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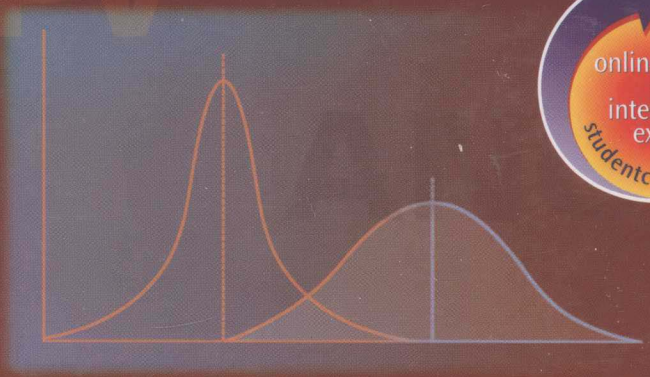

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EPIDEMIOLOGY, BIOSTATISTICS, and PREVENTIVE MEDICINE

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THIRD EDITION

Epidemiology, Biostatistics, and Preventive Medicine

Third Edition

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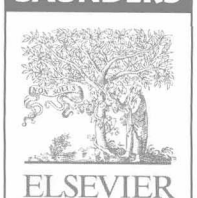

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Dorothea M.G. Wild, MD, MPH, is a Research Affiliate in Public Health at the Yale University Schools of Medicine and Public Health and Associate Program Director of the combined internal medicine/preventive medicine residency program at Griffin Hospital. Dr. Wild is Director of Quality Improvement at the Griffin Hospital Faculty Practice Plan, where she also works as a hospitalist. She has a special interest in health policy, cost-effectiveness analysis in medicine, and developing systems to reduce medical errors.

Preface

As the authors of the second edition of this textbook, we were pleased to be asked to write the third edition. The second edition has continued to be used for both courses and preventive medicine board review. Writing a revision every five years forces the authors to consider what the major developments have been since the last edition that need to be incorporated or emphasized. In the past five years, in addition to incremental developments in all health fields, some issues have become more urgent.

In the area of **medical care organization** and **financing**, after a period of relatively modest inflationary pressures following the introduction of the prospective payment system, we are now approaching a new crisis in the payment for medical care. In an attempt to remain globally competitive, employers either are not providing any medical insurance at all or are shifting an increasing proportion of the costs directly to the employees, many of whom cannot afford it. The costs are thus passed on to the providers, especially hospitals. In addition, the pressure for hospitals to demonstrate quality of care and avoid medical errors has become more intense.

Second, there have been major changes in **infectious diseases** since the last edition. Bovine spongiform encephalopathy has come to North America, and the world has experienced an epidemic of a new disease, severe acute respiratory syndrome (SARS). Even more significant, as this is being written the world is deeply concerned about the possibility of a true pandemic of the severe avian form of H5N1 influenza.

It has also become clear since the second edition that the United States and, to a lesser extent, much of the world are entering a time of **epidemic overweight** and **obesity**. This has already increased the incidence of many chronic diseases such as type II diabetes in adults and even in children.

In the past five years, questions about **screening for disease** have become more acute, because of both financial concerns and a better understanding of the use and limitations of screening in the prevention of symptomatic disease. The screening methods that have been subjected to the most study and debate have been mammography for breast cancer and determination of prostate-specific antigen and other techniques for prostate cancer.

Thus, major changes have occurred in the fields of health care policy and financing, infectious disease, chronic disease, and disease prevention technology. In this edition, we have sought to provide up-to-date guidance for these issues especially, and for preventive medicine generally. We wish to give special thanks to our developmental editor, Nicole DiCicco, for her helpful guidance throughout this process.

For this edition, we are pleased that Dr. Dorothea M.G. Wild, a specialist in health policy and management with a special interest in medical care quality, has joined us as a coauthor.

James F. Jekel
David L. Katz
Joann G. Elmore
Dorothea M.G. Wild

Preface to the Second Edition

The first edition of *Epidemiology, Biostatistics, and Preventive Medicine* was written by Dr. Jekel with the collaboration of Drs. Elmore and Katz. The first edition of the companion text, *Epidemiology, Biostatistics, and Preventive Medicine Review*, which included test questions associated with each chapter, was written by Dr. Katz. Both texts were greeted with highly favorable reactions by students and faculty in public health and medicine. In particular, the texts were praised for their ability to explain difficult concepts in clear and easy-to-understand terms. While the first editions were written explicitly for use in course work and USMLE (medical board) preparation, we were gratified that both of them came to be recommended by the American Board of Preventive Medicine as tools for preparing for its core specialty examination as well.

To enhance the value of the two texts for all of our readers, we have combined them into a single text. Thus, the second edition of *Epidemiology, Biostatistics, and Preventive Medicine* includes the following study tools: an examination at the end of each chapter; a 150-question comprehensive examination; detailed explanations about why answers to test questions are correct or incorrect; and a glossary of epidemiologic and medical terms.

Our guiding principles concerning the original 21 chapters of the book were to update all of the information, to improve or retain those aspects of the chapters that worked well in the first edition, and to include coverage of additional concepts. We substantially revised and updated the information on nutrition and genetics. We also updated the information on health counseling, disease screening, and immunizations, based on the latest recommendations of the US Preventive Services Task Force, the Department of Health and Human Services, and the Centers for Disease Control and Prevention. We added information on various topics, including the calculation and interpretation of the number needed to treat and the number needed to harm; the statistical analysis of incidence density; and the role of complementary and alternative medicine in modern health care delivery.

We are grateful for the many encouraging comments and suggestions that we received from our students and colleagues, both in the USA and elsewhere, concerning the first edition texts. We wish to thank Sharon Maddox, whose editing enhanced both the accuracy and clarity of this edition. And we continue to be thankful to our spouses and families for their support of our efforts.

James F. Jekel
David L. Katz
Joann G. Elmore

Preface to the First Edition

Epidemiology is the basic science of preventive medicine and public health, and biostatistics is the quantitative foundation of epidemiology. To separate these fields—as is usually done in texts for students of medicine, public health, and related disciplines—incurs the risks of providing incomplete coverage of each field and failing to integrate the subject matter.

In developing this book, the goal was to present a comprehensive view of the fields of epidemiology, biostatistics, preventive medicine, and public health by showing their interrelationships and emphasizing their relevance to clinical practice, research, and public health policy. In particular, the objectives were to combine theory and application in a manner that enables readers to interpret the scientific literature with understanding; to approach clinical practice with an emphasis on prevention; and to understand the social, organizational, financial, and governmental environments in which physicians and other health professionals must practice today.

Section I, Epidemiology, reviews the many ways in which epidemiology contributes to the medical sciences; discusses the sources of health data; incorporates numerous figures and graphs to illustrate how epidemiologic measurements are made and used; outlines the steps in epidemiologic surveillance, outbreak investigation, and assessment of causation and risks; and discusses common research designs used by epidemiologists.

Section II, Biostatistics, builds on the concepts introduced in the first section and emphasizes that an understanding of biostatistics is important not only for analyzing the results of research but also for understanding and reducing errors in clinical medicine. Biostatistical tests and equations are clearly explained and easy to follow, with special "boxes" used to illustrate the steps in calculating standard errors, *t* values, chi-square values, and other measurements.

Section III, Preventive Medicine and Public Health, focuses on methods of primary, secondary, and tertiary prevention; provides tables with up-to-date information on immunization schedules, available vaccines and antitoxins, screening recommendations, effects of toxic exposures, and similar topics; and discusses the nutritional, environmental, and behavioral factors that have an impact on health, as well as the socioeconomic and political climate that influences health care policy.

In addition to being a textbook for medical students and others taking courses in epidemiology, biostatistics, preventive medicine, and public health, this book is a source of information for health care professionals who wish to study these topics on their own or to review them for medical board examinations. The approach taken in this book evolved from my experiences in teaching a variety of courses to both students and professionals at Yale University School of Medicine, where the Department of Epidemiology and Public Health is an accredited school of public health and also serves as a department of epidemiology, biostatistics, and preventive medicine for the medical school. As a result, I have had the privilege of teaching many of these topics to public health students for 28 years, biostatistics to medical students for 13 years, public health to medical students for 8 years, and biostatistics and related topics to specialist physicians in the Robert Wood Johnson Clinical Scholars Program for 19 years, and directing the Yale Residency Program in General Preventive Medicine and Public Health for 17 years. These varied groups of outstanding individuals, from different backgrounds and levels of training and experience, have given me the best education a teacher could obtain. Any strength this book may have is due in significant measure to the challenges put forth by these students, who have numbered in the thousands during my three decades of university work.

I owe a tremendous debt to my collaborators, Dr. Joann Elmore and Dr. David Katz, both of whom are general internists with public health degrees and an orientation toward prevention. At first among my best students ever, they soon became trusted colleagues in teaching medical students and in research. They have achieved outstanding reputations at Yale University and are in considerable demand as teachers of medical and public health students and as research consultants. Dr. Elmore and Dr. Katz not only offered valuable suggestions regarding the book's general outlines but also provided extensive critiques of each chapter. Whenever we had differences, we resolved them in conference. For some chapters, the process of reviewing and revising was repeated several times. The final product was, therefore, a true collaboration. Any deficiencies, however, must be laid at my door alone.

Special thanks are also due to Dr. David Lane, a family practitioner and clinical epidemiologist, and to Michael Fischer, a medical student, for their insightful reviews of the epidemiology and biostatistics sections of the book. Dr. William Beckett, who has been a valued colleague for years in teaching public health to medical students, reviewed and made helpful suggestions about the information dealing with occupational health and exposure to toxins. Sharon Maddox, the

book's developmental editor, made major contributions to the organization, clarity, and accuracy of the text. William Schmitt of W.B. Saunders has been a patient and supportive editor from the time he first suggested this effort.

My intellectual debts to others are countless, and unfortunately, they cannot all be acknowledged here. The late Dr. Alexander Langmuir was the inspiration for me (as for hundreds of others) to enter epidemiology and public health as a career. Dr. Steven Helgerson, another student of Dr. Langmuir, was an inspiring colleague in efforts to improve the teaching of epidemiology, particularly the investigation of acute disease outbreaks. The late Dr. Edward M. Cohart first saw that I might make an academician and persisted until I agreed to give an academic career a try. Dr. Alvan Feinstein has been a continuous inspiration by his tireless and brilliant efforts to improve clinical epidemiology and biostatistics. His 1975 request for me to assist in the Robert Wood Johnson Clinical Scholars Program at Yale University was a major stimulus to become more involved in teaching biostatistics. Dr. Lowell Levin has consistently helped me to take a wide perspective regarding the sources of health and ways to improve health. Dr. David Allen was a coinvestigator in our research into the crack cocaine problem, and he has helped me to see the mental and spiritual aspects of many health problems.

I cannot count the lessons I have learned from my parents, who at this writing are preparing to celebrate their sixty-ninth wedding anniversary, and from my wife, Jan, who has been my loving and supportive companion for 37 years. They have taught me what it means to live in an environment filled with wholeness, peace, and health, perhaps best described by the Hebrew word *shalom*.

James F. Jekel

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SECTION

Epidemiology

1

1 Basic Epidemiologic Concepts and Principles

CHAPTER OUTLINE

WHAT IS EPIDEMIOLOGY?

Epidemiology has been defined in many ways. The word comes from the Greek language, in which *epi* means "upon," *demos* means "the population," and the combining form *-logy* means "the study of." Epidemiology is the study of something that afflicts (affects) a **population**. Usually, epidemiology is defined as the study of factors that determine the occurrence and distribution of disease in a population.

Epidemiology can be thought of as one of the ways in which disease, injury, and clinical practice are studied. The scientific study of disease can be approached at four levels: (1) the submolecular or molecular level (e.g., cell biology, genetics, biochemistry, and immunology); (2) the tissue or organ level (e.g., anatomic pathology); (3) the level of individual patients (e.g., clinical medicine); and (4) the level of populations (e.g., **epidemiology**). Perspectives gained from these four levels are related, and research should be coordinated among the various disciplines to maximize the scientific understanding of disease.

Some people distinguish between classical epidemiology and clinical epidemiology. **Classical epidemiology**, which is population-oriented, studies the community origins of health problems, particularly health problems related to infectious agents; nutrition; the environment; human behavior; and the psychologic, social, and spiritual state of a population. Classical epidemiologists are interested in discovering risk factors that might be altered in a population to prevent or delay disease, injury, and death.

Investigators involved in **clinical epidemiology** often use research designs and statistical tools that are similar to those used by classical epidemiologists. Clinical epidemiologists study patients in health care settings, however, to improve the prevention, early detection, diagnosis, and treatment and care of various diseases and the prognosis for patients already affected by a disease. Because clinical epidemiologists usually study people who are ill and are receiving medical attention, they must take special care to adjust for the presence of other diseases (comorbidity) and for any clinical treatments.[1]

The epidemiology section of this book is generally oriented toward classical epidemiology, although clinical examples also are used. Chapters 7 and 8 discuss several topics of special interest to clinical epidemiologists. The more statistical parts of epidemiology are found in Chapters 7 through 13, so that the basic concepts and methods of epidemiology can be introduced without undue complexity. Many of the illustrations from classical epidemiology concern infectious diseases because epidemiology originally was developed to study these diseases, and there is the most experience with them. Additionally, because of the increasing concern with **bioterrorism**, the classical methods of surveillance and outbreak investigation are drawn on, even while they are being modified to adapt to the new challenges. One example of new approaches is

called **syndromic epidemiology**, in which epidemiologists look for patterns of symptoms and signs that might indicate a form of bioterrorism.

Epidemiology also can be divided into **infectious disease epidemiology** and **chronic disease epidemiology**. Historically, infectious disease epidemiology has depended more heavily on laboratory support (especially microbiology and serology), and chronic disease epidemiology has depended more on complex sampling and statistical methods. This distinction is becoming less valid as molecular laboratory markers (genetic and otherwise) are being used increasingly in chronic disease epidemiology, and complex statistical analyses are being used more frequently in infectious disease epidemiology. Many illnesses, including tuberculosis and acquired immunodeficiency syndrome (AIDS), may be thought of as both infectious and chronic diseases.

The name of a medical discipline indicates a method of research into health and disease and the body of knowledge acquired by using that method of research. Pathology is a field of medical research with its own goals and methods, but investigators and clinicians also can speak of the "pathology of lung cancer." Similarly, epidemiology refers to a field of research that uses particular methods, but it also can be used to denote the resulting body of knowledge about the distribution and natural history of diseases—that is, about the nutritional, behavioral, environmental, and genetic sources of disease as identified through epidemiologic studies.

ETIOLOGY AND NATURAL HISTORY OF DISEASE

The way a disease progresses in the absence of medical or public health intervention is often called the natural history of the disease. Public health and medical personnel take advantage of available knowledge about the stages, mechanisms, and causes of disease to determine how and when to intervene. The goal of intervention, whether preventive or therapeutic, is to alter the natural history of a disease in a favorable way.

Stages of Disease

The development and expression of a disease occur over time and can be divided into three stages: the predisease, latent, and symptomatic stages. During the **predisease stage** (before the pathologic process begins), early intervention may prevent exposure to the agent of disease (e.g., lead, *trans*-fatty acids, or microbes), preventing the disease process from starting; this is called **primary prevention**. During the **latent stage** (when the disease process has begun, but is still asymptomatic), screening and appropriate treatment may prevent progression to symptomatic disease; this is called **secondary prevention**. During the **symptomatic stage** (when disease manifestations are evident), intervention may slow, arrest, or reverse the progression of disease; this is called **tertiary prevention**. These concepts are discussed in more detail in Chapter 14 and subsequent chapters.

Mechanisms and Causes of Disease

When discussing the etiology of disease, epidemiologists make a distinction between the **biologic mechanisms** of disease and the **social and environmental causes of disease**. Osteomalacia is a bone disease that may have social and biologic causes. For example, among women who observe the custom of purdah, which is observed by many Muslims, women who have reached puberty avoid public observation by spending most of their time indoors and by wearing clothing that covers virtually all of the body when they go outdoors. By blocking the action of the sun's radiation on the skin, these practices prevent the irradiation of ergosterol in the skin. Irradiated ergosterol is an important source of D vitamins, which are necessary for growth. If, as often happens, the diet of these women also is deficient in vitamin D during the rapid growth period of puberty, they may develop osteomalacia as a result of insufficient calcium absorption. Osteomalacia can affect future pregnancies by causing the pelvis to become distorted (more pear-shaped), making the pelvic opening too small for the fetus to pass through. In this example, the social, nutritional, and environmental *causes* set in motion the biochemical and other biologic *mechanisms* of osteomalacia that may lead to maternal and infant mortality.

Likewise, excessive fat intake, smoking, and lack of exercise are social factors that contribute to biologic mechanisms of atherogenesis, such as elevated blood levels of low-density lipoprotein cholesterol and very-low-density lipoprotein cholesterol and reduced blood levels of high-density lipoprotein cholesterol. These social risk factors have different effects depending of the genetic pattern of each individual and how the genes interact with the environment and other risk factors.

Epidemiologists attempt to go as far back as possible to discover the societal causes of disease, which offer clues to methods of prevention. Hypotheses introduced by epidemiologists frequently guide laboratory scientists as they seek biologic mechanisms of disease, which may suggest methods of treatment.

Host, Agent, and Environment

The causes of a disease often are considered in terms of a triad of factors: the host, the agent, and the environment. For many diseases, it is useful to add a fourth factor, the vector (Fig. 1-1). In measles, the host is a human being who is susceptible to measles infection, the agent is a highly infectious virus that can produce serious disease in humans, and the environment enables susceptible people to be exposed to infectious persons. In malaria, the host, agent, and environment are all important, but the vector, the *Anopheles* mosquito, also is crucial.

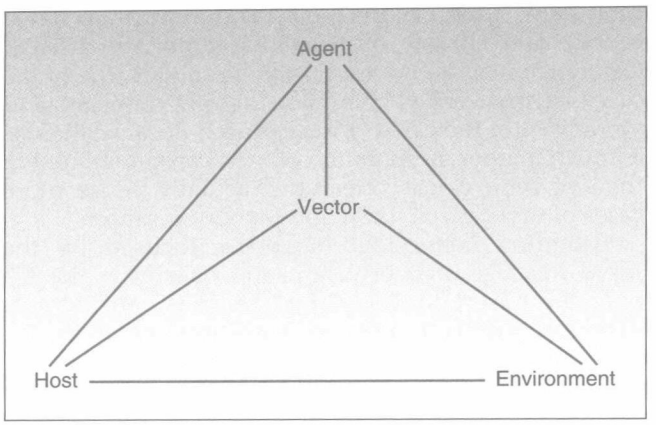

Figure 1–1 Factors involved in the natural history of disease.

Host factors are responsible for the degree to which the individual is able to adapt to the stressors produced by the agent. Host resistance is influenced by a person's genotype (e.g., dark skin reduces sunburn), nutritional status and body mass index (e.g., obesity increases susceptibility to many diseases), immune system (for resistance to cancer as well as microbial disease), and social behavior (e.g., physical exercise enhances resistance to many diseases, including depression). Several factors can work synergistically, such as nutrition and immune status. Measles is seldom fatal in well-nourished children, even in the absence of measles immunization and modern medical care. By contrast, 25% of children with marasmus (starvation) or kwashiorkor (protein-calorie malnutrition related to weaning) may die from complications of measles.

Agents of disease or illness can be divided into several categories. **Biologic agents** include allergens, infectious organisms (e.g., bacteria and viruses), biologic toxins (e.g., botulinum toxin), and foods (e.g., a high-fat diet). **Chemical agents** include chemical toxins (e.g., lead) and dusts, which can cause acute or chronic illness. **Physical agents** include kinetic energy (e.g., in cases involving bullet wounds, blunt trauma, and vehicular injuries), radiation, heat, cold, and noise. Epidemiologists now are studying the extent to which **social and psychologic stressors** can be considered agents in the production of health problems.

The **environment** influences the probability and circumstances of contact between the host and the agent. Poor restaurant sanitation increases the probability of patrons being exposed to *Salmonella* infections. Poor roads and bad weather conditions increase the number of automobile collisions and airplane crashes. The environment also includes social, political, and economic factors: Crowded homes and schools make exposure to infectious diseases more likely, and the political structure and economic health of a society influence the nutritional and vaccine status of the members of that society.

Vectors of disease commonly include insects (e.g., mosquitoes associated with the spread of malaria), arthropods (e.g., ticks associated with Lyme disease), and animals (e.g., raccoons associated with rabies in the eastern US). The concept of the *vector* can be applied more widely, however, to include groups of human beings (e.g., vendors of heroin and cocaine) and even objects (e.g., contaminated needles associated with hepatitis and AIDS). A vector may be considered part of the environment, or it may be treated separately (see Fig. 1-1). To be an effective transmitter of disease, the vector must have a specific relationship to the agent, the environment, and the host.

In the case of human malaria, mentioned briefly earlier, the vector is a mosquito of the genus *Anopheles*, the agent is a parasitic organism of the genus *Plasmodium*, the host is a human being, and the environment enables the mosquito to breed and to come into contact with the host. Specifically, the parasitic organism must go through part of its life cycle in the mosquito; the climate must be relatively warm and have standing water in which the mosquito can breed; the mosquito must bite humans and must be able to spread the disease; the host must be bitten by an infected mosquito (in the case of malaria, usually the biting occurs in houses at night, where sleeping people lack screens and mosquito nets); and the host must be susceptible to the disease.

Risk factors and preventable causes of disease, particularly life-threatening diseases such as cancer, have been the subject of much epidemiologic research. In 1964, an expert committee of the World Health Organization (WHO) estimated that "the majority" of cancer cases were potentially preventable and were due to "extrinsic factors." In the same year, the US Surgeon General released a report that indicated the risk of death from lung cancer among smokers was almost 11 times that among nonsmokers.[2] Doll and Peto[3] praised the 1964 WHO report on causes of cancer and made the following argument:

> In the years since that report was published, advances in knowledge have consolidated these opinions and few if any competent research workers now question its main conclusion. Individuals, indeed, have gone further and have substituted figures of 80% or even 90% as the proportion of potentially preventable cancers in place of the 1964 committee's cautious estimate of "the majority." Unfortunately, the phrase "extrinsic factors" (or the phrase "environmental factors," which is often substituted for it) has been misinterpreted by many people to mean only "man-made chemicals," which was certainly not the intent of the WHO committee. The committee included, in addition to man-made or natural carcinogens, viral infections, nutritional deficiencies or excesses, reproductive activities, and a variety of other factors determined wholly or partly by personal behavior.

The aforementioned conclusions are based on research from a variety of epidemiologic methods. Given the many different cell types of cancer, and the fact that there are many causal factors to be considered, how do epidemiologists estimate the percentage of deaths caused by preventable risk factors? One method looks at each type of cancer and determines

(from epidemiologic studies) the percentage of individuals with a specific type of cancer who have identifiable, preventable causes of that cancer. These percentages are added up in a weighted manner to determine the total percentage of all cancers having identifiable causes.

In the second method, annual age-specific and sex-specific cancer incidence rates are used from countries that have the lowest rates of a given cell type of cancer and have good disease detection. For a particular cell type of cancer, the low rate in such a country presumably is due to a low prevalence of the risk factors for that type of cancer. Researchers calculate the number of cases of each type of cancer that would be expected to occur annually in each age and gender group in the US, if these lowest observed rates had been true for the US population. Next, they add up the expected numbers for the various cancer types in the US. Finally, they compare this total number of expected cases with the total number of cases diagnosed in the US population. Using these methods, epidemiologists have estimated that the US has about five times as many total cancer cases as would be expected, based on the lowest rates in the world. Presumably, the excess cancer cases in the US are due to the prevalence of risk factors for cancer, such as smoking.

Risk Factors for Disease: BEINGS Model

The acronym **"BEINGS"** serves as a helpful device for remembering the major categories of risk factors for disease. Some of these factors, which are listed in Table 1-1 and discussed subsequently, are easier to change or eliminate than others. Currently, genetic factors are among the most difficult to change, although this field is rapidly developing and becoming more important to epidemiology and prevention. Immunologic factors are usually the easiest to change, if effective vaccines are available.

"B"—Biologic Factors and Behavioral Factors

The risk for particular diseases may be influenced by gender, age, weight, bone density, and numerous other biologic factors. In addition, human behavior is a central factor in health and disease. Smoking is an obvious example of a behavioral risk factor. It contributes to a variety of health problems, including myocardial infarction; lung, esophageal, and nasopharyngeal cancer; and chronic obstructive pulmonary disease. Cigarettes seem to be responsible for about 50% of the cases of myocardial infarction among smokers and about 90% of the cases of lung cancer. Because there is a much higher probability of myocardial infarction than of lung cancer, cigarettes actually cause more cases of myocardial infarction than lung cancer.

Attention increasingly is being focused on the rapid increase of overweight and obesity in the US over the past 1 to 2 decades. There is considerable debate about the number of deaths per year in the US that can be attributed to overweight and obesity. In 2004, Centers for Disease Control and Prevention (CDC) investigators estimated that 400,000 deaths were due to obesity and its major risk factors, inactivity and diet.[4] In 2005, using newer survey data and controlling for more potential confounders, other CDC investigators estimated that the number of deaths attributable to obesity and its risk factors was only 112,000.[5] Regardless, increasing obesity is found in all parts of the world and is part of a cultural transition related to the increased availability of calorie-dense foods and a simultaneous decline in physical activity, resulting in part from television and computer-related activities.[6] Obesity and overweight have negative health effects, particularly reducing the age of onset of, and increasing the prevalence of, type 2 diabetes. Obesity soon may become the leading cause of premature death in the US.

Multiple behavioral factors are associated with the spread of some diseases. In the case of AIDS, the spread of human immunodeficiency virus (HIV) can result from male homosexual activity and from intravenous drug abuse, which are the two predominant routes of transmission in the US. It also can result from heterosexual activity, which is the predominant route of spread in Africa and many other countries. Other examples of behavior that can lead to disease, injury, or premature death (i.e., death before the age of 65 years) are excessive intake of alcohol, abuse of illegal drugs, driving while intoxicated, and homicide and suicide attempts. In each of these cases, as in cigarette smoking and HIV-1 infection, changes in behavior could prevent the untoward outcomes. Many of the efforts in health promotion depend heavily on the modification of human behavior, which is discussed in detail in Chapter 15.

"E"—Environmental Factors

Epidemiologic studies were done during the outbreak of severe pneumonia among individuals attending a 1976 American Legion conference in Philadelphia. The studies suggested that the epidemic was caused by an infectious agent distributed through the air-conditioning and ventilation systems of the primary hotels hosting the conference. Only later, after *Legionella pneumophila* was identified, was the discovery made that this small bacterium thrives in air-conditioning cooling towers and in warm water systems. It also has been shown that respiratory therapy equipment that is merely rinsed with

Table 1–1 Beings: An Acronym for Remembering the Categories of Preventable Cause of Disease

Biologic factors and **B**ehavioral factors
Environmental factors
Immunological factors
Nutritional factors
Genetic factors
Services, **S**ocial factors, and Spiritual factors

water can become a reservoir for *Legionella*, causing hospital-acquired legionnaires' disease.

Early epidemiologic research concerning an illness that was first reported in 1975 in Old Lyme, Connecticut, suggested that the arthritis, rash, and other symptoms of the illness were caused by infection with an organism transmitted by a tick. This was enough information to enable preventive methods to be started. By 1977, it was clear that the disease, called Lyme disease, was spread by *Ixodes* ticks, and this opened the way for more specific prevention and research. Not until 1982, however, was the causative agent, *Borrelia burgdorferi*, discovered and shown to be spread by the *Ixodes* tick.

Epidemiologists frequently are called on to be the first professionals to respond to an apparent outbreak of new health problems, such as legionnaires' disease and Lyme disease. In their investigation, they describe the patterns of the disease in the affected population, develop and test hypotheses about causal factors, and introduce methods to prevent further cases of disease. The standard approach to investigating an epidemic is found in Chapter 3.

"I"—Immunologic Factors

Smallpox is the first infectious disease known to have been eradicated from the globe (although samples of the causative virus remain stored in laboratories in the US and Russia). Smallpox eradication was possible because vaccination against the disease conferred individual immunity and produced herd immunity. **Herd immunity** results when a vaccine reduces an immunized person's ability to spread a disease, leading to reduced disease transmission.

Most people now think of AIDS when they hear of a deficiency of the immune system, but **immunodeficiency** also may be caused by genetic abnormalities or by other factors. Transient immune deficiency has been noted after some infections (e.g., measles) and after the administration of certain vaccines (e.g., live measles vaccine). This is potentially serious in malnourished children. The use of cancer chemotherapy and the long-term use of corticosteroids produce immunodeficiency, which often may be severe.

"N"—Nutritional Factors

In the 1950s, it was shown that Japanese-Americans living in Hawaii had a much higher rate of myocardial infarction than did people of the same age and sex in Japan, and Japanese-Americans in California had a still higher rate of this disease compared with similar individuals in Japan.[7-9] The investigators believed that dietary differences were the most important factors producing the differences in disease rates, and their beliefs generally have been supported by subsequent research.

Before his death, Denis Burkitt, the physician after whom Burkitt lymphoma was named, spent many years doing epidemiologic research on the critical role that dietary fiber plays in good health. From his cross-cultural studies, he made some stunning statements, including the following:[10]

"By world standards, the entire United States is constipated."
"Don't diagnose appendicitis in Africa unless the patient speaks English."
"African medical students go through five years of training without seeing coronary heart disease or appendicitis."
"Populations with large stools have small hospitals. Those with small stools have large hospitals."

Based on cross-cultural studies, Burkitt observed that many of the diseases commonly seen in the US were rarely encountered in indigenous populations of tropical Africa (Table 1-2). This observation was true even of areas with good medical care, such as Kampala, Uganda, at the time Burkitt was there—a fact indicating that these diseases were not being missed because of lack of diagnosis. These differences were not primarily genetic in origin because African-Americans in the US experience these diseases at roughly the same rate as other groups in the US. The cross-cultural differences suggest that the current heavy burden of these diseases in the US is *not* inevitable. Burkitt suggested mechanisms by which a high intake of dietary fiber might prevent these diseases or markedly reduce their incidence.

"G"—Genetic Factors

It is well established that the genetic inheritance of individuals interacts with diet and environment in complex ways to promote or protect against a variety of illnesses, including heart disease and cancer. Genetic epidemiology is a growing field of research. Population genetics and genetic epidemiology are concerned with, among other things, the distribution of normal and abnormal genes in the population and whether or not these are in equilibrium. According to experts, population gene frequencies seem to be stable. Genetic epidemiology also is concerned with gene mutation rates, which do not seem to be changing.

Table 1–2 Diseases That Have Been Rare in the Indigenous Populations of Tropical Africa

Appendicitis
Breast cancer
Colon cancer
Coronary heart disease
Diabetes mellitus
Diverticulitis
Gallstones
Hemorrhoids
Hiatal hernia
Varicose veins

Data from Burkitt D. Lecture at Yale University School of Medicine, New Haven, Conn, April 28, 1989.

Considerable research involves studying the possible interaction of various genotypes with environmental, nutritional, and behavioral factors and pharmaceutical treatments. Ongoing research concerns the extent to which environmental adaptations can reduce the burden of diseases with a heavy genetic component.

Genetic disease now accounts for a higher proportion of disease than in the past, not because the incidence of genetic disease is increasing, but because the incidence of noninherited disease is decreasing. This point is illustrated by Scriver:[11]

> Heritability refers to ... the contribution of genes relative to all determinants of disease. Rickets, a genetic disease, recently showed an abrupt fall in incidence and an increase in heritability in Quebec. The fall in incidence followed universal supplementation of dairy milk with calciferol. The rise in heritability reflected the disappearance of a major environmental cause of rickets (vitamin D deficiency) and the persistence of Mendelian disorders of calcium and phosphate homeostasis without a change in their incidence.

Genetic screening is important for identifying problems in newborns, such as phenylketonuria and congenital hypothyroidism, for which therapy can be extremely beneficial if instituted early enough in life. Screening also is important for identifying other genetic disorders for which genetic counseling can be beneficial. In the future, the most important health benefits from genetics may come from the identification of individuals at high risk for specific problems or who would respond particularly well (or poorly) to specific drugs. Examples might include individuals at high risk for myocardial infarction; breast or ovarian cancer (*BrCA1* and *BrCA2* genes); environmental asthma; or reactions to certain foods, medicines, or behaviors. Screening for "susceptibility genes" undoubtedly will increase in the future, but there are ethical concerns about potential problems, such as medical insurance carriers hesitating to insure individuals with known genetic risks. For more on the prevention of genetic disease, see Section 3, particularly Chapter 19.

"S"—Services, Social Factors, and Spiritual Factors

Medical care services may be quite beneficial to health, but they also can be dangerous. One of the important tasks of epidemiologists is to determine the value and hazards of medical care in different settings. An Institute of Medicine report estimated that 2.9% to 3.7% of hospitalized patients experience "adverse events" during their hospitalization. Of these, about 19% are due to medication errors, and 14% are due to wound infections.[12] Based on the 3.6 million hospital admissions in a 1997 study, the Institute of Medicine study estimated that there were about 44,000 deaths each year secondary to medical errors in hospital. Other medical care-related causes of illness include unnecessary or inappropriate diagnostic or surgical procedures.

The effects of **social and spiritual factors** on disease and health have been less intensively studied than have the effects of other causal factors. Evidence is accumulating, however, that personal beliefs concerning the meaning and purpose of life, access to forgiveness, and the support received from members of a social network are powerful influences on health. Studies have shown that experimental animals and humans are better able to resist noxious stressors when they are with other members of the same species. Social support may be achieved through the family, friendship networks, and membership in various groups, such as clubs and churches. One study reviewed the literature concerning the association of religious faith with generally better health and found that strong religious faith was associated with better health and quality of life.[13] In AIDS patients, spiritual interventions may be more effective if they are combined with other types of treatment.[14]

Many investigators have explored factors related to health and disease in Mormons and Seventh-Day Adventists. Both of these religious groups have lower than average age-adjusted death rates from many common types of disease and specifically from heart disease, cancer, and respiratory disorders. Part of their protection undoubtedly arises from the behaviors proscribed or prescribed by the groups. Mormons prohibit the use of alcohol and tobacco. Seventh-Day Adventists likewise tend to avoid alcohol and tobacco, and they strongly encourage (but do not require) their members to eat a vegetarian diet. It is unclear, however, that these behaviors are solely responsible for the health differences: "It is difficult ... to separate the effects of health practices from other aspects of lifestyle common among those belonging to such religions, for example, differing social stresses and network systems."[15] In an earlier study, Berkman and Syme showed that for all age groups, the greater one's participation in churches and other groups and the stronger one's social networks, the lower the mortality that was observed.[16]

The work of the psychiatrist Frankl also documented the importance of a person's having a meaning and purpose in life, which can alleviate stress and improve coping.[17] Such factors are increasingly being studied as important in understanding the web of causation of diseases.

ECOLOGIC ISSUES IN EPIDEMIOLOGY

Classical epidemiologists have long seen their field as "human ecology," "medical ecology," or "geographic medicine" because an important characteristic of epidemiology is its **ecologic perspective**.[18] People are seen not only as individual organisms, but also as members of communities, in a social context. The world is understood as a complex ecosystem in which disease patterns vary greatly from one country to another. The types and rates of diseases in a country are a kind of "fingerprint" that indicates the standard of living, the lifestyle, the predominant occupations, and the climate, among other things. Owing to the tremendous growth in world population (>6 billion in 2005)