RAY M. MERRILL

INTRODUCTION TO EPIDEMIOLOGY

EIGHTH EDITION

RAY M. MERRILL, PhD, MPH
Brigham Young University, Utah

INTRODUCTION TO EPIDEMIOLOGY

EIGHTH EDITION

JONES & BARTLETT LEARNING

World Headquarters
Jones & Bartlett Learning
5 Wall Street
Burlington, MA 01803
978-443-5000
info@jblearning.com
www.jblearning.com

Jones & Bartlett Learning books and products are available through most bookstores and online booksellers. To contact Jones & Bartlett Learning directly, call 800-832-0034, fax 978-443-8000, or visit our website, www.jblearning.com.

Substantial discounts on bulk quantities of Jones & Bartlett Learning publications are available to corporations, professional associations, and other qualified organizations. For details and specific discount information, contact the special sales department at Jones & Bartlett Learning via the above contact information or send an email to specialsales@jblearning.com.

17110-5

Production Credits
VP, Product Management: Amanda Martin
Director of Product Management: Cathy Esperti
Product Manager: Sophie Fleck Teague
Product Specialist: Carter McAlister
Project Specialist: Kelly Sylvester
Project Specialist, Navigate: Lori Mortimer
Digital Project Specialist: Rachel Reyes
Senior Marketing Manager: Susanne Walker
Manufacturing and Inventory Control Supervisor: Amy Bacus
Composition: codeMantra U.S. LLC
Cover Design: Kristin E. Parker
Senior Media Development Editor: Shannon Sheehan
Rights Specialist: Maria Leon Maimone
Cover Image (Title Page): © Jamesbin/Shutterstock
Printing and Binding: LSC Communications
Cover Printing: LSC Communications

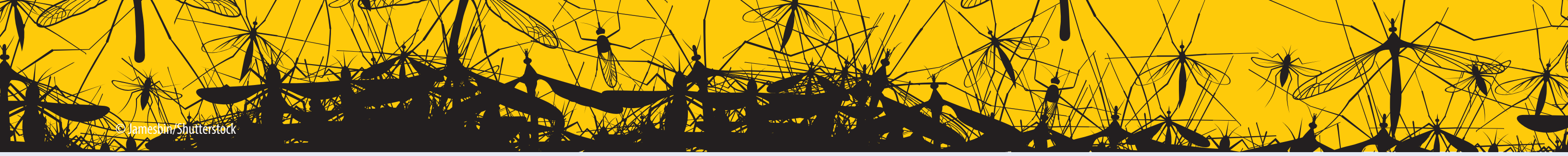
Library of Congress Cataloging-in-Publication Data
Names: Merrill, Ray M, author.
Title: Introduction to epidemiology / Ray M. Merrill.
Description: Eighth edition. | Burlington, Massachusetts: Jones & Bartlett Learning, [2021] | Includes bibliographical references and index.
Identifiers: LCCN 2019025620 | ISBN 9781284171105 (paperback) | ISBN 9781284170702 (paperback)
Subjects: | MESH: Epidemiologic Methods | Epidemiology
Classification: LCC RA651 | NLM WA 950 | DDC 614.4—dc23
LC record available at https://lccn.loc.gov/2019025620

6048

Printed in the United States of America
23 22 21 20 19 10 9 8 7 6 5 4 3 2 1

Dedication

To my uncle, Grant, who has inspired me throughout my life.



Brief Contents

Contents

Preface

Epidemiology is sometimes referred to as the basic science of public health. It is a scientifically driven discipline based on systematic observation and analysis of specified populations. The primary aim of epidemiology is to identify causes and risk factors of disease, events, and behaviors so as to successfully prevent and control health problems. Many individuals have helped shape this discipline, from Hippocrates, who attempted to explain disease from a rational perspective; to Thomas Sydenham (2,000 years later, in the 1600s), who studied diseases and epidemics from an observational viewpoint; to William Farr (200 years later, in the 1800s), who organized and developed a modern vital statistics system; to a number of people today who have identified various risk factors for disease, injury, and death and helped describe the natural history of many diseases and advanced methods for conducting epidemiologic research.

Historically, the main causes of death were due to a single pathogen, a single cause of disease. Epidemiologists had the challenge of isolating a single bacterium, virus, or parasite. In modern times, advances in nutrition, housing conditions, sanitation, water supply, antibiotics, and immunization programs have resulted in a decrease in infectious diseases as the primary cause of death, and an increase in many noninfectious diseases and conditions as the primary cause of death. Consequently, the scope of epidemiology has expanded to include the study of acute and chronic noninfectious diseases and conditions. Advances in biology, medicine, statistics, and social and behavioral sciences have greatly aided this progression in epidemiologic study.

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

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

New to the *Eighth Edition*

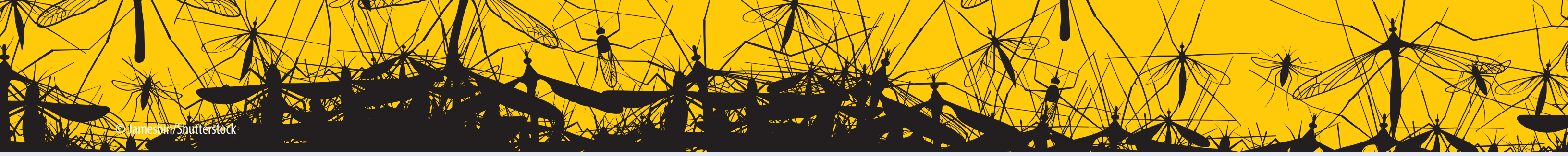
The eighth edition of this classic text, like its previous editions, continues its mission of providing a comprehensive introduction to the field of epidemiology. Emphasis is placed on application of the basic principles of epidemiology according to person, place, and time factors so as to solve current,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

Additions to this edition include an expanded discussion of incubation and latency periods, a more complete description of important health and population indicators, additional information on the role of vitamin and mineral deficiency/overdose in explaining disease, identification of key environmental risk factors associated with chronic disease, revised steps for conducting a field investigation, and study questions, as well as updated tables, figures, examples, and conclusions throughout the text. Current News Files are included in each chapter. Sections on life expectancy and the receiver operating characteristic (ROC) curve were added.

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

About the Author

Ray M. Merrill, PhD, MPH, received his academic training in statistics and public health. In 1995, he was named a Cancer Prevention Fellow at the National Cancer Institute, where he worked in the Surveillance Modeling and Methods Section of the Applied Research Branch. In 1998, he joined the faculty of the Department of Health Science at Brigham Young University in Provo, Utah, where he has been active in teaching and research. In 2001, he spent a sabbatical working in the Unit of Epidemiology for Cancer Prevention at the International Agency for Research on Cancer in Lyon, France. He has won various awards for his research and is a Fellow of the American College of Epidemiology and of the American Academy of Health Behavior. He is the author of more than 280 peer-reviewed publications, including *Environmental Epidemiology, Reproductive Epidemiology, Principles of Epidemiology Workbook, Fundamentals of Epidemiology and Biostatics, Behavioral Epidemiology, Statistical Methods in Epidemiologic Research,* and *Fundamental Mathematics for Epidemiology Study* (all with Jones & Bartlett Learning). Dr. Merrill teaches classes in epidemiology and biostatistics and is a full professor in the Department of Public Health, College of Life Sciences, at Brigham Young University.



Introduction

Epidemiology is a fun and challenging subject to study, as well as an interesting and important field to pursue as a career. There are many areas in which epidemiology can be applied, including cancer, cardiovascular disease, diabetes, injury, mental health, oral health, reproduction, respiratory, and more. Most undergraduate and graduate degree programs in public health, environmental health, occupational health and industrial hygiene, health education and health promotion, health services administration, nursing, and other health-related disciplines require a basic introductory course in epidemiology.

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

CHAPTER 1

Foundations of Epidemiology

OBJECTIVES

After completing this chapter, you will be able to:

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

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

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

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

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

The study of the distribution of health-related states or events involves identifying the frequency and pattern of the public health problem among people in the population. Frequency refers to the number of health-related states or events and their relationship to the size of the population. Typically, the number of cases or deaths is more meaningful when considered in reference to the size of the corresponding population, especially when comparing risks of disease among groups. For example, despite differences in population sizes across time or among regions, meaningful comparisons can be made of the burden of HIV/AIDS by using proportions or percentages. In 2017, HIV prevalence was 4.1% in Africa, 0.5% in the Americas, 0.4% in Europe, and 0.3% in Southeast Asia.[3]

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

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

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

Identifying causal associations is complex and typically requires making a "judgment" based on the totality of evidence, such as a valid statistical association, time sequence of events, biologic credibility, and consistency among studies. A step toward understanding causation is to identify relevant risk factors. A **risk factor** is a behavior, environmental exposure, or inherent human characteristic that increases the chance of developing an adverse health outcome.[6] For example, smoking is a risk factor for chronic conditions such as heart disease, stroke, and several cancers (including cancers of the oral cavity and pharynx, esophagus, pancreas, larynx, lung and bronchus, urinary bladder, kidney and renal pelvis, and cervix).[7–10] A risk factor is typically not sufficient to cause a disease; other contributing factors, such as personal susceptibility, may also be required before an adverse health outcome occurs. Thus, risk factor should not be equated with cause. The term "health-related states or events" is used in the definition of epidemiology to capture the fact that epidemiology involves more than just the study of disease (e.g., cholera, influenza, and pneumonia); it also includes the study of events (e.g., injury, drug abuse, and suicide) and of behaviors and conditions associated with health (e.g., physical activity, nutrition, seat belt use, and provision and use of health services).

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

Activities in Epidemiology

An epidemiologist is an investigator who studies the occurrence and causes of disease or other health-related events in specified populations and how various persons and places are affected, and uses relevant information to assist in preventing future health problems and controlling disease, injuries, and conditions. Epidemiologists may pursue jobs in research or seek practice-oriented employment. Careers in research involve responsibilities in grant and report writing, study design, data collection, data analysis and interpretation, publication preparation, and study coordination. Practice-oriented jobs often involve activities such as:

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

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

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

Role of Epidemiology in Public Health Practice

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

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

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

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

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

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

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

Epidemics, Endemics, and Pandemics

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

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

Several epidemics of cholera have been reported since the early 1800s. In 1816, an epidemic of cholera occurred in Bengal, India, and then became pandemic as it spread across India, extending as far as China and the Caspian Sea before receding in 1826.[14] Other cholera epidemics that also became pandemic involved Europe and North America (1829–1851), Russia (1852–1860), Europe and Africa (1863–1875), Europe and Russia (1899–1923), Indonesia, El Tor, and Bangladesh (India), and the Union of Soviet Socialist Republics (1961–1966).[14] During the last few months of 2018, cholera outbreaks occurred in the Borno, Adamawa, and Yobe states in Nigeria, with an estimated 11,000 cases and 175 deaths.[15] Examples of case reports of cholera, provided by John Snow, along with descriptions of two cholera epidemics investigated by Snow, are presented in Case Study I: Snow on Cholera (Appendix I).

In the United States, cholera is now classified as an endemic disease. From 2012 through 2016, the annual numbers of cases reported were 17, 14, 5, 5, and 15, respectively.[16] Other examples of diseases classified now as endemic in the United States include botulism, brucellosis, chickenpox, and plague.

Epidemics are often described by how they spread through the population. Two primary types of infectious-disease epidemics are common-source and propagated. A **common-source epidemic** arises from a specific source, whereas a **propagated epidemic** arises from infections transmitted from one infected person to another. Transmission can occur through direct or indirect routes. Common-source epidemics tend to result in cases occurring more rapidly during the initial phase as compared with host-to-host epidemics. Identifying the common source of exposure and removing it typically causes the epidemic to abate rapidly. By comparison, host-to-host epidemics rise and fall more slowly. Some examples of common-source epidemic diseases are anthrax, traced to milk or meat from infected animals; botulism, traced to soil-contaminated food; and cholera, traced to fecal contamination of food and water. Some examples of propagated epidemic diseases are tuberculosis, whooping cough, influenza, and severe acute respiratory syndrome.

In some diseases, natural immunity or death can decrease the susceptible population. Resistance to the disease can also occur with treatment

NEWS FILE

EBOLA VIRUS DISEASE

West Africa: The Largest Ebola Outbreak in History

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

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

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

1. Modified from World Health Organization. *Ebola virus disease*. http://www.who.int/mediacentre/factsheets/fs103/en/. Accessed July 8, 2015.
2. Horowitz E. How the Ebola outbreak spun out of control. *BostonGlobe.com*. October 8, 2014. https://www.bostonglobe.com/news/world/2014/10/08/how-this-ebola-outbreak-spun-out-control/b3Fea51l1oRs4c0gjN36EM/story.html. Accessed July 8, 2015.
3. Centers for Disease Control and Prevention. *Ebola (Ebola virus disease)*. http://www.cdc.gov/vhf/ebola/index.html. Accessed July 8, 2015.

or immunization, both of which reduce susceptibility. Disease transmission is usually a result of direct person-to-person contact or of indirect transmission through a vehicle (fomite) or vector. Syphilis and other sexually transmitted infections are examples of direct transmission of infectious agents. Hepatitis B and HIV/AIDS in needle-sharing drug users are examples of indirect or vehicle-borne transmission of infectious agents. Malaria spread by mosquitoes is an example of vector-borne transmission of the infectious agent.

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

Case Concepts in Epidemiology

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

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

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

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

If people become ill enough to require hospitalization, the severity of the illness is of concern. **Case severity** is found by looking at several variables that are effective measures of it. One such measure is the average length of stay in a hospital. The longer the hospital stay, the greater the severity of the illness. Subjectively, severity is also measured by how disabling or debilitating the illness is, the likelihood of recovery, how long the person is ill, and how much care the person needs.[17–20]

Epidemiology Triangle

When the colonists settled America, they introduced smallpox to the Native Americans. Epidemics became rampant, and entire tribes died as a result. In the 1500s, the entire native population of the island

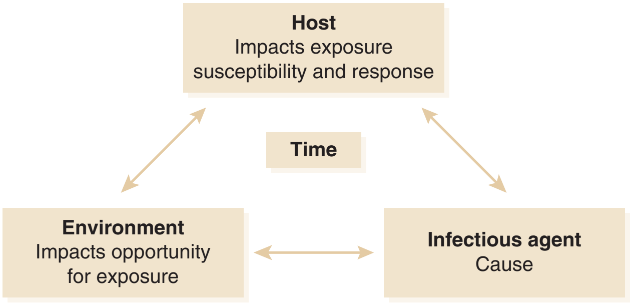


FIGURE 1-1 The Triangle of Epidemiology

of Jamaica died when smallpox was introduced. Poor sanitation and little basic knowledge of disease, low levels of immunity, various modes of transmission, and environmental conditions all allowed such epidemics to run wild and wipe out entire populations. A multitude of epidemiologic circumstances allowed such epidemics to happen. Four interrelated epidemiologic variables were involved and are present in an infectious outbreak: (1) the host; (2) the agent; (3) the environment; and (4) time-related factors.

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

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

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

Disease Transmission Concepts

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

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

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

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

Zoonosis is an infectious organism in vertebrate animals (e.g., rabies virus, *Bacillus anthracis*, Ebola virus, influenza virus) that can be transmitted to humans through direct contact, a fomite, or a vector. The World Health Organization states that zoonoses are those diseases and infections that can be naturally transmitted between vertebrate animals and humans.[21] For example, the rabies virus is transmitted from an infected animal (e.g., dog, cat, skunk, raccoon, monkey, bat, coyote, wolf, fox) to a human host through saliva by biting, or through scratches.

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

A **carrier** contains, spreads, or harbors an infectious organism. The infected person (or animal) harboring the disease-producing organism often lacks discernible clinical manifestation of the disease; nevertheless, the person or animal serves as a potential source of infection and disease transmission to other humans (or animals). For example, rodents or coyotes are often carriers of bubonic plague. Fleas serve as vectors in transmitting this disease to humans. The carrier condition can exist throughout the entire course of a disease if it is not treated, and its presence may not be apparent because the carrier may not be sick (healthy carrier). Some people can even be carriers for their entire lives. An example of this is Mary Mallon (Typhoid Mary), who was an asymptomatic carrier of the pathogen typhoid bacilli. Unfortunately, she worked as a cook, thereby contaminating the food she prepared. She was responsible for 51 cases, of which 3 resulted in death. Had she lived in modern times, antibiotics would have been effective treatment for Mary Mallon.[22,23] Tuberculosis is another example of a disease that is commonly known to have carriers.

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

1. **Active carrier**. An individual who has been exposed to and harbors a disease-causing organism (pathogen) and who has done so for some time, even though the person may have recovered from the disease.
2. **Convalescent carrier**. An individual who harbors a pathogen and who, although in the recovery phase of the course of the disease, is still infectious.
3. **Healthy carrier** (also called **passive carrier**). An individual who has been exposed to and harbors a pathogen but has not become ill or shown any of the symptoms of the disease. This could be referred to as a subclinical case.
4. **Incubatory carrier**. An individual who has been exposed to and harbors a pathogen, is in the beginning stages of the disease, is displaying symptoms, and has the ability to transmit the disease.
5. **Intermittent carrier**. An individual who has been exposed to and harbors a pathogen and who can spread the disease in different places or at different intervals.[24,25]

Modes of Disease Transmission

Identifying the methods by which a disease is transmitted allows for proper infection and control measures. The pathogens that cause disease have specific transmission characteristics. The two general **modes of disease transmission** are direct transmission and indirect transmission.

Direct transmission is the uninterrupted and immediate transfer of an infectious agent from one person to another. Direct transmission requires physical contact between an infected host and a susceptible person, and the physical transfer of a pathogen. Examples include sexually transmitted diseases (e.g., HIV/AIDS, chlamydia, gonorrhea, hepatitis B, herpes simplex virus, herpes), perinatal mother-to-child transmission (toxoplasmosis), and skin-to-skin (e.g., warts, impetigo, athlete's foot) transmission.

Indirect transmission occurs when an agent is transferred or carried by some intermediate item, organism, means, or process to a host, resulting in disease. Air currents, dust particles, water, food, oral–fecal contact, and other mechanisms that effectively transfer disease-causing organisms are means of indirect disease transmission. **Airborne transmission** occurs when droplets or dust particles carry the pathogen to the host and cause infection (e.g., respiratory viruses, pertussis, pneumococcal pneumonia, diphtheria, rubella). This may take place when a person sneezes, coughs, or talks, spraying microscopic pathogen-carrying droplets into the air that can be breathed in by nearby susceptible hosts. It also occurs when droplets are carried through a building's heating or air-conditioning ducts or are spread by fans throughout a building or complex of buildings. **Vector-borne transmission** occurs when an arthropod (e.g., mosquito, flea, tick, lice) conveys the infectious agent. It does not cause the disease itself but is responsible for transmitting the pathogen to a host. Vector-borne diseases include malaria, viral encephalitis, and Lyme disease. **Vehicle-borne transmission** involves an inanimate object that conveys an infectious agent to a host. For example, this occurs when a pathogen such as cholera or shigellosis is carried in drinking water, swimming pools, streams, or lakes used for swimming.

Some epidemiologists classify droplet spread as direct transmission because it usually takes place within a few feet of the susceptible host. Logically, however, the droplets from a sneeze or cough use the intermediary mechanism of the droplet to carry the pathogen; thus, it is an indirect transmission. This is also a form of person-to-person transmission, and influenza and the common cold are routinely spread this way. Droplets can also be spread by air-moving equipment and air-circulation processes (heating and air conditioning) within buildings, which carry droplet-borne disease great distances, often to remote locations, causing illness. Such equipment has been implicated in cases of tuberculosis and Legionnaires' disease.

Some vector-borne disease transmission processes are simple mechanical processes, such as when a pathogen spreads using a host (e.g., fly, flea, louse, rat) as a mechanism for a ride for nourishment, or as part of a physical transfer process. This is called **mechanical transmission**. **Biological transmission** is when the pathogen undergoes changes as part of its life cycle while within the host/vector and before being transmitted to the new host. Biological transmission is easily seen in malaria when the female *Anopheles* mosquito's blood meal is required for the *Plasmodium* protozoan parasite to complete its sexual development cycle. This can only occur with the ingested blood nutrients found in the intestine of the *Anopheles* mosquito.

Chain of Infection

There is a close association between the triangle of epidemiology and the **chain of infection** (**FIGURE 1-2**). Disease transmission occurs when the pathogen (infectious agent) leaves the reservoir (human, animal, or environment) through a **portal of exit** (e.g., nose, mouth, rectum, urinary tract, blood, or other bodily fluids if the reservoir is a human) and is spread by one of several modes of transmission. The pathogen or disease-causing agent then enters the body through a **portal of entry** of the susceptible host. The portal of exit from a source host to a new host may be the same (e.g., bodily fluid or respiratory tract) or different (e.g., fecal–oral route). Other portals of entry resulting in illness may involve infected skin or mucous membranes (sexually transmitted diseases) and blood (hepatitis viruses, human immunodeficiency virus).

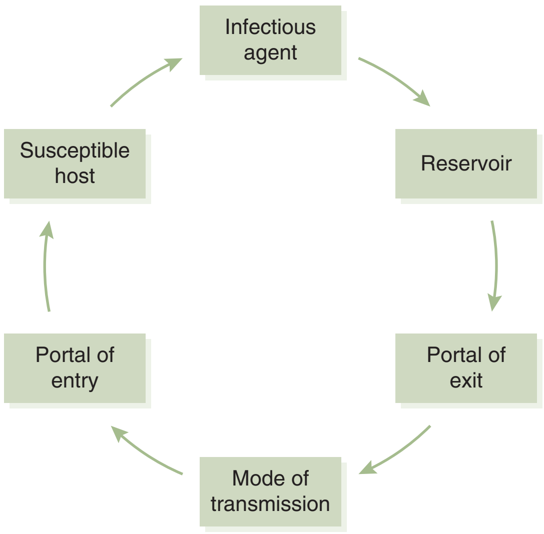


FIGURE 1-2 The Chain of Infection

Once a pathogen leaves its reservoir, it follows its mode of transmission to a host, either by direct transmission (person-to-person contact) or by indirect transmission (airborne droplets or dust particles, vectors, fomites, and food). The final link in the chain of infection is, thus, the susceptible individual or host, usually a human or an animal. The host is generally protected from invasion of pathogens by the skin, mucous membranes, and the body's physiological responses (weeping of mucous membranes to cleanse themselves, acidity in the stomach, cilia in the respiratory tract, coughing, and the natural response of the immune system). If the pathogen is able to enter the host, the result will most likely be illness if the host has no immunity to the pathogen.

Individuals who are young, who are elderly, who have underlying chronic diseases such as diabetes and asthma, who have a weakened immune system, or who are experiencing malnutrition are more susceptible to disease. A weakened immune system may be influenced by diet, exercise, stress, disease, and medications. Natural immunity can come from genetic makeup; that is, some people seem better able to resist disease than others. Active immunity occurs when the body develops antibodies and antigens in response to a pathogen invading the body. Passive immunity comes from antibodies entering the body, such as in a baby through the placenta or from antitoxin or immune globulin injections.[2]

Other Models of Causation

The epidemiology triangle as used in a discussion of infectious disease is basic and foundational to epidemiology; however, infectious diseases are no longer the leading cause of death in industrialized nations. In response, a more advanced model of the triangle

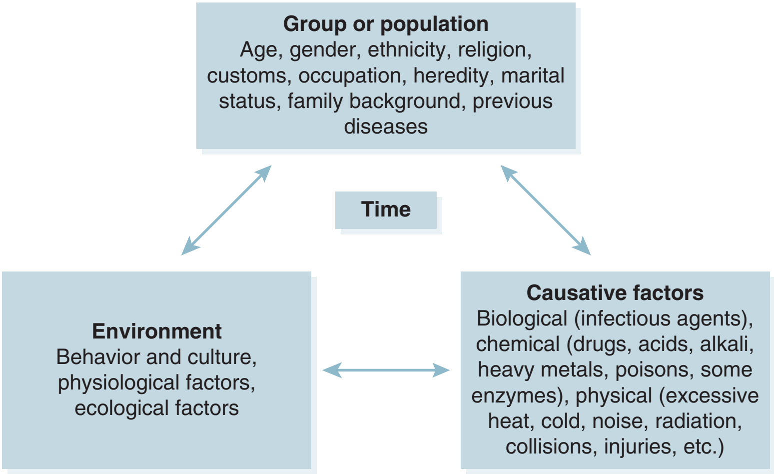


FIGURE 1-3 Advanced Model of the Triangle of Epidemiology

of epidemiology has been proposed. This new model includes all facets of the disease model. To make it more relevant and useful with regard to today's health-related states or events, behavior, lifestyle factors, environmental causes, ecologic elements, physical factors, and chronic diseases must be taken into account. **FIGURE 1-3** presents the adapted and advanced model of the triangle of epidemiology. This better reflects the behavior, lifestyle, and chronic disease issues found in modern times.

The advanced model of the triangle of epidemiology, like the traditional epidemiology triangle, is not comprehensive or complete; however, it recognizes that disease states and conditions affecting a population are complex and that there are many things that influence modern-day health-related states or events. The concept of infectious agent is replaced with causative factors, which implies the need to identify multiple causes or etiologic factors of disease, disability, injury, and death. The concept of host is replaced by group or population and their characteristics. The concept of environment is expanded to include factors that can impact the opportunity for exposure beyond the physical environment, such as behavior, culture, and lifestyle. Time accounts for the natural course of the health problem, taking into account the different elements of the triangle.

Another model that has been developed to capture the multifactorial nature of causation for many health-related states or events is Rothman's causal pies.[26] Assume the factors that increase the probability of the adverse health outcome are pieces of a pie, with the whole pie being sufficient to cause the health problem (**FIGURE 1-4**). More than one sufficient combination of factors may cause the health-related state or event, as illustrated in the figure. Each sufficient cause consists of multiple contributing factors called

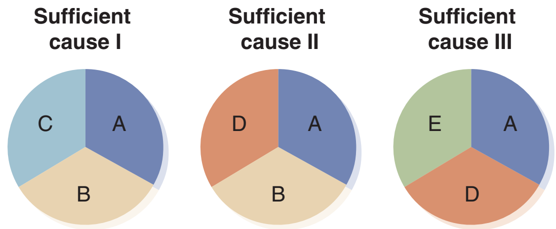


FIGURE 1-4 Three Sufficient Causes of an Adverse Health Outcome

component causes. The different component causes include elements of the triangle of epidemiology (i.e., agent, host, environment). When a given component cause is required in each of the different sufficient causes, it is referred to as a necessary cause. In Figure 1-4, the letter "A" represents a necessary cause because it is included in each of the three sufficient causes for the adverse health outcome. Exposure to the rubivirus is necessary for rubella-related birth defects to occur but is not sufficient to cause birth defects. Component causes required to make a sufficient cause may include a susceptible host who is not immune, and illness during the first few months of pregnancy.

Prevention and control measures do not require identifying every component of a sufficient cause because the health problem can be prevented by blocking any single component of a sufficient cause.

The web of causation is a graphical, pictorial, or paradigmatic representation of complex sets of events or conditions caused by an array of activities connected to a common core or common experience or event. It is an effective approach for investigating chronic disease and behaviorally founded causes of disease, disability, injury, and death. The web of causation shows the importance of looking for many causes or an array of contributing factors to various maladies. The web of causation will be illustrated in a later chapter.

Levels of Prevention

Three types of prevention have been established in public health: primary prevention, secondary prevention, and tertiary prevention.

Primary Prevention

Primary prevention is preventing a disease or disorder before it happens. Health promotion, health education, and health protection are three main facets of primary prevention.

Lifestyle changes, community health education, school health education, good prenatal care, good behavioral choices, proper nutrition, and safe and healthy conditions at home, school, and the workplace are all primary prevention activities. Fundamental public health measures and activities such as sanitation; infection control; immunizations; protection of food, milk, and water supplies; environmental protection; and protection against occupational hazards and accidents are all basic to primary prevention.

Personal hygiene and public health measures have had a major impact on halting communicable disease epidemics. Immunizations, infection control (e.g., handwashing), refrigeration of foods, garbage collection, solid and liquid waste management, water supply protection and treatment, and general sanitation have reduced infectious disease threats to populations.

Because of successes in primary prevention efforts directed at infectious diseases, noninfectious diseases are now the main causes of death in the United States and industrialized nations (**TABLE 1-2** and **FIGURE 1-5**).[27,28] In 1900, 40 of the 45 states had health departments. Treatment of drinking water using chlorination began in the early 1900s and became widely used thereafter. Animal and pest control contributed to lowering the occurrence of rabies, malaria, and plague. Malaria was reduced to very low levels by the late 1940s and outbreaks of plague, as well as human-to-human transmission of plague, last occurred in 1924–1925. In 1949, the licensure of combined diphtheria, tetanus, toxoids, and pertussis vaccines resulted in local and state health departments instituting vaccination programs. In 1955, the Salk poliovirus vaccine was introduced, which resulted in federal funding of local and state vaccination programs aimed

TABLE 1-2 Leading Causes of Death in the United States in 1900, 2000, and 2016

1900	2000	2016
Pneumonia and influenza 11.8%	Heart diseases 29.6%	Heart diseases 23.1%
Tuberculosis 11.3%	Cancer 23.0%	Cancer 21.8%
Diarrhea, enteritis, ulcerations of the intestines 8.3%	Cerebrovascular diseases 7.0%	Accidents 5.9%
Heart diseases 8.0%	Chronic lower respiratory diseases 5.1%	Chronic lower respiratory diseases 5.6%
Intracranial lesions of vascular origin 6.2%	Accidents 4.1%	Cerebrovascular diseases 5.2%
Nephritis 5.2%	Diabetes mellitus 2.9%	Alzheimer's disease 4.2%
Accidents 4.2%	Pneumonia and influenza 2.7%	Diabetes mellitus 2.9%
Cancer 3.7%	Alzheimer's disease 2.1%	Influenza and pneumonia 1.9%
Senility 2.9%	Nephritis 1.5%	Nephritis 1.8%
Diphtheria 2.3%	Septicemia 1.3%	Intentional self-harm (suicide) 1.6%

Data from Centers for Disease Control and Prevention. Leading causes of disease, 1900–1998. http://www.cdc.gov/nchs/data/statab/lead1900_98.pdf. Accessed February 9, 2019; Centers for Disease Control and Prevention. U.S. Mortality Public Use Data Tape, 2000. National Center for Health Statistics; 2002. http://webapp.cdc.gov/sasweb/ncipc/leadcaus10.html. Accessed February 9, 2019; Centers for Disease Control and Prevention. Health, United States, 2017–Data Finder. Table 019 Leading causes of death and number of deaths, by sex, race, and Hispanic origin: United States, 1980 and 2016.

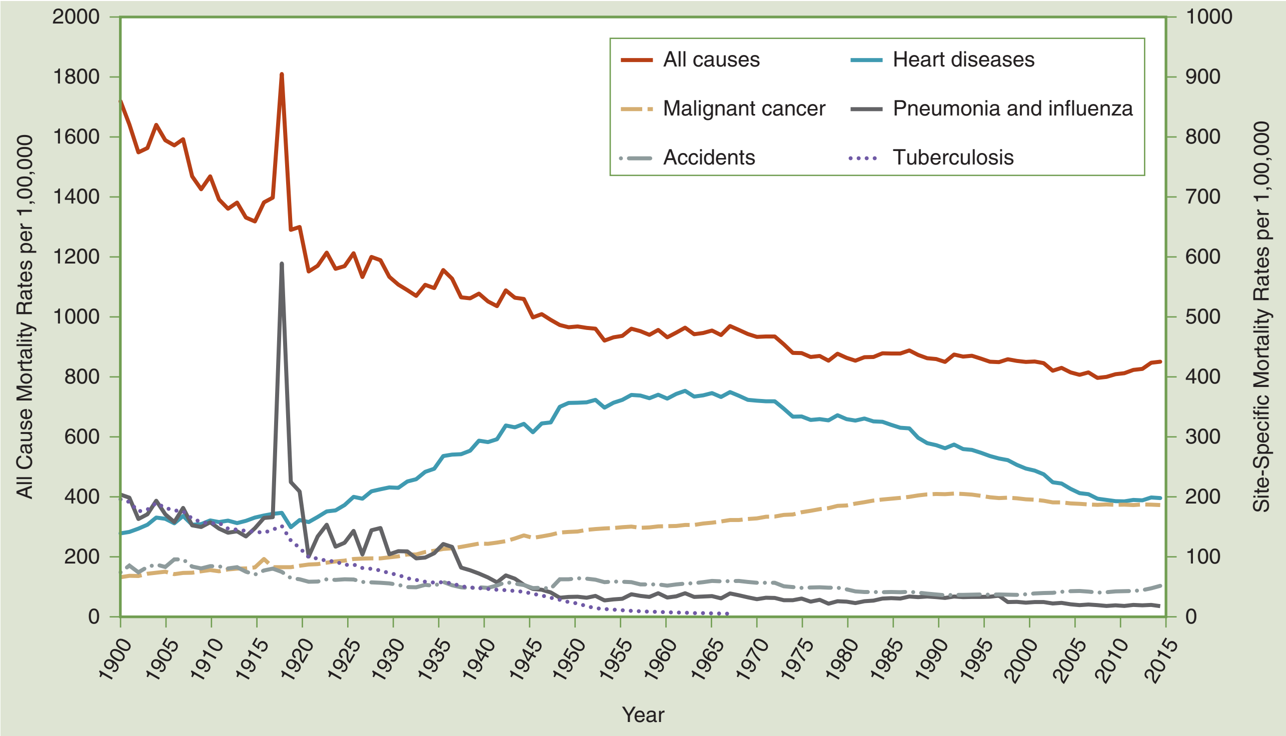


FIGURE 1-5 Infectious and Noninfectious Causes of Death in the United States, 1900–2016

Modified from Victoria Hansen, MS; Eyal Oren, PhD; Leslie K. Dennis, PhD; et al. *Infectious Disease Mortality Trends in the United States, 1980–2014*. American Medical Association, 2016.

at children. In 1962, the Vaccination Assistance Act supported the purchase and administration of several childhood vaccines. In 1942, penicillin began to be used for treating infections.[28]

The leading causes of death today throughout the world vary according to the income level of the country. In 2016, an estimated 56.9 million people died worldwide, with noncommunicable diseases explaining about 71% of all deaths (37% in low-income countries to 88% in high-income countries), up from 60% in 2000.[29] Ischemic heart disease (1st); stroke (2nd); chronic obstructive pulmonary disease (3rd); Alzheimer's disease and other dementias (5th); trachea, bronchus, and lung cancers (6th); and diabetes mellitus (7th) are the most common noncommunicable diseases.[29] Common risk factors for these diseases are environmental and behavior related (e.g., fine particulate matter in the air, smoking and tobacco use, alcohol and substance abuse, poor diet, and lack of physical fitness). The most common communicable causes of death were lower respiratory infections (4th), diarrheal diseases (9th), and tuberculosis (10th), with road injuries ranked 8th (74% of which were men and boys).[29] Given these leading causes of death, the World Health Organization's list of primary threats to global health are air pollution and climate change, noncommunicable diseases, global influenza pandemic, fragile and vulnerable settings, antimicrobial resistance, Ebola and other high-threat pathogens, weak primary health care, vaccine hesitancy, dengue, and HIV.[30]

Two related terms are active primary prevention and passive primary prevention. **Active primary prevention** requires behavior change in the individual (e.g., begin exercising, stop smoking, reduce dietary fat intake). **Passive primary prevention** does not require behavior change on the part of the individual (e.g., eating vitamin-enriched foods, drinking fluoridated water).

Secondary Prevention

Secondary prevention is aimed at the health screening and detection activities used to identify disease. If pathogenicity (the ability to cause disease) is discovered early, diagnosis and early treatment can prevent conditions from progressing and spreading within the population and can stop or at least slow the progress of disease, disability, disorders, or death.[1] Secondary prevention aims to block the progression of disease or prevent an injury from developing into an impairment or disability.[17,18,21] For example, early detection of cancer through screening may improve the effectiveness of treatment and decrease disability or disorders associated with the disease.

Tertiary Prevention

The aim of the third level of prevention is to retard or block the progression of a disability, condition, or disorder to keep it from advancing and requiring excessive care. **Tertiary prevention** consists of limiting any disability by providing rehabilitation when a disease, injury, or disorder has already occurred and caused damage. At this level, the goal is to help diseased, disabled, or injured individuals avoid wasteful use of healthcare services and not become dependent on healthcare practitioners and healthcare institutions. Prompt diagnosis and treatment, followed by proper rehabilitation and posttreatment recovery, proper patient education, behavior changes, and lifestyle changes are necessary to prevent reoccurrence of diseases or disorders. At the very minimum, the progression of the disease, disorder, or injury needs to be slowed and checked.[31,32] For example, tertiary prevention strategies for arthritis may include self-management strategies (e.g., weight control, physical activity), rehabilitation services (e.g., muscle strengthening, assistive devices), psychosocial strategies (e.g., telephone support interventions, cognitive behavioral therapies), and medical and surgical treatment (e.g., pain control, minimize joint damage).

Rehabilitation is any attempt to restore an afflicted person to a useful, productive, and satisfying lifestyle. Its purpose is to promote the highest quality of life possible, given the extent of the disease and disability. Rehabilitation is one component of tertiary prevention. Patient education, aftercare, health counseling, and some aspects of health promotion can play important roles in rehabilitation.

Conclusion

Epidemiology is the foundation of public health because of its important role in carrying out three core public health functions: assessment and monitoring of the health of populations at risk and identifying health problems and priorities; identifying risk factors for health problems; and providing a basis for predicting the effects of certain exposures. Epidemiology is the process of describing and understanding public health problems and of applying study findings to better prevent and control these problems. In addition, epidemiologic information is useful in guiding policies and setting priorities designed to solve public health problems and for allocating scarce health resources for protecting and promoting the public's health.

Exercises

Key Terms

Define the following terms.

Active carrier
Active primary prevention
Agent
Airborne transmission
Analytic epidemiology
Biological transmission
Carrier
Case
Case definition
Case severity
Cause
Chain of infection
Common-source epidemic
Convalescent carrier
Descriptive epidemiology
Direct transmission
Effectiveness
Efficacy
Endemic
Environment
Epidemic
Epidemiology
Fomite
Healthy carrier
Host
Incubatory carrier
Index case
Indirect transmission
Intermittent carrier
Mechanical transmission
Mixed epidemic
Modes of disease transmission
Pandemic
Passive carrier
Passive primary prevention
Pathogen
Portal of entry
Portal of exit
Primary case
Primary prevention
Propagated epidemic
Rehabilitation
Reservoir
Risk factor
Secondary case
Secondary prevention
Suspect case
Tertiary prevention
Time
Vector
Vector-borne transmission
Vehicle
Vehicle-borne transmission
Zoonosis

Study Questions

1. The definition of epidemiology includes the terms “distribution” and “determinants.” Describe the meaning of these terms.
2. Epidemiology involves the study of more than just infectious diseases. Explain.
3. Describe the chain of infection.
4. List four types of epidemiologic information useful for influencing public health policy and for planning individual health decisions.
5. Define “efficacy” and “effectiveness,” note their difference, and provide examples of both.
6. In what ways does epidemiology play a foundational role in public health?
7. Distinguish between a necessary cause and a sufficient cause.
8. Explain the epidemiology triangle and compare and contrast it with the advanced epidemiology triangle.
9. Describe how primary prevention, secondary prevention, and tertiary prevention may be used to deal with cancer.
10. HIV/AIDS can be transmitted from an infected person to another person through blood, semen, vaginal fluids, and breastmilk. High-risk behaviors include homosexual practices; unprotected oral, vaginal, or anal sexual intercourse; and needle sharing. Discuss how this information can be used in public health action and in individual decision making.

References

1. *Stedman's Medical Dictionary for the Health Professions and Nursing.* 5th ed. Baltimore, MD: Lippincott Williams & Wilkins; 2005.
2. Page RM, Cole GE, Timmreck TC. *Basic Epidemiologic Methods and Biostatistics: A Practical Guide Book*. Sudbury, MA: Jones and Bartlett Publishers; 1995.
3. World Health Organization. Prevalence of HIV among adults aged 15 to 49, 2017. Estimates by WHO region. http://apps.who.int/gho/data/view.main.22500WHOREG?lang=en. Accessed February 13, 2019.
4. Centers for Disease Control and Prevention. Pneumocystis pneumonia—Los Angeles. *MMWR Morb Mortal Wkly Rep*. 1981;30:250–252.
5. Centers for Disease Control and Prevention. Possible transfusion-associated acquired immune deficiency syndrome (AIDS)—California. *MMWR Morb Mortal Wkly Rep*. 1982;31:652–654.
6. Last JM, ed. *A Dictionary of Epidemiology.* 4th ed. New York, NY: Oxford University Press; 2001.
7. Rigotti NA, Pasternak RC. Cigarette smoking and coronary heart disease: risks and management. *Cardiol Clin*. 1996;14:51–68.
8. Shinton R. Lifelong exposures and the potential for stroke prevention: the contribution of cigarette smoking, exercise, and body fat. *J Epidemiol Community Health*. 1997;51:138–143.
9. U.S. Department of Health and Human Services. *The Health Benefits of Smoking Cessation: A Report of the Surgeon General, 1990*. Rockville, MD: Centers for Disease Control, Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 1990. (DHHS Publication No. [CDC] 90-8416).
10. U.S. Department of Health and Human Services. *Reducing the Health Consequences of Smoking: 25 Years of Progress. A Report of the Surgeon General, 1989.* Rockville, MD: Centers for Disease Control, Office on Smoking and Health; 1989. (DHHS Publication No. [CDC] 89-8411).
11. Merrill RM, White GL Jr. Why health educators need epidemiology. *Educ Health*. 2002;15:215–221.
12. Thacker SB, Berkelman RL. Public health surveillance in the United States. *Epidemiol Rev*. 1988;10:164–190.
13. Oleckno WA. *Essential Epidemiology: Principles and Application*. Long Grove, IL: Waveland Press; 2002.
14. Merrill RM. *Introduction to Epidemiology.* 5th ed. Sudbury, MA: Jones and Bartlett Publishers; 2010.
15. World Health Organization. Nigeria. Borno, Adamawa, and Yobe states declare end of cholera outbreaks. https://www.afro.who.int/news/borno-adamawa-and-yobe-states-declare-end-cholera-outbreaks. Accessed February 20, 2019.
16. Centers for Disease Control and Prevention. Notifiable diseases and mortality tables. *MMWR Morb Mortal Wkly Rep*. 2018;66(52), Table 1. http://www.cdc.gov/mmwr/volumes/66/wr/mm6652md.htm#table-1. Accessed February 19, 2019.
17. Timmreck TC. *Health Services Cyclopedic Dictionary.* 3rd ed. Sudbury, MA: Jones and Bartlett Publishers; 1997.
18. Mausner J, Bahn AK. *Epidemiology: An Introductory Text*. Philadelphia, PA: WB Saunders; 1974.
19. Shindell S, Salloway JC, Oberembi CM. *A Coursebook in Health Care Delivery*. New York, NY: Appleton-Century-Crofts; 1976.
20. Lilienfeld AM, Lilienfeld DE. *Foundations of Epidemiology.* 2nd ed. New York, NY: Oxford University Press; 1980.
21. World Health Organization. *Zoonoses: Second Report of the Joint WHO/FAO Expert Committee*. Geneva, Switzerland: World Health Organization; 1959.
22. “Typhoid Mary” dies of a stroke at 68. Carrier of disease, blamed for 51 cases and 3 deaths, but she was held immune. *New York Times*. November 12, 1938. http://select.nytimes.com/gst/abstract.html?res=F10D15FE3859117389DDAB0994D9415B888FF1D3. Accessed January 2, 2012.
23. Soper GA. The work of a chronic typhoid germ distributor. *JAMA*. 1907;48:2019–22.
24. Thomas CL, ed. *Taber's Cyclopedic Medical Dictionary.* 14th ed. Philadelphia, PA: FA Davis; 1981.
25. Nester EW, McCarthy BJ, Roberts CE, Pearsall NN. *Microbiology*. New York, NY: Holt, Rinehart & Winston; 1973.

26. Rothman KJ. Causes. *Am J Epidemiol*. 1976;104:587–592.
27. Hansen V, Oren E, Dennis LK, Brown HE. Infectious disease mortality trends in the United States, 1980–2014. *JAMA*. 2016;316(20):2149–2151.
28. Centers for Disease Control and Prevention. Achievements in Public Health, 1900–1999: Control of Infectious Diseases. *MMWR Morb Mortal Wkly Rep*. 1999;48(29):621–629.
29. World Health Organization. *Global Health Estimates 2016: Deaths by Cause, Age, Sex, by Country and by Region, 2000–2016*. Geneva, Switzerland: World Health Organization; 2018.
30. World Health Organization. Ten Threats to Global Health in 2019. https://www.who.int/emergencies/ten-threats-to-global-health-in-2019. Accessed February 22, 2019.
31. Picket G, Hanlon JJ. *Public Health: Administration and Practice*. St. Louis, MO: Times Mirror/Mosby; 1990.
32. McMahon B, Pugh TF. *Epidemiology Principles and Methods*. Boston, MA: Little, Brown and Company; 1970.

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 contributions made by several key individuals to 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 perspective 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 BCE), who attempted to explain disease occurrence from a rational viewpoint, to John Graunt (1620–1674 CE), 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 rather than a theoretical one, was 2,000 years. Approximately 200 years later, William Farr (1807–1883) advanced John Graunt's work to better describe epidemiologic problems; John Snow laid the groundwork for descriptive and analytic epidemiology; Robert Koch and Louis Pasteur provided scientific evidence for germ theory; Ignaz Semmelweis discovered that handwashing standards in obstetrical clinics could reduce the incidence of puerperal fever; and Florence Nightingale showed that certain environmental conditions (e.g., fresh air, light, cleanliness) could improve recovery among patients in hospitals. In the early 1900s, Edgar Sydenstricker classified morbidity statistics to improve the value of this information and conducted community health surveys to provide valuable public health information; Janet Lane-Claypon developed study designs for identifying risk factors for breast cancer; Alice Hamilton pioneered the field of toxicology; and Wade Hampton Frost showed that epidemiology is an analytical science closely integrated with biology and medicine. Since then, the science of epidemiology has rapidly progressed. Although it is impossible to identify all the contributors to the field of epidemiology here, several of these individuals and their contributions are considered in this chapter.

Hippocrates, the First Epidemiologist

Hippocrates was a physician who is commonly regarded as the father of medicine. He may also be thought of as the first epidemiologist. In his three books, *Epidemic I*, *Epidemic III*, and *On Airs, Waters, and Places*, he attempted to describe disease from a rational perspective rather than from 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 Walter Reed, MD, a U.S. Army physician working in the tropics, made the connection in 1900. Hippocrates also introduced terms like *epidemic* and *endemic*.[1–4]

Hippocrates gave advice to people 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 people's behavior, such as eating, drinking, and other activities. Did they eat lunch, eat too much, or drink too little? Were they industrious?

Hippocrates suggested that traveling physicians 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 of and a cure for disease. Cures for illness and protection from disease came from maintaining a balance and avoiding imbalance in the constitution.

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 season. 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, Sydenham became acquainted with Robert Boyle, a colleague who sparked his 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 (**FIGURE 2-1**). 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.

FIGURE 2-1 Thomas Sydenham

Sydenham, detail of an oil painting by Mary Beale, 1688; in the National Portrait Gallery, London.

Sydenham published his observations in a book in 1676 titled *Observationes Medicae*.[4]

One of Sydenham's major works 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 erred in identifying the cause of the disease.[4]

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 noted 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 noted that the most common months for scurvy were April, May, and June. He also observed that cold, rainy, foggy, and thick weather was 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 for the cause of disease and, most of all, the cause of scurvy.[5] Although he was 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 experiences with the experiences of those who were healthy.

When Lind began to look at the mariners' diet, 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 wherein he assigned different supplemental dietary interventions to 12 ill patients who had all 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 said 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 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 limes or lime juice be included in seamen's diet, resulting in the nickname "limeys" to refer to British seamen.

Lind's epidemiologic contributions 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 also 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 that 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. At the time, smallpox was common in Europe, with 400,000 people dying annually from the disease and a third of the cases going blind.[6] 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]

Jesty's experiment 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. In May 1796, Jenner identified a young dairymaid, Sarah Nelms, who had fresh cowpox lesions on her hand. With the matter from Nelms's lesions, Jenner inoculated an 8-year-old boy, James Phipps. James developed a mild fever and a loss of appetite, but was soon feeling much better. In July 1796, Jenner inoculated the boy with a fresh smallpox lesion. No disease developed. Cowpox was thus found to shield against smallpox. Jenner invented a vaccination for smallpox with this knowledge. The vaccine was used to protect populations from this disease.[3,4,6–8]

FIGURE 2-2 Picture of a Boy with Smallpox Taken by Dr. Stan Foster, EIS Officer, Class of 1962

Courtesy of Centers for Disease Control and Prevention, Atlanta, Georgia.

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 people proliferate, so does the risk of future smallpox epidemics.

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.[9]

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 a few years of observing the course of the disease and the symptoms associated with childbed fever, Semmelweis began a series of investigations.[9]

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 5 times greater than that of the second clinic, and over a 6-year period, it was 3 times greater. Semmelweis observed that the mothers became ill either immediately during birth or within 24–36 hours after delivery. The mothers died quickly of rapid-developing childbed fever. Often the children would soon die as well. This was not the case in the second clinic.[9]

Semmelweis observed it was not the actual labor that was the problem, but the examination of the patients that 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 in the second clinic, the medical students who worked in the first clinic would come directly from 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. Handwashing or any form of infection control was not a common practice. Student doctors conducted the routine daily pelvic exams with putrefied cadaver material on their hands, and the practice was never questioned. There was no reason to be concerned about clean hands because the theory of medicine 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.[9]

Semmelweis discovered that any infected or putrefied tissue, whether from a living patient or a cadaver, could cause disease to spread. To destroy the cadaverous or putrefied matter on the hands, it was necessary that every person—physician or midwife—performing an examination wash his or her hands in chlorinated lime on entering the labor ward of the first clinic. 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, so Semmelweis required washing with chlorinated lime between each examination. When strict adherence to handwashing was followed by 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.[9]

At this time in the history of public health, the causes of disease were unknown, yet suspected. It was known that handwashing 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.[9] Today, it is known that handwashing is still one of the best sanitation practices. 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 for 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

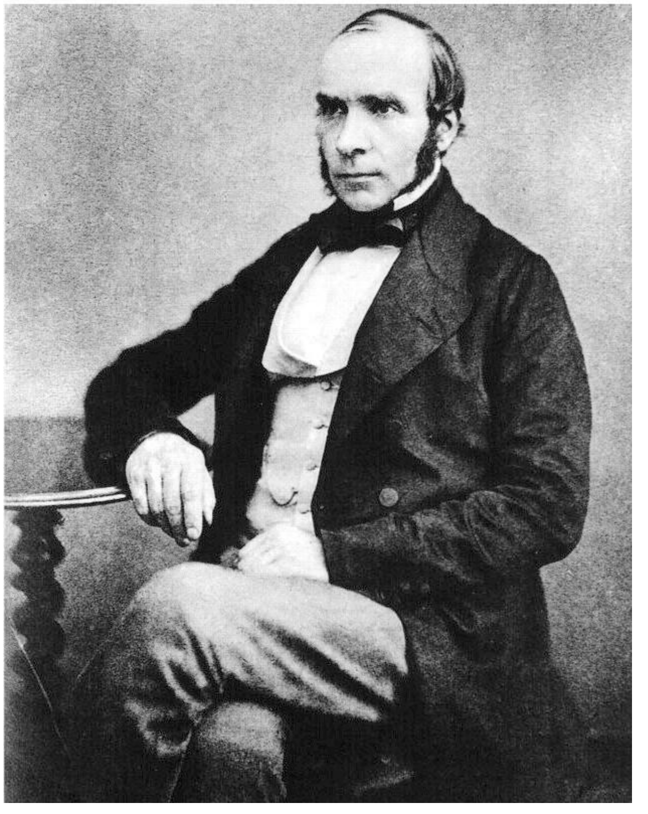


FIGURE 2-3 John Snow

National Library of Medicine.

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.[10–12]

Throughout his medical career, Snow studied cholera. **Cholera** is an acute infectious 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.[10–12]

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 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, as protection from any reoccurrence, and as a political statement to the community, Snow removed the handle from the Broad Street pump.[10–12]

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. Some 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.[10–12]

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 its 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 that had occurred by chance.[10–12]

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 and mostly by Southwark and Vauxhall Water Company, was associated with very high death rates.[10–12]

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. By sampling water from within the houses of those he contacted, Snow developed a test that used chloride of silver to identify the water source for each household. Snow was eventually able to tell the source of water by appearance and smell.[10–12]

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 people 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 8–9 times greater than that 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 people's homes, produced cholera throughout

NEWS FILE

Preventing Cholera

A Simple Filtration Procedure Produces a 48% Reduction in Cholera

Cholera continues to plague developing countries and surfaces sporadically throughout the world. An estimated 1.3–4.0 million cases of cholera and as many as 143,000 deaths from cholera occur each year. Provision of safe water and sanitation is the primary way to reduce the impact of cholera and other waterborne diseases. Oral cholera vaccines may also be taken in conjunction with conventional control measures.

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 and 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.

Modified from World Health Organization. Cholera. https://www.who.int/en/news-room/fact-sheets/detail/cholera. Accessed February 22, 2019; Colwell RR, Huq A, Islam MS, et al. Reduction of cholera in Bangladeshi villages by simple filtration. *Proc Natl Acad Sci.* 2003;100(3):1051–1055.

the community. Snow showed that cholera was a waterborne disease that traveled in both surface and groundwater supplies.[10–12]

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.[3,4,10–12] Because of John Snow's contributions, many have referred to him as the Father of Epidemiology.

Epidemiologic Work of Pasteur and Koch

In the 1870s, on journeys into the countryside in Europe, it was not uncommon to see dead sheep lying in the fields. These sheep had died from anthrax, a bacterial disease that most commonly afflicts animals (e.g., cattle, sheep, horses) but can also occur in humans. **Anthrax** is a serious bacterial infection, usually fatal, caused by *Bacillus anthracis*. 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 (although 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? 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 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 effective 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 that 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 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 methods 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. Koch became a key medical research scientist in Germany in the period marked by the explosion of knowledge in medicine and public health, and he used photography to take the first pictures of microbes to show the world that microorganisms do in fact exist and that they are what cause disease.[3,4,13]

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. 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 largely be prevented by proper water filtration.[3,4,13]

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 identification of the tuberculosis and cholera microorganisms, and 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.[3,4,13,14]

Both Pasteur and Koch were successful in putting to rest a major misguided notion of medicine at the time: that disease was 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.[10]

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 *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 more than 247 microscopes and more than 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 developed because of the advent of the microscope, which influenced advances in the study and control of diseases.[4,15]

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, 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.[4,13]

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 *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 (occurred over a long period).[4,13]

When Graunt died, little was done to continue his good work until 200 years later, when William

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

The Diseases and Casualties This Year Being 1632			
Abortive and Stillborn	445	Chrisomes, and Infants	2,268
Afrighted	1	Cold and Cough	55
Aged	628	Colick, Stone, and Strangury	56
Ague	43	Consumption	1,797
Apoplex, and Meagrom	17	Convulsion	241
Bit with a mad dog	1	Cut of the Stone	5
Bloody flux, Scowring, and Flux	348	Dead in the street and starved	6
Brused, Issues, Sores, and Ulcers	28	Dropsie and Swelling	267
Burnt and Scalded	5	Drowned	34
Burst, and Rupture	9	Executed and Prest to Death	18
Cancer, and Wolf	10	Falling Sickness	7
Canker	1	Fever	1,108
Childbed	171	Fistula	13

Flox and Small Pox	531	Plague	8
French Pox	12	Planet	13
Gangrene	5	Pleurisie, and Spleen	36
Gowt	4	Purples, and Spotted Fever	38
Grief	11	Quinsie	7
Jaundies	43	Rising of the Lights	98
Jawfain	8	Sciatica	1
Impostume	74	Scurvey, and Itch	9
Killed by Several Accident	46	Suddenly	62
King's Evil	38	Surfet	86
Lethargie	2	Swine Pox	6
Lunatique	5	Teeth	470
Made away themselves	15	Thrush, Sore Mouth	40
Measles	80	Tissick	13
Murthered	7	Tympany	34
Over-laid/starved at nurse	7	Vomiting	1
Palsie	25	Worms	27
Piles	8		
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			

Data from Hull CH, ed. In *The Economic Writings of Sir William Petty*. New York, NY: Cambridge University Press; 1899.

Farr (1807–1883) was appointed registrar general in England. Farr built on Graunt's ideas. The concept of "political arithmetic" was replaced by a new term, "statistics." Farr extended the use of vital statistics, and he organized and developed a modern vital statistics system, much of which is still in use today. Another of Farr's important contributions was the promotion of the idea that some diseases, especially chronic diseases, can have a **multifactorial etiology**.[16]

Occupational Health and Industrial Hygiene

Bernardino Ramazzini (1633–1714) was born in Carpi near Modena, Italy. 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 climbing down into 80-foot wells to take temperature and barometric readings so as 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 (typhus, an infectious disease caused by one of the bacteria in the family rickettsiae, is characterized by high fever, a transient rash, and severe illness).[3,4,13,15]

Ramazzini came upon 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 cesspool 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.[3,4,13,15]

Encountering the cesspool worker turned Ramazzini's 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 provide related epidemiologic implications. He completed *The Diseases of Workers* in 1690, but it was not published until 1703. It was not acceptable to pity the poor or simple laborers during this period, so Ramazzini delayed publication because he thought it would not be accepted.[3,4,13,15]

Ramazzini observed that disease among workers had 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 was ascribed to certain violent and irregular motions and unnatural postures imposed on the body while working.[3,4,13,15]

Ramazzini described the dangers of poisoning from lead that potters used in their glaze. He also identified the danger posed by mercury, which was 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.[3,4,13,15]

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.[3,4,13,15]

Ramazzini's major epidemiologic contributions were not only his investigation into and description of work-related maladies, but also 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, to 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.[3,4,13,15]

Florence Nightingale

Florence Nightingale (1820–1910) was the daughter of upper-class British parents (**FIGURE 2-4**). 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.[17–21]

After reading a correspondence series 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 designated her head of an official delegation of nurses. Nightingale worked for the next

FIGURE 2-4 Florence Nightingale

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.[17–21]

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.[17–21]

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 she 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.[17–21]

Her outspoken *Notes on Matters Affecting the Health, Efficiency and Hospital Administration of the British Army* (1858) 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, she became the first woman to receive the Order of Merit.[17]

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. 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.[17–21]

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 51 cases of typhoid fever in a 15-year period.[14]

George Soper, a sanitary engineer studying several outbreaks of typhoid fever in New York City in the 1900s, found that 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 obvious 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.[14,22]

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, but 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. She died at 70 years of age from pneumonia.[14,22]

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

Vitamins are organic components in food that are needed in very small amounts for metabolism, growth, and maintaining good health. The discovery of vitamins and the role they play in life and health have an interesting history. 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 populations around the world. It was believed in 1870 that as many as one-third 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 until then had been 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.[13,23,24]

The first major epidemiologic implications of deficiency illnesses came in 1886, when the Dutch commissioned the firm of C. A. Pekelharing and Winkler, which sent Christiaan 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. Gerrit Grijns (1865–1944), a physiologist, correctly identified that beriberi was a result of a deficiency of an essential nutrient in the outer layers of grain that is removed by polishing.

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, Elmer McCollum (1879–1967) 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 nonfatty 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.[13,23]

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 found 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.[13,23–25]

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 (1793–1859) published the first report on sanitation and public health problems in the Commonwealth of Massachusetts. Shattuck was a teacher, sociologist, and statistician, and he served in the state legislature. He was the chair of a legislative committee to study 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 were epidemiologic in nature. To ensure that epidemiology, its investigations, and the all-important control and prevention aspects of its work are achieved, an organized and structured effort is needed. 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 schoolchildren 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.[26,27]

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*.[26,27]

FIGURE 2-5 The Mosquito and Yellow Fever. 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, MD, a U.S. Army physician working in the tropics, made the epidemiological connection between the mosquito (*Aedes aegypti* species) and yellow fever.

Courtesy of Centers for Disease Control and Prevention, Atlanta, Georgia.

The infectious nature of yellow fever was established in 1900 (**FIGURE 2-5**). In 1902, the United States Public Health Service was founded, and in 1906, the Pure Food and Drug Act 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 the same year, the first school of public health, the Harvard School of Public Health, was established.[26,27]

Alice Hamilton (1869–1970) received a doctor of medicine degree from the Medical School at the University of Michigan. She then completed internships at the Minneapolis Hospital for Women and Children and the New England Hospital for Women and Children. She became a leading expert in occupational health and a pioneer in the field of toxicology. In 1919, she became the first woman appointed to the faculty at Harvard Medical School, joining a new department in Industrial Medicine.[28]

Wade Hampton Frost (1880–1938) received a medical degree from the University of Virginia. He later became the first professor of epidemiology at the Johns Hopkins School of Hygiene and Public Health. Frost created an epidemiology curriculum for the new academic discipline. He also worked closely with Lowell Reed of the Department of Biostatistics, which established the close working relationship between the two disciplines for addressing public health problems. He showed that epidemiology is an analytical science closely integrated with biology and medical science. His work focused on the epidemiology of poliomyelitis, influenza, diphtheria, and tuberculosis. In 1918, Frost, along with Edgar Sydenstricker, investigated the impact of the influenza pandemic on 18 different localities in the United States, providing important insights for public health experts. Because of his contributions to our understanding of the natural history of selected diseases and advances in the methods and scientific discipline of epidemiology, Wade Hampton Frost is often considered the father of modern epidemiology.[29]

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 (1881–1936). 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 as death (mortality) statistics. 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.[30]

In the early 1900s, morbidity statistics of any given kind were not regularly collected on a large scale. Interest in disease statistics came only after the demand for them arose from special populations and when the statistics would prove useful socially and economically. In addition, 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.[30]

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 were deemed 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 were 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 to determine the existence of an incidence of various diseases as they were manifested under normal conditions within the community.[30]

A morbidity study by Sydenstricker and his colleagues under the direction of the United States Public Health Service in Hagerstown, Maryland, was conducted in 1921–1924. The study involved 16,517 person-years of observation or an equivalent population of 1,079 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 were that only 5% of illnesses were of a short duration of 1 day or less, and 40% were not only disabling but caused bed confinement as well. An accurate data-gathering process was developed from the experience.[30]

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.[30]

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 of age. The lowest resistance to disease was in early childhood, birth through 4 years, and toward the end of life.[30,31]

Breast Cancer Epidemiology

Janet Lane-Claypon (1877–1967) was an English physician who received a doctorate in physiology and an MD at the London School of Medicine for Women (**FIGURE 2-6**). In her early career, she applied her skills in the research lab, investigating the biochemistry of milk and reproductive physiology, but later focused her thinking on the epidemiology of breast cancer.[32,33]

In 1912, Lane-Claypon published the results from a novel cohort study showing that babies fed breastmilk gained more weight than those fed cow's milk. She used statistical methods to show that the difference in weight between the two groups was unlikely to be due to chance. She also assessed whether confounding factors could explain the difference. She was a strong advocate for breastfeeding, midwife training, and prenatal services to reduce premature births, stillbirths, and maternal mortality.[32,33]

FIGURE 2-6 Janet Lane-Claypon

In 1923, Lane-Claypon conducted a case-control study that involved 500 women with a history of breast cancer (cases) and 500 women without a history of breast cancer (controls). She then investigated whether the cases differed from the controls with respect to occupation and infant mortality (proxies of social status), nationality, marital status, and age. She also investigated reproductive health histories. Until this study, no large-scale review of this type had been conducted.[32,33]

In 1926, Lane-Claypon conducted another cohort study, which followed a large group of surgically treated women with pathologically confirmed breast cancer for up to 10 years. The study showed that disease stage at the time of diagnosis was directly related to survival. Lane-Claypon recognized the importance of accurate staging and the potential bias that inaccurate staging could have on the results. Further, she showed that breast cancer risk was greater for women who did not have children, who married at a later-than-average age, or who did not breastfeed. She also recognized that genes could influence cancer risk.[32,33]

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 people between 30 and 62 years of age. These people were recruited to participate in a cohort study that spanned 30 years, with 5,100 residents completing the study. In the 30 years, medical exams and other related testing activities were conducted with the participants. The study was initially sponsored by the National Institutes of Health, the Massachusetts Department of Public Health, and the Framingham Department of Health.[34–36]

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.[34–36]

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.[34–36]

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. The study advanced understanding of the epidemiology of hypertensive or arteriosclerotic cardiovascular disease. It also identified much of what we know today about the effects of diet, exercise, and common medications such as aspirin on heart disease.

Cigarette Smoking and Cancer

After World War II, vital statistics indicated a sharp increase in deaths attributed to lung cancer. The first epidemiologic reports indicating a link between cigarette smoking and lung cancer appeared in the early 1950s.[37–41] 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.[42]

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).[43,44] 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 a history of smoking.

The first cohort study assessing the association between smoking and lung cancer was conducted in 1951 by Doll and Hill.[45,46] 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.

Modern Epidemiology

The expanding role of epidemiology has been accompanied by an increasing number of methods for conducting epidemiologic research. In the 1960s and 1970s, epidemiologists tended to be physicians with a primary interest in disease etiology. Some of these physicians were effective in collaborating with statisticians. Olli S. Miettinen (1936–) is a statistician who developed and published several landmark papers on causal, design, and statistical approaches in epidemiology.[47–50] Several other statisticians contributed to modern epidemiologic thinking: Sir Austin Bradford Hill (1897–1991), who pioneered the randomized clinical trial and presented criteria for determining causal associations;[51,52] Jerome Cornfield (1912–1979), who contributed to the development of clinical trials, Bayesian inference, and the relationship between statistical theory and practice;[53] Joseph L. Fleiss (1937–2003), who contributed to mental health statistics and developed a statistical measure of interrater reliability called kappa;[54,55] Sander Greenland (1951–), who contributed primarily to meta-analysis, Bayesian inference, and causal inference; Norman Breslow (1941–), who developed and promoted greater use of the case-control matched sample research design; Nathan Mantel (1919–2002), who, with William Haenszel, developed the Mantel-Haenszel test and the Mantel-Haenszel odds ratio;[56] and William G. Cochran (1909–1980), who developed and advanced research in experimental designs and sampling techniques.[57–60]

Conclusion

This chapter describes the contributions of many key players to the field of epidemiology who sought to explain illness, injury, and death from an observational, scientific perspective. Individuals were presented who helped shape the discipline as we know it today. These people were physicians, statisticians, engineers, sociologists, chemists, and more. Pioneers in the area of epidemiology introduced germ theory, the microscope, vaccinations, study designs, evaluation methods, sources and modes of disease transmission, and the importance of monitoring and evaluating health-related states or events.

Exercises

Key Terms

Define the following terms.

Anthrax
Atomic theory
Childbed fever
Cholera
Multifactorial etiology
Scurvy
Smallpox
Typhoid fever
Typhus
Variolation
Vitamins

Study Questions

1. Match the individuals in the left-hand column of **TABLE 2-2** with their contributions.
2. List some of the contributions of the microscope to epidemiology.
3. What two individuals contributed to the birth of vital statistics?
4. What type of epidemiologic study was used by James Lind?
5. What types of epidemiologic studies were used by Doll and Hill?
6. What types of epidemiologic studies were used by Janet Lane-Claypon?

TABLE 2-2 History of Epidemiology: Names and Contributions

Hippocrates	A. Identified various modes of transmission and incubation times for cholera
Thomas Sydenham	B. Provided classifications of morbidity statistics to improve the value of morbidity information
James Lind	C. Observed in the 17th century that certain jobs carried a high risk for disease
Benjamin Jesty	D. Introduced the words "epidemic" and "endemic"
Edward Jenner	E. Advanced useful treatments and remedies including exercise, fresh air, and a healthy diet, which other physicians rejected at the time
Ignaz Semmelweis	F. Through an experimental study, showed that lemons and oranges were protective against scurvy
John Snow	G. Invented a vaccination for smallpox
Louis Pasteur	H. The father of modern epidemiology
Robert Koch	I. Used data as a tool for improving city and military hospitals
John Graunt	J. Conducted the first cohort study investigating the association between smoking and lung cancer
William Farr	K. Promoted the idea that some diseases, especially chronic diseases, can have a multifactorial etiology
Bernardino Ramazzini	L. Observed that milkmaids did not get smallpox, but did get cowpox
Edgar Sydenstricker	M. Developed a vaccine for anthrax

(*continues*)

TABLE 2-2 History of Epidemiology: Names and Contributions *(continued)*

Doll and Hill	N. Pioneered the use of cohort and case-control studies to identify risk factors for breast cancer
Florence Nightingale	O. A pioneer in the field of toxicology
Janet Lane-Claypon	P. Credited with producing the first life table
Alice Hamilton	Q. Used photography to take the first pictures of microbes to show the world that microorganisms existed and that they caused many diseases
Wade Hampton Frost	R. A statistician who was a pioneer in developing the theory of epidemiologic study design and causal inference
Olli S. Miettinen	S. Discovered that the incidence of puerperal fever could be drastically cut by using handwashing standards in obstetrical clinics

References

1. Hippocrates. Airs, waters, places. In: Buck C, Llopis A, Najera E, Terris M, eds. *The Challenge of Epidemiology: Issues and Selected Readings*. Washington, DC: World Health Organization; 1988:18–19.
2. Dorland WA, ed. *Dorland's Illustrated Medical Dictionary*. 25th ed. Philadelphia, PA: Saunders; 1974.
3. Cumston CG. *An Introduction to the History of Medicine*. New York, NY: Alfred A. Knopf; 1926.
4. Garrison FH. *History of Medicine*. Philadelphia, PA: Saunders; 1926.
5. Lilienfeld AM, Lilienfeld DE. *Foundations of Epidemiology*. 2nd ed. New York, NY: Oxford University Press; 1980:30–31.
6. Barquet N, Domingo P. Smallpox: the triumph over the most terrible of the ministers of death. *Ann Intern Med*. 1997;127(8, pt. 1):635–642.
7. Willis NJ. Edward Jenner and the eradication of smallpox. *Scott Med J*. 1997;42:118–121.
8. Jenner E. An inquiry into the causes and effects of the variolae vaccine. In: Buck C, Llopis A, Najera E, Terris M, eds. *The Challenge of Epidemiology: Issues and Selected Readings*. Washington, DC: World Health Organization; 1988:31–32.
9. Semmelweis I. The etiology, concept, and prophylaxis of childbed fever. In: Buck C, Llopis A, Najera E, Terris M, eds. *The Challenge of Epidemiology: Issues and Selected Readings*. Washington, DC: World Health Organization; 1988:46–59.
10. Benenson AS, ed. *Control of Communicable Diseases in Man*. 15th ed. Washington, DC: American Public Health Association; 1990:367–373.
11. Snow J. *On the Mode of Communication of Cholera*. 2nd ed. London, UK: John Churchill; 1955.
12. Vinten-Johansen P, Panera N, Rip M, Zuck D, Brody H. *Cholera, Chloroform, and the Science of Medicine: A Life of John Snow*. New York, NY: Oxford University Press; 2003.
13. Rosen G. *A History of Public Health*. Baltimore, MD: Johns Hopkins University Press; 1958.
14. Nester EW, McCarthy BJ, Roberts CE, Pearsall NN. *Microbiology: Molecules, Microbes and Man*. New York, NY: Holt, Rinehart and Winston; 1973.
15. Seelig MG. *Medicine: An Historical Outline*. Baltimore, MD: Williams and Wilkins; 1925.
16. Fox JP, Hall CE, Elveback LR. *Epidemiology: Man and Disease*. New York, NY: Macmillan Company; 1970.
17. Cohen IB. Florence Nightingale. *Scientific American*. 1984;250:128–137.
18. Cohen IB. *The Triumph of Numbers: How Counting Shaped Modern Life*. New York, NY: W. W. Norton & Company; 2006.
19. Kopf EW. Florence Nightingale as a statistician. *J Am Stat Assoc*. 1916;15:388–404.
20. Nuttal P. The passionate statistician. *Nurs Times*. 1983; 28:25–27.
21. Grier MR. Florence Nightingale and statistics. *Res Nurs Health*. 1978;1:91–109.
22. Health News. *Medical Milestone: Mary Mallon, Typhoid Mary, November 1968*. New York, NY: New York Department of Health; 1968.
23. Krause MV, Hunscher MA. *Food, Nutrition and Diet Therapy*. 5th ed. Philadelphia, PA: Saunders; 1972.
24. Guthrie HA. *Introductory Nutrition*. St. Louis, MO: Mosby; 1975.
25. Clayton T, ed. *Taber's Medical Dictionary*. 14th ed. Philadelphia, PA: Davis; 1981:762.
26. Green L, Anderson C. *Community Health*. 5th ed. St. Louis, MO: Times Mirror/Mosby; 1986.
27. Picket G, Hanlon J. *Public Health: Administration and Practice*. 9th ed. St. Louis, MO: Times Mirror/Mosby; 1990.
28. Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health (NIOSH). *History of Alice Hamilton, M.D.* http://www.cdc.gov/niosh/awards/hamilton/HamHist.html. Accessed January 3, 2012.

29. Daniel TM. *Wade Hampton Frost, Pioneer Epidemiologist 1880–1938: Up to the Mountain*. Rochester, NY: University of Rochester Press; 2004.
30. Sydenstricker E. A study of illness in a general population. *Public Health Rep*. 1926;61:12.
31. Sydenstricker E. Sex difference in the incidence of certain diseases at different ages. *Public Health Rep*. 1928;63:1269–1270.
32. Winkelstein W Jr. Vignettes of the history of epidemiology: three firsts by Janet Elizabeth Lane-Claypon. *Am J Epidemiol*. 2004;160(2):97–101.
33. Morabia A. Janet Lane-Claypon: interphase epitome. *Epidemiology*. 2010;21(4):573–576.
34. Miller DF. *Dimensions of Community Health*. 3rd ed. Dubuque, IA: William C. Brown; 1992.
35. Hennekens CH, Buring JE. *Epidemiology in Medicine*. Boston, MA: Little, Brown and Company; 1987.
36. Dawber TR, Kannel WB, Lyell LP. An approach to longitudinal studies in a community: the Framingham study. *Ann NY Acad Sci*. 1963;107:539–556.
37. Doll R, Hill AB. Smoking and carcinoma of the lung: preliminary report. *BMJ*. 1950;2:739–748.
38. Norr R. Cancer by the carton. *Read Dig*. December 1952:7–8.
39. Cigarettes. What CU's test showed: the industry and its advertising, and how harmful are they? *Consum Rep*. 1953:58–74.
40. Miller LM, Monahan J. The facts behind the cigarette controversy. *Read Dig*. 1954:1–6.
41. Tobacco smoking and lung cancer. *Consum Rep*. 1954:54, 92.
42. United States Department of Health and Human Services. *Smoking and Health: Report of the Advisory Committee to the Surgeon General of the Public Health Service*. Publication PHS 1103. Washington, DC: U.S. Government Printing Office; 1964.
43. Wynder EL, Graham EA. Tobacco smoking as a possible etiologic factor in bronchiogenic carcinoma: a study of six hundred and eighty-four proved cases. *JAMA*. 1950;143:329–336.
44. Doll R, Hill AB. Smoking and carcinoma of the lung: preliminary report. *BMJ*. 1950;2:739–748.
45. Doll R, Hill AB. Mortality in relation to smoking: ten years' observations of British doctors. *BMJ*. 1964;1:1399–1410.
46. Doll R, Peto R. Mortality in relation to smoking: twenty years' observations on male British doctors. *BMJ*. 1976;2:1525.
47. Miettinen OS. Individual matching with multiple controls in the case of all-or-none responses. *Biometrics*. 1969;22: 339–355.
48. Miettinen OS. *Principles of Epidemiologic Research*. Unpublished manuscript. Cambridge, MA: Harvard University; 1975.
49. Miettinen OS. Estimability and estimation in case-referent studies. *Am J Epidemiol*. 1976;103(2):226–235.
50. Miettinen OS, Wang JD. An alternative to the proportionate mortality ratio. *Am J Epidemiol*. 1981;114:144–148.
51. Farewell V, Johnson T. Woods and Russell, Hill, and the emergence of medical statistics. *Stat Med*. 2010;29:1459–1476. doi:10.1002/sim.3893
52. Armitage P. Obituary: Sir Austin Bradford Hill, 1897–1991. *J Royal Stat Soc*. 1991;154(3):482–484.
53. Greenhouse SW, Greenhouse JB, Cornfield J. *Encyclopedia of Biostatistics*. New York, NY: John Wiley & Sons; 2005.
54. Scott W. Reliability of content analysis: the case of nominal scale coding. *Public Opin Q*. 1955;19(3):321–325.
55. Fleiss JL. Measuring nominal scale agreement among many raters. *Psychol Bull*. 1971;76(5):378–382.
56. Mantel N, Haenszel W. Statistical aspects of the analysis of data from the retrospective analysis of disease. *J Natl Cancer Inst*. 1959;22(4):719–748.
57. Cochran WG, Cox GM. *Experimental Designs.* 2nd ed. New York, NY: John Wiley & Sons; 1992.
58. Cochran WG. *Sampling Techniques.* 3rd ed. New York, NY: John Wiley & Sons; 1977.
59. Snedecor GW, Cochran WG. *Statistical Methods, Applied to Experiments in Agriculture and Biology.* 5th ed. Ames, IA: Iowa State College Press; 1956.
60. Moses LE, Mosteller F, eds. *Planning and Analysis of Observational Studies*. New York, NY: John Wiley & Sons; 1983.


© sdecoret/Shutterstock

CHAPTER 3

Practical Disease Concepts in Epidemiology

OBJECTIVES

After completing this chapter, you will be able to:

- Define disease and identify common sources and modes of disease transmission.
- Classify acute and chronic diseases according to infectivity and communicability.
- Understand the major stages in the disease process.
- Know the five major categories of disease.
- Define zoonosis and identify selected zoonotic diseases and potential carriers of infectious organisms that may be zoonotic.
- Describe notifiable disease reporting in the United States.
- Discuss immunity and immunizations against infectious diseases.
- Identify the changing emphasis of epidemiologic study.
- Describe common nutritional deficiency diseases and disorders.
- Describe selected chronic diseases and conditions.

Disease is an interruption, cessation, or disorder of body functions, systems, or organs.[1] Diseases arise from infectious agents, inherent weaknesses, lifestyle, or environmental stresses. Often, a combination of these factors influences the onset of disease. The early development of epidemiology was based on the investigation of infectious disease outbreaks. Today, epidemiologic studies also consider diseases that are influenced by noninfectious causes such as genetic susceptibility, lifestyle, and selected environmental factors.

Identifying the causes of disease and the mechanisms by which disease is spread remains a primary focus of epidemiology. The science and study of the causes of disease and their mode of operation is referred to as **etiology**.[1] Disease processes are complex and require an understanding of several factors, which may include anatomy, physiology, histology, biochemistry, microbiology, and related medical sciences. This chapter cannot provide a comprehensive foundation of all these fields of study. Thus, only the basics of diseases, their classification, and processes are presented.

Communicable and Noncommunicable Diseases and Conditions

Infectious diseases are caused by invading organisms called pathogens. Infectious diseases may or may not be contagious. When an infectious disease is contagious, or capable of being communicated or transmitted, it is called a **communicable disease**.[1] Examples of infectious communicable diseases are HIV/AIDS, cholera, and influenza. Although all communicable diseases are infectious diseases, not all infectious diseases are communicable diseases. An example of an infectious noncommunicable disease is tetanus, caused by the bacterium *Clostridium tetani*, which is found in the environment. Spores of the bacterium live in the soil, may remain infectious for more than 40 years, and are found throughout the world. Similarly, anthrax exposure may result from breathing spores that have been in the soil for, in some cases, many years. Another example is Legionnaires' disease, which is caused by inhaling *Legionella* bacteria from the environment. Noninfectious diseases may be referred to as noncommunicable diseases and conditions, such as heart disease, cancer, mental illness, and injuries from accidents.

Infectious communicable diseases may be transmitted through vertical or horizontal transmission. **Vertical transmission** refers to transmission from an individual to its offspring through sperm, placenta, milk, or vaginal fluids.[1] **Horizontal transmission** refers to transmission of infectious agents from an infected individual to a susceptible contemporary.[1] Horizontal transmission may involve direct transmission (e.g., sexually transmitted diseases), a common vehicle (e.g., waterborne, food-borne, or blood-borne diseases), an airborne pathogen (e.g., tuberculosis), or a vector-borne pathogen (e.g., malaria).

Pathogens are defined as organisms or substances such as bacteria, protozoa, viruses, fungi, abnormal or infectious prions (proteins produced by mutated genes), and parasites that are capable of producing disease.[1] Infectious diseases are those in which the pathogen is capable of entering, surviving in, and multiplying in the host. **Infectivity** refers to the capability of a disease agent to enter, survive in, and multiply in a susceptible host.[1] The host plays a major part in the ability of an organism to cause disease by providing nutrients and a life-sustaining environment. The disease-evoking power of a pathogen is called **virulence**.[1]

Antibiotics work against pathogens because of their toxicity—that is, the antibiotic substance contains elements that are more toxic to bacteria than to the human body. A **toxin** is a poison and consequently kills pathogens by poisoning them. For example, arsenic is a toxin once used to treat syphilis.[2] The strength of a substance or chemical is measured by how little of it is required for it to work as a poison and how quickly it acts. The shorter the duration and the less of the substance needed to cause the organism to die, the higher the level of toxicity.

Diseases are classified as acute or chronic:

Acute: relatively severe disorder with sudden onset and short duration of symptoms.[1]
Chronic: less severe but of continuous duration, lasting over long periods, if not a lifetime.[1]

Infectious and noninfectious diseases can be acute or chronic. To help clarify acute and chronic disease classification according to infectivity and communicability, some examples are presented in **TABLE 3-1**.

Natural History of Disease

Each disease has a natural history of progression if no medical intervention is taken and the disease is allowed to run its full course. There are four common stages relevant to most diseases:

1. Stage of susceptibility
2. Stage of presymptomatic disease
3. Stage of clinical disease
4. Stage of recovery, disability, or death

The stage of susceptibility precedes the disease and involves the likelihood a host has of developing an ill effect from an external agent. The stage of presymptomatic disease begins with exposure to or accumulation of factors sufficient to cause the disease process to begin and subsequent pathologic changes to occur in a