Foundations of Epidemiology

SECOND EDITION

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Preface

The purpose of this book is to present the concepts and methods of epidemiology as they are applied to a variety of disease problems. The broad scope of epidemiology is liberally illustrated with studies of specific diseases. Emphasis is placed on the integration of biological and statistical elements in the sequence of epidemiologic reasoning that derives inferences about the etiology of disease from population data. The epidemiologist's role in integrating knowledge obtained from a variety of scientific disciplines is described.

A knowledge of biostatistics is indispensable in the conduct of epidemiologic studies and the analysis of their results. This information can be found in many textbooks of biostatistics. To provide the minimal background necessary for understanding the epidemiologic methods that are discussed, however, we have added a new appendix of selected statistical procedures used frequently by epidemiologists.

This book has been designed as a text for introductory courses in epidemiology wherever they are offered. Thus, it can be used in schools of medicine, public health, allied health sciences, dentistry, nursing, and veterinary medicine, as well as in environmental health sciences and other programs offered by colleges of arts and sciences.

The text can be divided into four parts. Chapters 1 to 3 review the historical background and conceptual basis of epidemiology. Chapters 4 to 7 discuss demographic studies, including mortality and morbidity, and their application to epidemiologic problems.

The next four chapters, 8 to 11, consider the epidemiologic study, both observational and experimental. The last chapter illustrates the ways and means by which the types of data obtained from the various studies are integrated into a conceptual whole and focused on the derivation of biologic inferences.

Though several changes have been made in this edition, the book's structure remains basically the same. Many chapters have been extensively revised to include findings from recent epidemiologic studies. These chapters have been expanded, using many new examples from a greater variety of epidemiologic problems. New chapters on clinical and community trials have been added to strengthen the discussion of experimental epidemiology. The chapter on theoretical epidemiology has been modified and placed in an appendix.

To enhance the teaching value of the book, sets of study problems have been added to all appropriate chapters. These problems are not limited to reviewing topics discussed in the same chapter in which they appear. Rather, they cumulatively review material from preceding chapters, helping readers to integrate this material. The problems give students an opportunity to apply the method, and reasoning patterns that constitute epidemiology. Some of them invite broad consideration of various epidemiologic issues and viewpoints.

Some Comments on Terminology. The terms we have used to describe the different types of demographic and epidemiologic studies and their resultant measures are unchanged from those of the previous edition. During the past several years, however, the number of terms in use has proliferated considerably, causing much confusion, particularly to students. To remedy this problem, several committees have been constituted in an attempt to standardize epidemiologic terminology.

Here we should like to list some synonyms for several of the more frequently used terms; others are noted in the text. This list is by no means complete:

1. *Retrospective studies,* in addition to being called "case-control" studies, are also referred to as "case-referrent" studies.
2. *Prospective studies* are also termed "longitudinal" studies, as well as "cohort" studies. What we call "non-concurrent prospective" studies are also referred to as "historical cohort,"

"retrospective cohort," "retrospective longitudinal" and "historical prospective" studies.

3. *Relative risk* is also termed the "risk ratio."
4. *Attributable risk,* as it is used in the book, is sometimes called "population attributable risk."

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A.M.L.

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D.E.L.

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Contents

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1 Laying the Foundations: The Epidemiologic Approach to Disease

Epidemiology is concerned with the patterns of disease occurrence in human populations and of the factors that influence these patterns. The epidemiologist is primarily interested in the occurrence of disease by time, place, and persons. He tries to determine whether there has been an increase or decrease of the disease over the years; whether one geographical area has a higher frequency of the disease than another; and whether the characteristics of persons with a particular disease or condition distinguish them from those without it.

The personal characteristics with which the epidemiologist is concerned are the following:

1. Demographic characteristics such as age, sex, color, ethnic group.
2. Biological characteristics such as blood levels of antibodies, chemicals, enzymes; cellular constituents of the blood; measurements of physiological function of different organ systems of the body.
3. Social and economic factors such as socioeconomic status, educational background, occupation, nativity.
4. Personal habits such as tobacco and drug use, diet, physical exercise.
5. Genetic characteristics such as blood groups.

These areas of endeavor are well described by Hirsch's definition of historical and geographical pathology as a

> science which . . . will give, firstly, a picture of the occurrence, the distribution and the types of the diseases of mankind, in distinct epochs of time and at various points of the earth's surface; and secondly, will render an account of the relations of these diseases to the external conditions surrounding the individual and determining his manner of life. (12, 14)

This statement has commonly served as a base for defining epidemiology as "the study of the distribution of a disease or a physiological condition in human populations and of the factors that influence this distribution" (16). A more inclusive description was given by Wade Hampton Frost, one of the architects of modern epidemiology, who noted that "epidemiology is essentially an inductive science, concerned not merely with describing the distribution of disease, but equally or more with fitting it into a consistent philosophy" (12). Thus, epidemiology can be regarded as a sequence of reasoning concerned with biological inferences derived from observations of disease occurrence and related phenomena in human population groups. To this we can add that epidemiology is an integrative, eclectic discipline deriving concepts and methods from other disciplines, such as statistics, sociology, and biology, for the study of disease in populations.

A. GENERAL PURPOSES OF EPIDEMIOLOGIC STUDIES

The information obtained from an epidemiologic study can be utilized in several ways:

1. To elucidate the etiology of a specific disease or group of diseases by combining epidemiologic data with information from other disciplines such as genetics, biochemistry, and microbiology.
2. To evaluate the consistency of epidemiologic data with etiological hypotheses developed either clinically (at the bedside) or experimentally (in the laboratory).
3. To provide the basis for developing and evaluating preventive procedures and public health practices.

Examples of each of these three general purposes will be presented.

Etiological Studies of Disease

A simple example of the use of epidemiologic data to determine etiological factors would be the investigation of an outbreak of food poisoning to determine which food was contaminated with the microorganism or chemical responsible for the epidemic. Another example would be the study of a disease that occurs with higher frequency among workers in occupations exposing them to particular chemicals, as illustrated by the study of arsenic and cancer by Mabuchi (18). In this study, lists were obtained of all men who had been employed in a pesticide plant. The workers were divided into those who had been predominantly exposed to arsenical compounds and those whose major exposure was to nonarsenical chemicals. Approximately 87 percent of 1,050 male and 67 percent of 343 female employees were traced to determine their mortality experience. The observed numbers of deaths from specific causes were then compared with those expected based on the death rates of the community in which the plant was located. A significantly larger number of deaths from lung cancer was found to have occurred in the group exposed to arsenic than would have been expected; further, this relationship between lung cancer and exposure to arsenic indicated a dose-response effect, i.e., the longer an employee was exposed to arsenical compounds, the greater was his or her chance of dying from lung cancer. The investigators concluded that a causal relationship existed between exposure to arsenical compounds and lung cancer.

Only occasionally do investigators find that the increased exposure of individuals to certain agents results in a decreased frequency of disease. A classical example of this kind of relationship is that between the presence of fluorides in the water supply and dental caries. The investigation of this relationship is worth recounting, as it illustrates in concise form how a sequence of studies can be conducted to develop a preventive measure for a disease.

By the late 1930s, it had been recognized that mottled enamel of teeth was due to the use of a water supply with a high fluoride concentration (5, 7, 8). Earlier, a practicing dentist had formed a clinical impression that persons with mottled teeth had less caries than usual (2, 21, 22). This led the Public Health Service to conduct surveys of children 12–14 years of age in thirteen cities in four states where the fluoride concentration in the water supply varied considerably (6). The results indicated that dental caries decreased

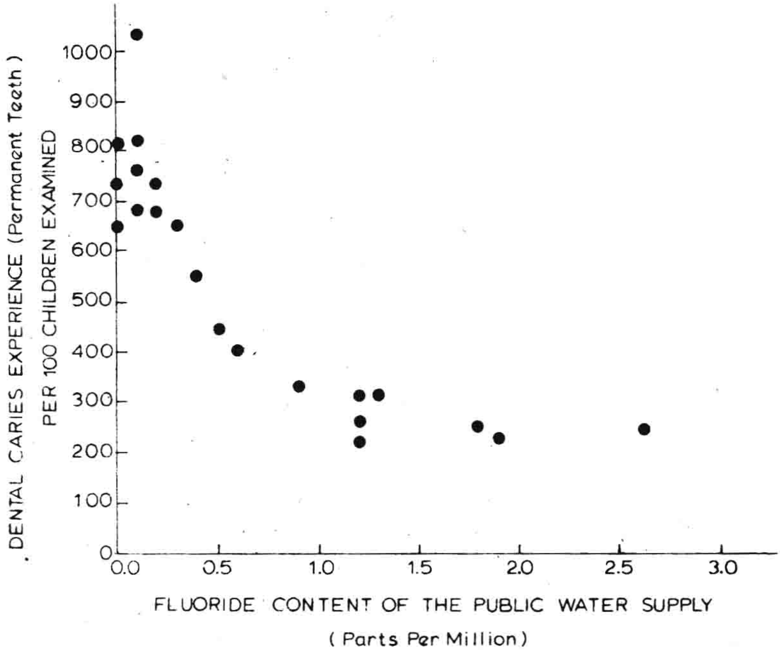

Figure 1–1. Relationship between the amount of dental caries in permanent teeth and fluoride content in the public water supply

Source: Dean, Arnold, and Elvove (6).

with increasing content of fluoride in the water, thus suggesting that the addition of fluorides to the water supply should decrease the frequency of dental caries (Fig. 1–1). This could best be demonstrated by a comparative experiment, where fluorides were added to the water supply of one community and the water supply remained untouched in a comparable community where the fluoride concentration was naturally low. The dental caries experience of school children in these communities could then be determined by periodic examinations over a number of years, and compared. Several such studies were initiated, including one comparing Kingston and Newburgh, New York (Table 1–1) (1). In the town with fluorides in the water supply, the index of dental caries (DMF) was found to be lower than in the one without fluorides. In this instance, a clinical impression led to both an epidemiologic survey and a comparative experiment, both of which demonstrated the relationship between a population characteristic, fluoride consumption, and a disease, dental caries.

Table 1–1. DMF* Teeth per 100 Children, Ages 6–16, Based on Clinical and Roentgenographic Examinations—Newburgh† and Kingston, New York, 1954–1955

Age‡	Number of Children with Permanent Teeth		Number of DMF Teeth		DMF Teeth per 100 Children with Permanent Teeth§		
	Newburgh	Kingston	Newburgh	Kingston	Newburgh	Kingston	Percent Difference K–N
6–9‖	708	913	672	2,134	98.4	233.7	—57.9
10–12	521	640	1,711	4,471	328.1	698.6	—53.0
13–14	263	441	1,579	5,161	610.1	1,170.3	—47.9
15–16	109	119	1,063	1,962	975.2	1,648.7	—40.9

* DMF includes permanent teeth decayed, missing (lost subsequent to eruption), or filled.
† Sodium fluoride was added to Newburgh's water supply beginning May 2, 1945.
‡ Age at last birthday at time of examination.
§ Adjusted to age distribution of children examined in Kingston who had permanent teeth in the 1954–1955 examination.
‖ Newburgh children of this age group were exposed to fluoridated water from the time of birth.

Source: Ast and Schlesinger (1).

Table 1–2. Oral Contraceptive Practice Among Women Aged 40–44 Years Who Died from Myocardial Infarction (MI), and Controls

Oral Contraceptive Practice	Patients with Myocardial Infarction No.	Patients with Myocardial Infarction Percent		Controls No.	Controls Percent	
Never used	78	73.6		86	84.3	
Current users (used during month before death or during same calendar period for controls)	18	17.0	28 (26.4%)	7	6.9	16 (15.7%)
Ex-users (used only more than one month before death or during same calendar period for controls)	10	9.4		9	8.8	
Total	106	100.0		102	100.0	
Not known	2			8		
Comparison between users and women not currently using oral contraceptives	$\chi^2 = 4.35$; $P < 0.05$					

Source: Mann et al. (20).

Consistency with Etiological Hypotheses

The investigator attempts to determine whether an etiological hypothesis developed clinically, experimentally, or from other epidemiologic studies is consistent with the epidemiologic characteristics of the disease in a human population group(s). Many studies of the relationship between oral contraceptive use and various forms of cardiovascular disease illustrate this approach. Over a period of years, epidemiologic studies had shown a relationship between oral contraceptive use and both venous thromboembolism and thrombotic stroke (4, 27). Soon after these studies started to appear, the first of a series of case reports associated oral contraceptive use with myocardial infarction (3). This stimulated several investigators to conduct epidemiologic studies of this issue (19, 20). The statistically significant results of one recent study by Mann, Inman, and Thorogood for women aged 40–44 who died from myocardial infarction are presented in Table 1–2 (20).