Plague	8
Cold and Cough	55	Planet	13
Colick, Stone, and Strangury	56	Pleurisie, and Spleen	36
Consumption	1,797	Purples, and Spotted Fever	38
Convulsion	241	Quinsie	7
Cut of the Stone	5	Rising of the Lights	98
Dead in the street and starved	6	Sciatica	1
Dropsie and Swelling	267	Scurvey, and Itch	9
Drowned	34	Suddenly	62
Executed and Prest to Death	18	Surfet	86
Falling Sickness	7	Swine Pox	6
Fever	1,108	Teeth	470
Fistula	13	Thrush, Sore Mouth	40
Flox and Small Pox	531	Tympany	13
French Pox	12	Tissick	34
Gangrene	5	Vomiting	1
Gowt	4	Worms	27
Grief	11		

Christened	**Buried**
Males 4,994	Males 4,932
Females 4,590	Females 4,603
In All 9,584	In All 9,535

Increased in the Burials in the 122 Parishes, and at the Pesthouse this year—993

Decreased of the Plagues in the 122 Parishes, and at the Pesthouses this year—266

From Johns Hopkins Press: Baltimore, 1937.

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and gender, who died, what killed them, and where and when the deaths occurred. Graunt also recorded how many persons died each year and the cause of death.[4,11]

Through the analysis of the bills of mortality already developed for London, Graunt summarized mortality data and developed a better understanding of diseases as well as sources and causes of death. Using the data and information he collected, Graunt wrote a book, *Natural and Political Observations Made Upon the Bills of Mortality*. From the bills of mortality, Graunt identified variations in death according to gender, residence, season, and age. Graunt was the first to develop and calculate life tables and life expectancy. He divided deaths into two types of causes: acute (struck suddenly) and chronic (lasted over a long period of time).[4,11]

When Graunt died, little was done to continue his good work until 200 years later, when William Farr (1807–1883) was appointed registrar general in England. Farr built on the ideas of Graunt. The concept of "political arithmetic" was replaced by a new term, "statistics." Farr extended the use of vital statistics and organized and developed a modern vital statistics system, much of which is still in use today. Another important contribution of Farr was to promote the idea that some diseases, especially chronic diseases, can have a **multifactorial etiology**.[14]

OCCUPATIONAL HEALTH AND INDUSTRIAL HYGIENE

Bernardino Ramazzini (1633–1714) was born in Carpi near Modena, Italy (**Figure 2-4**). He received his medical training at the University of Parma and did postgraduate studies in Rome. Ramazzini eventually returned to the town of Modena, where he became a professor of medicine at the local university. He was interested in the practical problems of medicine and not in the study of ancient theories of medicine, a fact not well received by his colleagues. Through Ramazzini's continuous curiosity and his unwillingness to confine himself to the study of ancient medical theories, he became recognized for his innovative approaches to medical and public health problems. For example, in 1692, at the age of 60, Ramazzini was

FIGURE 2-4 Bernardino Ramazzini. Picture courtesy of the United States National Library of Medicine, National Institutes of Health, History of Medicine. http://wwwihm.nlm.nih.gov/ihm/images/B/21/633.jpg or http://wwwihm.nlm.nih.gov/ihm/images/B/21/634.jpg. Accessed January 13, 2009.

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climbing down into 80-foot wells, and taking temperature and barometric readings in order to discover the origin and rapid flow of Modena's spring water. He tried to associate barometric readings with the cause of disease by taking daily readings during a typhus epidemic (infectious disease characterized by high fever, a transient rash, and severe illness).[3,4,11,13]

Ramazzini came on a worker in a cesspool. In his conversation with the worker, Ramazzini was told that continued work in this environment would cause the worker to go blind. Ramazzini examined the worker's eyes after he came out of the cesspit and found them bloodshot and dim. After inquiring about other effects of working in cesspools and privies, he was informed that only the eyes were affected.[3,4,11,13]

The event with the cesspool worker turned his mind to a general interest in the relationship of work to health. He began work on a book that would become influential in the area of occupational medicine and provided related epidemiologic implications. The book, titled *The Diseases of Workers*, was completed in 1690 but not published until 1703. It was not acceptable to pity the poor or simple laborers in this period of time, which caused Ramazzini to delay the publication because he thought it would not be accepted.[3,4,11,13]

Ramazzini observed that disease among workers arose from two causes. The first, he believed, was the harmful character of the materials that workers handled because the materials often emitted noxious vapors and very fine particles that could be inhaled. The second cause of disease was ascribed to certain violent and irregular motions and unnatural postures imposed on the body while working.[3,4,11,13]

Ramazzini described the dangers of poisoning from lead used by potters in their glaze. He also identified the danger posed by the use of mercury as used by mirror makers, goldsmiths, and others. He observed that very few of these workers reached old age. If they did not die young, their health was so undermined that they prayed for death. He observed that many had palsy of the neck and hands, loss of teeth, vertigo, asthma, and paralysis. Ramazzini also studied those who used or processed organic materials such as mill workers, bakers, starch makers, tobacco workers, and those who processed wool, flax, hemp, cotton, and silk—all of whom suffered from inhaling the fine dust particles in the processing of the materials.[3,4,11,13]

Ramazzini further examined the harmful effects of the physical and mechanical aspects of work, such as varicose veins from standing, sciatica caused by turning the potter's wheel, and ophthalmia found in glassworkers and blacksmiths. Kidney damage was seen to be suffered by couriers and those who rode for long periods, and hernias appeared among bearers of heavy loads.[3,4,11,13]

Major epidemiologic contributions made by Ramazzini were not only his investigation into and description of work-related maladies but his great concern for prevention. Ramazzini suggested that the cesspool workers fasten transparent bladders over their eyes to protect them and take long rest periods or, if their eyes were weak, get into a different line of work. In discussing the various trades, he suggested changing posture, exercising, providing adequate ventilation in workplaces, and avoiding extreme temperatures in the workplace.

Ramazzini was an observant epidemiologist. He described the outbreak of lathyrism in Modena in 1690. He also described the malaria epidemics of the region and the Paduan cattle plague in 1712.[3,4,11,13]

FLORENCE NIGHTINGALE

Florence Nightingale (1820–1910) was the daughter of upper-class British parents (**Figure 2-5**). She pursued a career in nursing, receiving her initial training in Kaiserworth at a hospital run by an order of Protestant Deaconesses. Two years later, she gained further experience as the superintendent at the Hospital for Invalid Gentlewomen in London, England.

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FIGURE 2-5 Florence Nightingale. Picture courtesy of the United States National Library of Medicine, National Institutes of Health, History of Medicine. http://wwwihm.nlm.nih.gov/ihm/images/B/20/486.jpg or http://wwwihm.nlm.nih.gov/ihm/images/B/20/488.jpg

After reading a series of correspondence from the *London Times* in 1854 on the plight of wounded soldiers fighting in the Crimea, Nightingale asked the British secretary of war to let her work in military hospitals at Scutari, Turkey. In addition to granting her permission, he also designated her head of an official delegation of nurses. Nightingale worked for the next 2 years to improve the sanitary conditions of army hospitals and to reorganize their administration. The *Times* immortalized her as the "Lady with the Lamp" because she ministered to the soldiers throughout the night.

When she returned to England, Nightingale carried out an exhaustive study of the health of the British Army. She created a plan for reform, which was compiled into a 500-page report entitled *Notes on Matters Affecting the Health, Efficiency, and Hospital Administration of the British Army* (1858). In 1859, she published *Notes on Hospitals*, which was followed in 1860 by *Notes on Nursing: What It Is and What It Is Not*. That same year she established a nursing school at St. Thomas's Hospital in London.

Nightingale wanted to make nursing a respectable profession and believed that nurses should be trained in science. She also advocated strict discipline and an attention to cleanliness, and felt that nurses should possess an innate empathy for their patients. Although Nightingale became an invalid after her stay in the Crimea, she remained an influential leader in public health policies related to hospital administration until her death on August 13, 1910.

Her outspoken *Notes on Matters Affecting the Health, Efficiency and Hospital Administration of the British Army* (1857) and *Notes on Hospitals* (1859) helped to create changes in hygiene and overall treatment of patients. She also founded the groundbreaking Nightingale Training School for nurses and in later years published dozens of books and pamphlets on public health. Nightingale was awarded the Royal Red Cross by Queen Victoria in 1883 and in 1907 became the first woman to receive the Order of Merit.

With the encouragement of her father, Nightingale received an education, studying Italian, Latin, Greek and history, and received excellent training in mathematics. During her time at Scutari, she collected data and systematized record-keeping practices. She used the data as a tool for improving city and military hospitals. She collected and generated data and statistics by developing a Model Hospital Statistical Form for hospitals.

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Nightingale's monitoring of disease mortality rates showed that with improved sanitary methods in hospitals death rates decreased. Nightingale developed applied statistical methods to display her data, showing that statistics provided an organized way of learning and improving medical and surgical practices. In 1858, she became a Fellow of the Royal Statistical Society, and in 1874 became an honorary member of the American Statistical Association.[15–19]

TYPHOID MARY

In the early 1900s, 350,000 cases of typhoid occurred each year in the United States. **Typhoid fever** is an infectious disease characterized by a continued fever, physical and mental depression, rose-colored spots on the chest and abdomen, diarrhea, and sometimes intestinal hemorrhage or perforation of the bowel. An Irish cook, Mary Mallon, referred to as Typhoid Mary, was believed to be responsible for 53 cases of typhoid fever in a 15-year period.[12]

George Soper, a sanitary engineer studying several outbreaks of typhoid fever in New York City in the 1900s, found the food and water supply was no longer suspect as the primary means of transmission of typhoid. Soper continued to search for other means of communication of the disease. He began to look to people instead of fomites, food, and water.

He discovered that Mary Mallon had served as a cook in many homes that were stricken with typhoid. The disease always seemed to follow, but never precede, her employment. Bacteriologic examination of Mary Mallon's feces showed that she was a chronic carrier of typhoid. Mary seemed to sense that she was giving people sickness, because when typhoid appeared, she would leave with no forwarding address. Mary Mallon illustrated the importance of concern over the chronic typhoid carrier causing and spreading typhoid fever. Like 20% of all typhoid carriers, Mary suffered no illness from the disease. Epidemiologic investigations have shown that carriers might be overlooked if epidemiologic searches are limited to the water, food, and those with a history of the disease.[12,20]

From 1907 to 1910, Mary was confined by health officials. The New York Supreme Court upheld the community's right to keep her in custody and isolation. Typhoid Mary was released in 1910, through legal action she took, and she disappeared almost immediately. Two years later, typhoid fever occurred in a hospital in New Jersey and a hospital in New York. More than 200 people were affected. It was discovered that Typhoid Mary had worked at both hospitals as a cook but under a different name. This incident taught public health officials and epidemiologists the importance of keeping track of carriers. It also showed that typhoid carriers should never be allowed to handle food or drink intended for public consumption. In later years, Typhoid Mary voluntarily accepted isolation. Typhoid Mary died at age 70 years.[12,20]

The investigating, tracking, and controlling of certain types of diseases that can affect large populations were epidemiologic insights gained from the Typhoid Mary experience. The importance of protecting public food supplies and the importance of the investigative aspects of disease control were again reinforced and further justified as public health measures. Today, antibiotic therapy is the only effective treatment for typhoid fever.

VITAMINS AND NUTRITIONAL DISEASES

In the mid to late 1800s, bacteria were being identified as the major causes of disease; however, the discovery of microorganisms and their connection to disease clouded the discovery of the causes of other life-threatening diseases. Beriberi, rickets, and pellagra were still devastating the populations around the world. It was believed in 1870 that up to one third

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of poor children in the inner city areas of major cities in the world suffered from serious rickets. Biochemistry was being advanced, and new lines of investigation were opening up. In the 1880s, it was observed that when young mice were fed purified diets, they died quickly. When fed milk, they flourished. In 1887, a naval surgeon, T. K. Takaki, eradicated beriberi from the Japanese navy by adding vegetables, meat, and fish to their diet, which up until then was mostly rice. In 1889, at the London Zoo, it was demonstrated that rickets in lion cubs could be cured by feeding them crushed bone, milk, and cod liver oil.[11,21,22]

The first major epidemiologic implications of deficiency illnesses came in 1886 when the Dutch commissioned the firm of C. A. Pekelharing and Winkler who sent Christian Eijkman (1858–1930), an army doctor, to the East Indies to investigate the cause of beriberi. Eijkman observed that chickens fed on polished rice developed symptoms of beriberi and recovered promptly when the food was changed to whole rice, but he mistakenly attributed the cause of the disease to a neurotoxin. Eijkman and G. Grijns (1865–1944), a physiologist, suggested that beriberi was a result of the lack of some essential substance in the outer layer of the rice grain. In 1905, Pekelharing conducted a series of experiments based on Eijkman's observations, was more thorough in his work, and came to the same conclusions.

In 1906, Frederick Gowland Hopkins (1861–1947), a British biochemist, did similar studies with a concern for the pathogenesis of rickets and scurvy. Hopkins suggested that other nutritional factors exist beyond the known ones of protein, carbohydrates, fat, and minerals, and these must be present for good health.

In 1911, Casimir Funk (1884–1967), a Polish chemist, isolated a chemical substance that he believed belonged to a class of chemical compounds called amines. Funk added the Latin term for life, *vita*, and invented the term "vitamine." He authored the book *Vitamines*. In 1916, E. V. McCollum showed that two factors were required for the normal growth of rats, a fat-soluble "A" factor found in butter and fats and a water-soluble "B" factor found in non-fatty foods such as whole grain rice. These discoveries set the stage for labeling **vitamins** by letters of the alphabet. McCollum in the United States and E. Mellanby in Great Britain showed that the "A" factor was effective in curing rickets. It was also demonstrated that the "A" factor contained two separate factors. A heat-stable factor was identified and found to be the one responsible for curing rickets. A heat-labile factor that was capable of healing xerophthalmia (dryness of the conjunctiva leading to a diseased state of the mucous membrane of the eye resulting from vitamin A deficiency) was also discovered. The heat-stable factor was named vitamin D, and the heat-labile factor was termed vitamin A.[11,21–23]

The discovery of vitamin D connected observations about rickets and cod liver oil. Cod liver oil cured rickets because it contains vitamin D. It was observed that children exposed to sunshine were less likely to get rickets. In Germany in 1919, Kurt Huldschinsky (1883–1940) also showed that exposing children to artificial sunshine cured rickets. It was shown that vitamin D was produced in the body when sunshine acted on its fats. It was later discovered that the antiberiberi substance vitamin B was also effective against pellagra.[11,21,22]

In this era, the role of social and economic factors was observed to contribute much to the causation of disease, especially poverty conditions, which clearly contributed to nutritional deficiencies.[11]

BEGINNING OF EPIDEMIOLOGY IN THE UNITED STATES

In 1850, Lemuel Shattuck published the first report on sanitation and public health problems in the Commonwealth of Massachusetts. Shattuck was a teacher, sociologist, and statistician, and served in the state legislature. He was chair of a legislative committee to study

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sanitation and public health. The report set forth many public health programs and needs for the next century. Of the many needs and programs suggested, several of them were epidemiologic in nature. One of the things needed to ensure that epidemiology, its investigations, and the all-important control and prevention aspects of its work be achieved is an organized and structured effort. The organized effort has to come through an organization sponsored by the government.

Shattuck's report set forth the importance of establishing state and local boards of health. It recommended that an organized effort to collect and analyze vital statistics be established. Shattuck also recommended the exchange of health information, sanitary inspections, research on tuberculosis, and the teaching of sanitation and prevention in medical schools. The health of school children was also of major concern. As a result of the report, boards of health were established, with state departments of health and local public health departments soon to follow, organizations through which epidemiologic activities took place.[24,25]

Quarantine conventions were held in the 1850s. The first in the United States was in Philadelphia in 1857. The prevention of typhus, cholera, and yellow fever was discussed. Port quarantine and the hygiene of immigrants were also of concern. Public health educational activities began at this time. In 1879, the first major book on public health, which included epidemiologic topics, was published by A. H. Buck. The book was titled *Hygiene and Public Health*.[24,25]

The infectious nature of yellow fever was established in 1900 (**Figure 2-6**). In 1902, the United States Public Health Service was founded, and in 1906, the Pure Food and Drug Act was passed. Standard methods of water analysis were also adopted in 1906. The pasteurization of milk was shown to be effective in controlling the spread of disease in 1913, and in this same year, the first school of public health, the Harvard School of Public Health, was established.[24,25]

FIGURE 2-6 It has been said that of all the people who ever died, half of them died from the bite of the mosquito. For thousands of years it was not known that the mosquito was responsible for diseases such as yellow fever and malaria. These two diseases are still not fully contained in many parts of the world. In 1900, Walter Reed, M.D., a U.S. Army physician working in the tropics, made the epidemiological connection between the mosquito (Aedes aegypti species) and yellow fever. Pictures courtesy of Centers for Disease Control and Prevention, Atlanta, Georgia.

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HISTORICAL DEVELOPMENT OF MORBIDITY IN EPIDEMIOLOGY

An epidemiology professional of the early 1900s who helped advance the study of disease statistics (morbidity) was Edgar Sydenstricker. The development of a morbidity statistics system in the United States was quite slow. One problem was that morbidity statistics cannot be assessed and analyzed in the same manner that death (mortality) statistics are. Sydenstricker struggled with the mere definition of sickness and recognized that to all persons disease is an undeniable and frequent experience. Birth and death come to a person only once but illness comes often. This was especially true in Sydenstricker's era when sanitation, public health, microbiology, and disease control and prevention measures were still being developed.[26]

In the early 1900s, morbidity statistics of any given kind were not regularly collected on a large scale. Interest in disease statistics came only when the demand for them arose from special populations and when the statistics would prove useful socially and economically. Additionally, Sydenstricker noted that there were barriers to collecting homogeneous morbidity data in large amounts: differences in data collection methods and definitions, time elements, and the existence of peculiar factors that affect the accuracy of all records.[26]

Sydenstricker suggested that morbidity statistics be classified into five general groups in order to be of value.

1. Reports of communicable disease—notification of those diseases for which reasonably effective administrative controls have been devised.
2. Hospital and clinical records. These records were viewed as being of little value in identifying incidence or prevalence of illness in populations (at this time, most people were treated at home unless they were poor and in need of assistance). Such records are only of value for clinical studies.
3. Insurance and industrial establishment and school illness records. The absence of records of illnesses in workers in large industries in the United States was of concern because it added to the difficulty of defining and explaining work-related illness. Criteria for determining disability from illness or injury at work and when sick benefits should be allowed were not well developed. Malingering was also considered, as was its effect on the illness rates of workers. It was suggested that if illness records showing absence from school were kept with a degree of specificity, they could be of value to the understanding of the effect of disease on these populations.
4. Illness surveys. These have been used by major insurance companies to determine the prevalence of illness in a specific population. House-to-house canvass approaches have been used. Incidence of diseases within a given period is not revealed by such methods, whereas chronic-type diseases are found to be of higher incidence (which should be expected and predicted).
5. Records of the incidence of illness in a population continuously or frequently observed. To benefit epidemiologic studies, two study methods have been employed: (1) determination of the annual illness rate in a representative population and (2) development of an epidemiologic method whereby human populations could be observed in order to determine the existence of an incidence of various diseases as they were manifested under normal conditions within the community.[26]

A morbidity study by Sydenstricker and his colleagues under the direction of the United States Public Health Service in Hagerstown, Maryland, was conducted in the years 1921–1924. The study involved 16,517 person-years of observation or an equivalent population of 1,079

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individuals who were observed for 28 months beginning in 1921. Illnesses discovered in field investigations, when family members reported being sick or when researchers observed a sick person, were recorded during each family visit. A fairly accurate record of actual illness was obtained by a community interview method. Two findings included were that only 5% of illnesses were of a short duration of 1 day or less and that 40% were not only disabling but caused bed confinement as well. An accurate data-gathering process was developed from the experience.[26]

In the study, 17,847 cases of illness were recorded in a 28-month period. An annual rate of 1,081 per 1,000 person-years was observed, being about one illness per person-year. The illness rate was 100 times the annual death rate in the same population.[26]

The most interesting results of this first morbidity study were the variations of incidence of illness according to age. The incidence of frequent attacks of illness, four or more a year, was highest (45%) in children aged 2–9 years and lowest in those aged 20–24 years (11%). By 35 years old, the rate rose again, to 21%. When severity of illness was looked at, it was found that the greatest resistance to disease was in children between 5 and 14 years. The lowest resistance to disease was in early childhood, 0–4 years, and toward the end of life.[26,27]

THE FRAMINGHAM HEART STUDY

In 1948, the Framingham, Massachusetts cardiovascular disease study was launched. The aim of the study was to determine which of the many risk factors contribute most to cardiovascular disease. At the beginning, the study involved 6,000 persons between 30 and 62 years of age. These persons were recruited to participate in a cohort study that spanned 30 years, with 5,100 residents completing the study. In each of the 30 years, medical exams and other related testing activities were conducted with the participants. The study was initially sponsored by the National Health Institute of the United States Public Health Service and the Massachusetts Department of Public Health, along with the local Framingham Health Department.[28–30]

The site for the study was determined by several factors. It was implied that Framingham was a cross-section of America and was a typical small American city. Framingham had a fairly stable population. One major hospital was used by most of the people in the community. An annual updated city population list was kept, and a broad range of occupations, jobs, and industries were represented. The study approach used in the Framingham study was a prospective cohort study.[28–30]

The diseases of most concern in the study were coronary heart disease, rheumatic heart disease, congestive heart failure, angina pectoris, stroke, gout, gallbladder disease, and eye conditions. Several clinical categories of heart disease were distinguished in this study: myocardial infarction, angina pectoris, coronary insufficiency, and death from coronary heart disease, as shown by a specific clinical diagnosis.[28–30]

Many study design methods and approaches were advanced in the investigation, such as cohort tracking, population selection, sampling, issues related to age of the population, mustering population support, community organization, a specific chronic disease focus, and analysis of the study findings.

CIGARETTE SMOKING AND CANCER

After World War II, vital statistics indicated a sharp increase in deaths attributed to lung cancer. The first epidemiologic reports suggesting a link between cigarette smoking and lung cancer appeared in the early 1950s.[31–35] By the time of the 1964 report by the Surgeon General of the United States, there had been 29 case-control studies and 7 prospective cohort studies published, all showing a significantly increased risk of lung cancer among tobacco smokers.[36]

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The first case-control studies that assessed the association between smoking and lung cancer were conducted in the late 1940s by Wynder and Graham in the United States (1950) and Doll and Hill in Great Britain (1950).[37,38] These studies first identified cases with lung cancer and controls and then investigated whether people with lung cancer differed from others without the disease with respect to their smoking history. Both studies showed that lung cancer patients were more likely to have been smokers.

The first cohort study assessing the association between smoking and lung cancer was conducted in 1951 by Doll and Hill.[39,40] Physicians in Great Britain were sent a questionnaire to determine their smoking habits. They were then followed over a 25-year period with death certificate information collected to determine whether deaths were attributed to lung cancer or some other cause. The study found that smokers were 10 times more likely to die of lung cancer than nonsmokers.

The case-control and cohort study designs used by these researchers remain commonly used in epidemiologic research today.

CONCLUSION

This chapter describes the contributions of many key players to the field of epidemiology. Individuals were presented who helped shape the discipline as we know it toady. Pioneers in the area of epidemiology introduced germ theory, the microscope, vaccination, study designs, sources and modes of disease transmission, and the importance of monitoring and evaluating health-related states or events.

NEWS FILE

Contribution of Pasteur and Koch to Epidemiology: Preventing Cholera

A Simple Filtration Procedure Produces a 48% Reduction in Cholera

Cholera continues to plague developing countries and surfaces sporadically throughout the world. In 2001, an estimated 184,311 cases and 2,728 deaths were reported by the World Health Organization; nevertheless, the number of cases and deaths may be much higher because illness and death associated with Vibrio cholerae tends to be underreported as a result of surveillance difficulties and threat of economic and social consequences.

Researchers developed a simple filtration procedure involving both nylon filtration and sari cloth (folded four to eight times) filtration for rural villagers in Bangladesh to remove Vibrio cholerae attached to plankton in environmental water. The research hypothesis was that removing the copepods (with which Vibrio cholerae is associated) from water used for household purposes, including drinking, would significantly reduce the prevalence of cholera. The study was conducted over a 3-year period.

Both the nylon filtration group and the sari filtration group experienced significantly lower cholera rates than the control group. Both filters were comparable in removing copepods as well as particulate matter from the water. The study estimated that the sari cloth filtration reduced the occurrence of cholera by about 48%. Given the low cost of sari cloth filtration, this prevention method has considerable potential in lowering the occurrence of cholera in developing countries.

From Colwell RR, Huq A, Islam MS, et al. Reduction of cholera in Bangladeshi villages by simple filtration. *Proc Natl Acad Sci USA* 2003;100(3):1051–1055.

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EXERCISES

Key Terms

Define the following terms.

Anthrax	Scurvy
Atomic theory	Smallpox
Childbed fever	Typhoid fever
Cholera	Typhus
Hot and cold diseases	Variolation
Multifactorial etiology	Vitamin
Necropsy	Waterborne

STUDY QUESTIONS

2.1 Match the individuals in Column A with their historical contributions in Column B.

Column A	Column B
____ Hippocrates	A. Identified the cause of rabies
____ Thomas Sydenham	B. Invented a vaccination for smallpox
____ James Lind	C. Published the first report on sanitation and public health problems
____ Benjamin Jesty	D. Introduced the terms epidemic and endemic
____ Edward Jenner	E. Showed an association between smoking and lung cancer using case-control and cohort study designs
____ Ignaz Semmelweis	F. Chronic healthy (passive) carrier of typhoid fever, causing numerous cases
____ John Snow	G. Applied experimental methods to identify that oranges and lemons were effective remedies for scurvy at sea
____ Louis Pasteur	H. Insisted that observation should drive the study of the course of disease
____ Robert Koch	I. With Pasteur, established the germ theory of disease
____ John Graunt	J. Exposed his wife and children to cowpox
____ William Farr	K. Eradicated beriberi in a group with certain foods
____ Bernardino Ramazzini	L. Associated certain occupational exposures to disease
____ Mary Mallon	M. Conducted descriptive and analytic epidemiologic studies investigating cholera epidemics in London
____ T. K. Takaki	N. Developed and calculated life tables and life expectancy
____ Lemuel Shattuck	O. Lady with the Lamp
____ Edgar Sydenstricker	P. Developed a modern vital statistics system
____ Doll and Hill	Q. Developed morbidity statistics
____ Florence Nightingale	R. Identified the importance of washing hands to prevent the spread of disease

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2.2 List some of the contributions of the microscope to epidemiology.

2.3 What two individuals contributed to the birth of vital statistics?

2.4 What type of epidemiologic study was used by James Lind?

2.5 What types of epidemiologic studies were used by Doll and Hill?

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