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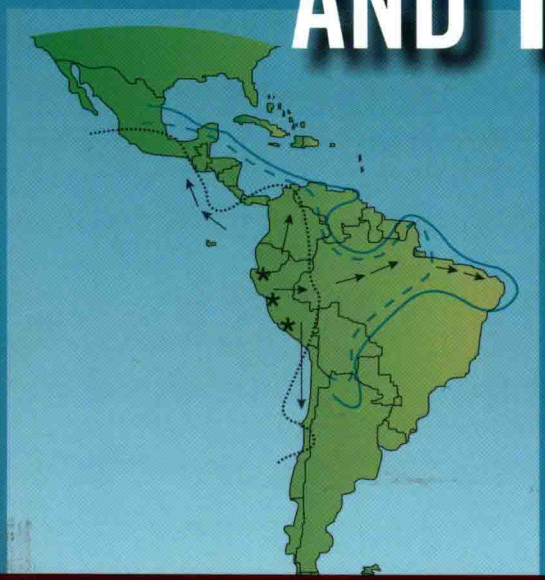
JEKEL'S EPIDEMIOLOGY, BIOSTATISTICS, PREVENTIVE MEDICINE, AND PUBLIC HEALTH



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FOURTH EDITION

Jekel's Epidemiology, Biostatistics, Preventive Medicine, and Public Health

Fourth Edition

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JEKEL'S EPIDEMIOLOGY, BIOSTATISTICS, PREVENTIVE MEDICINE AND PUBLIC HEALTH

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I acknowledge the important influence students have had in shaping our text and the meticulous and valuable editorial assistance that Raymond Harris, PhD, provided on the epidemiology chapters for this fourth edition. I personally thank my son, Nicholas R. Ransom, for his support and patience during the preparation of each new edition of this text. —*JE*

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Preface

We are very pleased and proud to bring you this fourth edition of what proved to be in earlier editions a best-selling title in its content area of epidemiology, biostatistics, and preventive medicine. We are, as well, a bit nervous about our efforts to honor that pedigree because this is the first edition not directly overseen by Dr. James Jekel, who set this whole enterprise in motion almost 20 years ago. We hasten to note that Dr. Jekel is perfectly well and was available to help us out as the need occasionally arose. But after some years of a declared retirement that looked like more than a full-time job for any reasonable person, Jim has finally applied his legendary good sense to himself and is spending well-earned time in true retirement with his large extended family. A mentor to several of us, Jim remains an important presence in this edition, both by virtue of the content that is preserved from earlier editions, and by virtue of the education he provided us. When the book is at its best, we gratefully acknowledge Dr. Jekel's influence. If ever the new edition falls short of that standard, we blame ourselves. We have done our best, but the bar was set high!

To maximize our chances of clearing the bar, we have done the prudent thing and brought in reinforcements. Most notable among them is Dr. Sean Lucan, who joined us as the fourth member of the main author team. Sean brought to the project an excellent fund of knowledge, honed in particular by the Robert Wood Johnson Clinical Scholars program at the University of Pennsylvania, as well as a keen editorial eye and a sharp wit. The book is certainly the better for his involvement, and we are thankful he joined us.

Also of note are five new chapters we did not feel qualified to write, and for which we relied on guest authors who most certainly were. Their particular contributions are noted in the contents list and on the title page of the chapters in question. We are grateful to this group of experts for bringing to our readers authoritative treatment of important topics we could not have addressed half so well on our own.

Readers of prior editions, and we thank you for that brand loyalty, will note a substantial expansion from 21 chapters to 30. This was partly the result of unbundling the treatment of preventive medicine and public health into separate sections, which the depth and breadth of content seemed to require. These domains overlap substantially, but are distinct and are now handled accordingly in the book. The expansion also allowed the inclusion of important topics that were formerly neglected: from the epidemiology of mental health disorders, to disaster planning, to health care reform, to the One Health concept that highlights the indelible links among the health of people, other species, and the planet itself.

Return readers will note that some content is simply preserved. We applied the "if it ain't broke, don't fix it!" principle to our efforts. Many citations and illustrations have stood the test of time and are as informative now as they ever were. We resisted the inclination to "update" such elements simply for the sake of saying we had done so. There was plenty of content that did require updating, and readers will also note a large infusion of new figures, tables, passages, definitions, illustrations, and citations. Our hopes in this regard will be validated if the book feels entirely fresh and current and clear to new and return readers alike, yet comfortably familiar to the latter group.

Any book is subject to constraints on length and scope, and ours is no exception. There were, therefore, predictable challenges regarding inclusions and exclusions, depth versus breadth. We winced at some of the harder trade-offs and did the best we could to strike the optimal balance.

Such, then, are the intentions, motivations, and aspirations that shaped this new edition of *Epidemiology, Biostatistics, Preventive Medicine, and Public Health*. They are all now part of a process consigned to our personal histories, and the product must be judged on its merits. The verdict, of course, resides with you.

David L. Katz
for the authors

Preface to the Third Edition

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

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SECTION

Epidemiology

1

1 Basic Epidemiologic Concepts and Principles

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I. WHAT IS EPIDEMIOLOGY?

Epidemiology is usually defined as the study of factors that determine the occurrence and distribution of disease in a population. As a scientific term, epidemiology was introduced in the 19th century, derived from three Greek roots: *epi,* meaning "upon"; *demos,* "people" or "population"; and *logos,* "discussion" or "study." Epidemiology deals with much more than the study of **epidemics,** in which a disease spreads quickly or extensively, leading to more cases than normally seen.

Epidemiology can best be understood as the basic science of public health. It provides methods to study disease, injury, and clinical practice. Whereas health care practitioners collect data on a single patient, **epidemiologists** collect data on an entire population. The scientific methods used to collect such data are described in the Epidemiology section of this text, Chapters 1 to 7, and the methods used to analyze the data are reviewed in the Biostatistics section, Chapters 8 to 13.

The scientific study of disease can be approached at the following four levels:

1. Submolecular or molecular level (e.g., cell biology, genetics, biochemistry, and immunology)
2. Tissue or organ level (e.g., anatomic pathology)
3. Level of individual patients (e.g., clinical medicine)
4. Level of populations (e.g., epidemiology).

Perspectives gained from these four levels are related, so the scientific understanding of disease can be maximized by coordinating research among the various disciplines.

Some people distinguish between classical epidemiology and clinical epidemiology. **Classical epidemiology,** which is population oriented, studies the community origins of health problems, particularly those related to infectious agents; nutrition; the environment; human behavior; and the psychological, social, economic, 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 similar to those used by classical epidemiologists. However, clinical epidemiologists study patients in health care settings rather than in the community at large. Their goal is to improve the prevention, early detection, diagnosis, treatment, prognosis, and care of illness in individual patients who are at risk for, or already affected by, specific diseases.[1]

Many illustrations from classical epidemiology concern infectious diseases, because these were the original impetus for the development of epidemiology and have often been its focus. Nevertheless, classical methods of surveillance and outbreak investigation remain relevant even for such contemporary concerns as **bioterrorism**, undergoing modification as they are marshaled against new challenges. One example of such an adapted approach is **syndromic epidemiology,** in which epidemiologists look for patterns of signs and symptoms that might indicate an origin in bioterrorism.

Epidemiology can also 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), whereas chronic disease epidemiology has depended on complex sampling and statistical methods. However, this distinction is becoming less significant with the increasing use of molecular laboratory markers (genetic and other) in chronic disease epidemiology and complex

statistical analyses in infectious disease epidemiology. Many illnesses, including tuberculosis and acquired immunodeficiency syndrome (AIDS), may be regarded as both infectious and chronic.

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

II. ETIOLOGY AND NATURAL HISTORY OF DISEASE

The term **etiology** is defined as the cause or origin of a disease or abnormal condition. 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.

A. Stages of Disease

The development and expression of a disease occur over time and can be divided into three stages: predisease, latent, and symptomatic. During the **predisease stage,** before the disease process begins, early intervention may avert exposure to the agent of disease (e.g., lead, *trans*-fatty acids, microbes), preventing the disease process from starting; this is called **primary prevention.** During the **latent stage,** when the disease process has already begun but is still asymptomatic, screening for the disease and providing 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 Chapters 15 to 17.

B. Mechanisms and Causes of Disease

When discussing the etiology of disease, epidemiologists distinguish between the **biologic mechanisms** and the **social, behavioral, and environmental causes** of disease. For example, *osteomalacia* is a bone disease that may have both social and biologic causes. Osteomalacia is a weakening of the bone, often through a deficiency of vitamin D. According to 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, or by wearing clothing that covers virtually all of the body when they go outdoors. Because these practices block the action of the sun on bare skin, they prevent the irradiation of ergosterol in the skin. However, irradiated ergosterol is an important source of D vitamins, which are necessary for growth. If a woman's diet is also deficient in vitamin D during the rapid growth period of puberty, she may develop osteomalacia as a result of insufficient calcium absorption. Osteomalacia can adversely 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, which may ultimately lead to maternal and infant mortality.

Likewise, excessive fat intake, smoking, and lack of exercise are behavioral factors that contribute to the biologic mechanisms of *atherogenesis,* such as elevated blood levels of low-density lipoprotein (LDL) cholesterol or reduced blood levels of high-density lipoprotein (HDL) cholesterol. These behavioral risk factors may have different effects, depending on the genetic pattern of each individual and the interaction of genes with the environment and other risk factors.

Epidemiologists attempt to go as far back as possible to discover the social and behavioral 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.

C. Host, Agent, Environment, and Vector

The causes of a disease are often considered in terms of a triad of factors: the host, the agent, and the environment. For many diseases, it is also useful to add a fourth factor, the vector (Fig. 1-1). In measles, the *host* is a human who is susceptible to measles infection, the *agent* is a highly infectious virus that can produce serious disease in humans, and the *environment* is a population of unvaccinated individuals, which enables unvaccinated susceptible individuals to be exposed to others who are infectious. The *vector* in this case is relatively unimportant. In malaria, however, the host, agent, and environment are all significant, but the vector, the *Anopheles* mosquito, assumes paramount importance in the spread of disease.

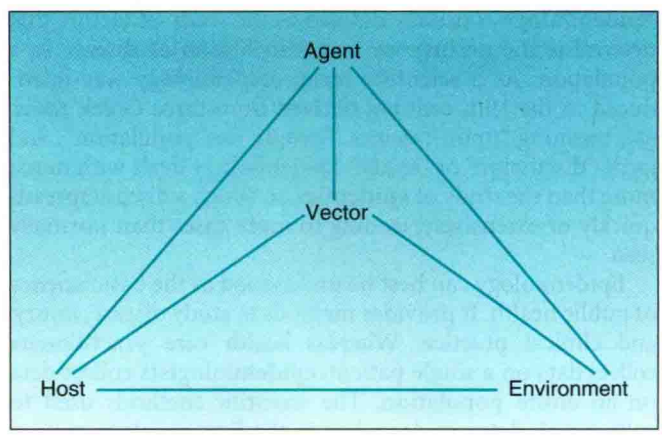

Figure 1-1 Factors involved in natural history of disease.

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 (e.g., compromised immunity reduces 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, viruses), biologic toxins (e.g., botulinum toxin), and foods (e.g., 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., involving bullet wounds, blunt trauma, and crash injuries), radiation, heat, cold, and noise. Epidemiologists now are studying the extent to which **social and psychological stressors** can be considered agents in the development of health problems.

The **environment** influences the probability and circumstances of contact between the host and the agent. Poor restaurant sanitation increases the probability that patrons will be exposed to *Salmonella* infections. Poor roads and adverse 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 its members.

Vectors of disease include insects (e.g., mosquitoes associated with spread of malaria), arachnids (e.g., ticks associated with Lyme disease), and mammals (e.g., raccoons associated with rabies in eastern U.S.). The concept of the *vector* can be applied more widely, however, to include human groups (e.g., vendors of heroin, cocaine, and methamphetamine) and even inanimate objects that serve as vehicles to transmit disease (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, the vector is a mosquito of the genus *Anopheles,* the agent is a parasitic organism of the genus *Plasmodium,* the host is a human, and the environment includes standing water that enables the mosquito to breed and to come into contact with the host. Specifically, the plasmodium must complete part of its life cycle within the mosquito; the climate must be relatively warm and provide a wet environment in which the mosquito can breed; the mosquito must have the opportunity to bite humans (usually at night, in houses where sleeping people lack screens and mosquito nets) and thereby spread the disease; the host must be bitten by an infected mosquito; and the host must be susceptible to the disease.

D. Risk Factors and Preventable Causes

Risk factors for disease and preventable causes of disease, particularly life-threatening diseases such as cancer, have been the subject of much epidemiologic research. In 1964 a World Health Organization (WHO) expert committee estimated that the *majority* of cancer cases were potentially preventable and were caused by "extrinsic factors." Also that year, the U.S. Surgeon General released a report indicating that the risk of death from lung cancer in smokers was almost 11 times that in nonsmokers.[2]

Advances in knowledge have consolidated the WHO findings to the point where few, if any, researchers now question its main conclusion.[3] Indeed, some have gone further, substituting figures of 80% or even 90% as the proportion of potentially preventable cancers, in place of WHO's more cautious estimate of the "majority." Unfortunately, the phrase "extrinsic factors" (or its near-synonym, "environmental factors") has often been misinterpreted to mean only man-made chemicals, which was certainly not the intent of the WHO committee. In addition to man-made or naturally occurring carcinogens, the 1964 report included viral infections, nutritional deficiencies or excesses, reproductive activities, and a variety of other factors determined "wholly or partly by personal behavior."

The WHO conclusions are based on research using a variety of epidemiologic methods. Given the many different types of cancer cells, and the large number of causal factors to be considered, how do epidemiologists estimate the percentage of deaths caused by preventable risk factors in a country such as the United States?

One method looks at each type of cancer and determines (from epidemiologic studies) the percentage of individuals in the country 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.

A second method examines annual age-specific and gender-specific cancer incidence rates in countries that have the lowest rates of a given type of cancer and maintain an effective infrastructure for disease detection. For a particular cancer type, the low rate in such a country presumably results from a low prevalence of the risk factors for that 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 United States, if the lowest observed rates had been true for the U.S. population. Next, they add up the expected numbers for the various cancer types in the U.S. They then compare the total number of expected cases with the total number of cases actually diagnosed in the U.S. population. Using these methods, epidemiologists have estimated that the U.S. 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 U.S. are caused by the prevalence of risk factors for cancer, such as smoking.

I. BEINGS Model

The acronym **BEINGS** can serve as a mnemonic device for the major categories of risk factors for disease, some of which are easier to change or eliminate than others (Box 1-1). Currently, genetic factors are among the most difficult

Box 1-1 BEINGS Acronym for Categories of Preventable Cause of Disease

Biologic factors and Behavioral factors
Environmental factors
Immunologic factors
Nutritional factors
Genetic factors
Services, Social factors, and Spiritual factors

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 AND BEHAVIORAL FACTORS

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

Increasing attention has focused on the rapid increase in *overweight* and *obesity* in the U.S. population over the past two decades. The number of deaths per year that can be attributed to these factors is controversial. In 2004 the U.S. Centers for Disease Control and Prevention (CDC) estimated that 400,000 deaths annually were caused by obesity and its major risk factors, *inactivity* and an *unhealthy 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 rates of obesity are found worldwide as 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 mechanized transportation and sedentary lifestyles.[6-11]

Obesity and overweight have negative health effects, particularly by reducing the age at onset of, and increasing the prevalence of, *type 2 diabetes.* Obesity is established as a major contributor to premature death in the United States,[12,13] although the exact magnitude of the association remains controversial, resulting in part from the complexities of the causal pathway involved (i.e., obesity leads to death indirectly, by contributing to the development of chronic disease).

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 unprotected sexual intercourse between men and from shared syringes among intravenous drug users, which are the two predominant routes of transmission in the United States. HIV infection can also result from unprotected vaginal intercourse, which is the predominant transmission route in Africa and other parts of the world. Other behaviors that can lead to disease, injury, or premature death (before age 65) are excessive intake of alcohol, abuse of both legal and illegal drugs, driving while intoxicated, and homicide and suicide attempts. In each of these cases, as in cigarette smoking and HIV infection, changes in behavior could prevent the untoward outcomes. Many efforts in health promotion depend heavily on modifying human behavior, as discussed in Chapter 15.

"E"—ENVIRONMENTAL FACTORS

Epidemiologists are frequently the first professionals to respond to an apparent outbreak of new health problems, such as *legionnaires' disease* and *Lyme disease,* which involve important environmental factors. In their investigations, epidemiologists 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. Chapter 3 describes the standard approach to investigating an epidemic.

During an outbreak of severe pneumonia among individuals attending a 1976 American Legion conference in Philadelphia, epidemiologists conducted studies suggesting that the epidemic was caused by an infectious agent distributed through the air-conditioning and ventilation systems of the primary conference hotels. Only later, after the identification of *Legionella pneumophila*, was it discovered that this small bacterium thrives in air-conditioning cooling towers and warm-water systems. It was also shown that respiratory therapy equipment that is merely rinsed with water can become a reservoir for *Legionella*, causing hospital-acquired legionnaires' disease.

An illness first reported in 1975 in Old Lyme, Connecticut, was the subject of epidemiologic research suggesting 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 measures to begin. By 1977 it was clear that the disease, then known as Lyme disease, was spread by *Ixodes* ticks, opening 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.

"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 U.S. and Russian laboratories). Smallpox eradication was possible because vaccination against the disease conferred individual immunity and produced herd immunity. **Herd immunity** results when a vaccine diminishes 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 and 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 result is potentially serious in malnourished children. The use of

cancer chemotherapy and the long-term use of corticosteroids also produce immunodeficiency, which may often be severe.

"N"—NUTRITIONAL FACTORS

In the 1950s it was shown that Japanese Americans living in Hawaii had a much higher rate of MI than people of the same age and gender in Japan, while Japanese Americans in California had a still higher rate of MI than similar individuals in Japan.[14-16] The investigators believed that dietary variations were the most important factors producing these differences in disease rates, as generally supported by subsequent research. The Japanese eat more fish, vegetables, and fruit in smaller portions.

Denis Burkitt, the physician after whom Burkitt's lymphoma was named, spent many years doing epidemiologic research on the critical role played by dietary fiber in good health. From his cross-cultural studies, he made some stunning statements, including the following[17]:

"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 United States, such as diabetes and hypertension, were rarely encountered in indigenous populations of tropical Africa (Box 1-2). This observation was true even of areas with good medical care, such as Kampala, Uganda, when Burkitt was there, indicating that such diseases were not being missed because of lack of diagnosis. These differences could not be primarily genetic in origin because African Americans in the United States experience these diseases at about the same rate as other U.S. groups. Cross-cultural differences suggest that the current heavy burden of these diseases in the United States is *not* inevitable. Burkitt suggested mechanisms by which a high intake of dietary fiber might prevent these diseases or greatly 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. As a result, **genetic epidemiology** is a growing field of research that addresses, among other things, the distribution of normal and abnormal genes in a population, and whether or not these are in equilibrium. Considerable research examines the possible interaction of various genotypes with environmental, nutritional, and behavioral factors, as well as with 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 illness than in the past, not because the incidence of genetic disease is increasing, but because the incidence of noninherited disease is decreasing and our ability to identify genetic diseases has improved. Scriver[18] illustrates this point as follows:

> 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 any 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. Screening is also important for identifying other genetic disorders for which counseling can be beneficial. In the future, the most important health benefits from genetics may come from identifying individuals who are 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 MI; breast or ovarian cancer (e.g., carriers of *BRCA1* and *BRCA2* genetic mutations); 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 20.

"S"—SERVICES, SOCIAL FACTORS, AND SPIRITUAL FACTORS

Medical care services may be beneficial to health but also can be dangerous. One of the important tasks of epidemiologists is to determine the benefits and hazards of medical care in different settings. **Iatrogenic disease** occurs when a disease is induced inadvertently by treatment or during a diagnostic procedure. A U.S. Institute of Medicine report estimated that 2.9% to 3.7% of hospitalized patients experience "adverse events" during their hospitalization. Of these events, about 19% are caused by medication errors and 14% by wound infections.[19] Based on 3.6 million hospital admissions cited in a 1997 study, this report estimated that about 44,000 deaths each year are associated with medical errors in hospital. Other medical care–related causes of illness include unnecessary or inappropriate diagnostic or surgical

Box 1-2 Diseases that Have Been Rare in Indigenous Populations of Tropical Africa

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

Data from Burkitt D: Lecture, Yale University School of Medicine, 1989.