

PRINCIPLES OF FIELD STUDY OF HUMAN POPULATIONS

Introduction

The evidence thus far introduced for an interaction of nutrition and infection has derived mainly from clinical investigation, from laboratory studies, and from animal experiments. This emphasis by investigators is a natural outgrowth of the development of experimental medicine during the past half century, the improved biochemical and biophysical methods of measuring life processes, and the fact that clinical research is now solidly based on scientific principles. The original concern with an interaction between nutrition and infection, however, arose out of observations in nature of the common association of war, famine, and pestilence. The community effect is still the dominant consideration if the knowledge gained, whatever its source, is to be applied to the benefit of the public health. The evaluation of community effect requires field investigation by epidemiologic methods.

Epidemiologic field study, too, has progressed in the course of years from a descriptive to an analytical discipline, and important advances have resulted from the application of modern methods of laboratory and clinical investigation to field observations. Formerly restricted to infectious diseases transmissible from person to person, epidemiologic investigation has now extended to practically all community diseases and injuries. In this transition, nutritional disorders have had a prominent part, especially through prevalence surveys of the nutritional state of representative groups of people. Nevertheless, several aspects of the epidemiologic field study of nutrition and its relationship to infectious and other diseases still remain largely untouched. Further progress depends heavily on good field studies.

As chronic disease processes came to be viewed from an epidemiologic standpoint, the technical methods of field study naturally developed along fresh lines. An outstanding feature was recognition that the procedures so well suited to sharply marked epidemics and to acute infectious diseases that run a rapid course did not wholly suffice for chronic diseases, of which mal-

nutrition is one (Anderson, 1965). The need was for long-term prospective study, for years instead of weeks or months, if incidence were to be accurately determined and causative factors identified. That method has become an essential part of chronic-disease epidemiology, and is being applied to a variety of morbid processes.

Field Study of Human Nutrition and Nutritional Disease

Field study has a long-established place in nutritional investigations. Lind's observations (1757) on scurvy are an early example, although the "field" in this case was a ship on the high seas. Since then, changes in the nature of field studies are as many as in the other two fundamental approaches to knowledge of malnutrition: clinical investigation and laboratory experimentation.

Gordon & Le Riche (1950) distinguished three phases in the development of field work in nutrition and nutritional diseases. Initially, interest centered on food and its effect on the nutritional state of populations. The method was the dietary survey, although the procedure differed so much from present practice that it might better have been termed "food consumption survey".

Identification of specific nutrients and an improved definition of nutritional disease entities led to a second stage, the study of the prevalence of individual dietary deficiencies and specific nutritional disorders. Laboratory tests were incorporated into field practice, and clinical methods were enlarged to give more precise measurements. Field study attained a new level of importance.

The current trend expands the nutritional survey to make it the nucleus of a general health survey. The emphasis is not only on nutritional disorders and the nutritional state as such, but also on the effect exerted by nutrition on the characteristics and behavior of other community disease (Gilles, 1964). Nutrition of the host influences resistance through a variety of mechanisms. Less appreciated is the fact that other mass diseases have a decided impact on the frequency and severity of nutritional disorders.

The range of interaction becomes increasingly apparent. In dealing with nutrition and infection, this monograph touches on only one of many such relationships. Others include such diverse interactions as that between calcium deficiency and fractures in the aged (Harrison et al., 1961) and the controversial connection between nutritional factors and chronic degenerative, metabolic or neoplastic disorders, such as coronary heart disease (Miller et al., 1956), diabetes (Wilkerson & Krall, 1947), and cancer (Jolliffe, 1962).

Nutrition has thus followed the course of other scientific disciplines concerned with health. Initially, there was emphasis on its own particular problems, but later these were considered as part of the general pattern of

clinical and epidemiologic effort toward community health and welfare. In the case of nutrition (Young & Trulson, 1960), this marked a return to the objectives of the original nutrition survey, but with better methods and greater achievement (Hankin et al., 1967; Keys, 1967).

As nutritional interests expanded from clinical management of patients to prevention and control of disease in general populations, epidemiologic techniques became an integral part of practice. At first, the methods were elementary and directed to case-finding—to identifying patients with nutritional deficiencies and assuring adequate treatment. Occasional outbreaks of nutritional disease brought into play the more complicated measures needed for epidemic control (Morley, 1963). Both endeavors are essentially operational, designed to remedy an existing situation, with minor concern for cause or effect.

The enlarged scope of the nutrition survey involved determinations of prevalence, accompanied by a need to know the characteristics of host and environment that determine the origin, course, and extent of nutritional disease in population groups. The result was a descriptive epidemiology.

As activities extended to the correlation of nutritional disorders with other diseases of a population, the straightforward methods of operational and descriptive epidemiology were insufficient. Changing incidence over time, multiple environmental factors, and cultural characteristics of the human host were important variables requiring a more sophisticated epidemiology (Williams, 1964; Ramos-Galván, 1965). Hypotheses to explain the complex pattern of causality had to be recognized and defined, then tested under representative conditions, with adequate controls, using quantitative measurements. At its best, this is field research in nutrition, and the method, that of analytical epidemiology.

In many countries, the effort expended on epidemiologic investigation of nutritional health and disease now ranks closely with that devoted to communicable diseases and injuries. Field studies have also extended to primitive places, ill-defined environmental conditions, and people whose customs and habits are little known (Jyothi et al., 1963; Marsden, 1964; Pharaon et al., 1965). Such investigations are informative, since the problems of nutrition are not only universal, but often clearest in less developed areas. Epidemiologic procedures find further application in food science and food technology—for example, in establishing the value of the iodization of salt (Marine et al., 1923). The incentive to develop Incaparina (Scrimshaw et al., 1961) as a cheap protein-rich food for young children and the demonstration of its desirable characteristics came largely from field investigations.

This does not imply that reliance has to be placed mainly on field study for furthering knowledge of nutritional disorders or any group of diseases. As Winslow (1948) stated, in the laboratory all factors can be held constant except the one studied, the influence of which can thus be determined in

definite and precise fashion. But the factors kept constant in the laboratory experiment may vary critically under natural conditions. Elimination of this variability may lead to conclusions that do not correspond to actual phenomena in nature. In both the laboratory and the field, serious errors are possible unless clinical identification of the condition studied is sound. All three approaches—laboratory, clinical and field—are essential and interdependent. Emphasis in a particular investigation frequently turns from one approach to another or combines all three. Clinical investigation requires laboratory support (Todd, 1960), and laboratory experiment without the test of applicability in clinic and field (Francis et al., 1955) lacks full proof. So, too, field procedure uses laboratory and clinical facilities in the measurements made, although modifications are often necessary to fit field conditions.

These interlocking interests are the main justification for presenting here the principles of the field practice of epidemiology. Many investigators competent in clinical or laboratory research are called upon to supplement their investigations by field trial. Too often this is done without appreciation that a well-ordered experiment in the field requires the same scientific exactness and care as a clinical or laboratory investigation. The essentials are adequate controls, appropriate selection of sample, and the use of statistically significant numbers. Careful definition of criteria for recognition of observed phenomena and established methods of measurement are indispensable. Sir George Pickering, in his Harveian Oration (1964) before the Royal College of Physicians of London, characterized science as an occupation not peculiar to laboratories: "The fact is that there are some questions that can be answered only by work in the field, which includes the clinic. Because a piece of work is done in the field does not make it less scientific. Because a piece of work is done in the laboratory and with elaborate apparatus, does not make it good science."

Field studies are individually distinctive. Each has its motivation, incentives, procedures, and mode of attack. Each varies with time, place, and person. Some are associated with emergencies of short duration, the primary aim being practical control or amelioration of the situation. Others deal with persisting problems in which the need is to know origin and behavior as a means toward effective prevention. By its nature, epidemiology involves geographic pathology and is international in its interests. Sociologic and anthropologic considerations are also prominent, because so much of human disease is man-made. The three kinds of field study—operational, descriptive, and analytical—nevertheless share a common plan of action.

The Epidemiological Society of London was formed a hundred years ago, an event that conveniently marks recognition of epidemiology as a scientific discipline. The study of disease in nature is far older, for it reaches back more than two millennia to the *Airs, Waters, and Places* of Hippocrates (Adams, 1849). And yet, in 1942, the *Journal of the American Public*

Health Association asked editorially: "What and who is an epidemiologist?" The answers differed so greatly (Winslow, 1948) that the question generally remained unsettled. Indeed, much the same query was repeated by Terris (1962), and the answers were equally diverse (Payne, 1962; Schweitzer, 1963; Stallones, 1963).

An expanding field of interests within the past fifty years (Winslow et al., 1952) accounts as much as anything for the varied interpretation of the scope and content of epidemiology. The acute infectious diseases were once the sole concern. Epidemiology now includes within its sphere of interests all major community disease, notably chronic degenerative, metabolic, and neoplastic processes, nutritional deficiencies, injuries, and mental and behavioral disorders. Epidemiologic method, too, has progressed from simple observation and description to analytic procedures designed to identify through experiment (Hill, 1953) the causes of origin and behavior of community disease. These developments have resulted in complicated techniques drawing on many more scientific disciplines than just microbiology. Epidemiology today is specialized in so many directions that at times the appreciation of its fundamental characteristic comes close to being lost.

This primary attribute is the study of disease under natural conditions in which a human population is the basis for observation. Within a general population, the typical unit is a family or other group living together. Epidemiology recognizes no boundaries as to the size or nature of the populations it studies, the "field" comprising such general populations as residents of a village, town, or city; of an apartment house or a neighborhood; or of a province, district, or nation, along with their associated environments. Selected populations are persons within an institution, a factory or industry, a hospital ward, or an army. The principle that epidemiology deals with populations living under "field" or natural conditions and viewed collectively rather than as an assembly of individuals is about the limit of common agreement.

Scope and Content of Epidemiology

The epidemiologist approaches his field in a number of different ways and with a variety of objectives. In his judgment of scope and content, he usually evidences the wholly human propensity of favoring that with which he is most familiar.

Any appreciable experience in epidemiology soon dissipates the rash belief that agreement on "What and who is an epidemiologist?" will result from deductive reasoning or any form of logic. But it may be worth while to describe what happened and what has been seen in our collective experience, which has taken us from Hammerfest to Cape Town and circled the tropics and the Arctic. Inevitably, a concept of principle in field work

evolves from interests as diverse as the acute communicable diseases, chronic non-communicable disorders, nutritional deficiencies, and the population problem. If illustrations used in this discussion are often from communicable diseases, it is because that is where most epidemiologic principles originated, despite the wider application today of field investigation.

The views expressed are far from wholly personal. They derive in large part from scores of former associates, more than any other from F.F. Russell. In his direction of investigations of yellow fever for the Rockefeller Foundation (Strode, 1951), he set an enduring pattern for study of disease — disease as exhibited broadly in clinic, field, and laboratory.

Tracing reservoirs and sources of infection

Early field work was largely operational epidemiology in communicable disease, an emphasis that still holds globally. The practical purpose was to identify sources of infection in the origin of epidemics (Goffman, 1965), to introduce indicated control measures, and to formulate preventive practices to ward off subsequent outbreaks. It soon acquired the highly descriptive name of "shoe-leather" epidemiology: the method was house-to-house enquiry, and the procedure was observational and descriptive. Where the source of the epidemic was traced to contaminated water, milk, or food, identification of the immediate source of infection was often enough for institution of proper control measures. Further recognition of reservoirs of infection, usually man—either as a patient or as a carrier—increased the chances of avoiding future epidemics.

An improving public health practice soon permitted the addition of individual case study, the epidemiologic case having as the unit of observation the household, which includes the patient and familial and other close contacts, along with the immediate environment (Gordon, 1965). Case study began with sporadic infectious diseases likely to evolve into epidemics. It came to include industrial poisonings, cancer, and other non-infectious processes. Eventually, as with tuberculosis, case study developed into case finding, with the purpose of discovering unrecognized illness. The gradual incorporation of laboratory procedures into field practice was an important result of these more complex activities.

Epidemics in the USA and many other countries are now less frequent, yet their investigation continues as the major obligation of epidemiology in official health agencies. With local differences, the prescribed diseases requiring case study also include nutritional deficiencies, poisonings, air pollution, and traumatic accidents. The tracing of sources of infection is not wholly routine; from time to time the epidemiologist faces the unknown as a fresh disease invades—St Louis encephalitis in Florida (Bond et al., 1963), hepatitis in New Delhi (India, Ministry of Health 1956) or cholera in Bangkok (Siddhichai & Grayston, 1960).

Administrative control of disease

In most health departments, the application of control measures, as determined by field analysis, is also the epidemiologist's obligation (Rogers, 1963; Hilleboe & Larimore, 1965), especially emergency measures to remedy a deficiency in water supply, milk production, distribution of food, or the management of disease carriers. Other administrative duties (Anderson et al., 1962) include the planning and conduct of programs for specific immunization against diseases such as smallpox and diphtheria, based, in turn, on a preceding evaluation of existing levels of protection. Periodic surveys of disease occurrence are necessary to determine efficiency in disease reporting (Feemster, 1947). Recognition of changes in periodicity of endemic disease (Sartwell, 1965) and watchfulness for newly introduced infections (Comings et al., 1962) are continuing obligations.

All activities thus far noted fall within the scope of operational epidemiology. They are the means by which official health agencies seek to restrict disease. The larger goals of prevention require understanding of the broad biological behavior of disease. Thus, epidemiologic divisions of health departments increasingly assume investigative responsibilities, of greater or lesser complexity, commonly in collaboration with voluntary health organizations or academic centers concerned with medical research. This brings into play a descriptive epidemiology, still based on observations in nature, but emphasizing one of several other approaches.

Identification of agents of disease

Epidemiologists long ago added laboratory procedures in order to support the findings of traditional field study through identification of the inciting agent. Observations starting in the field are often carried to the laboratory, and those starting in the laboratory may end in the field. Both approaches are epidemiologic if they pertain to disease as it affects a human population.

There are differences in the relative emphasis placed on the two approaches, determined usually by the particular problem. When an outbreak of intestinal disease is clearly the result of food poisoning (Rubenstein & MacCreedy, 1953; Googins et al., 1961; Cockburn et al., 1962), the invaded population and the environment are the obvious objects of study in determining the source and instituting control. The laboratory identifies and confirms the suspected agent, although frequently not until the explosive episodes have ended. But, if the objective is to define the frequency and distribution of the reservoirs of infection, as in prevalence surveys of *Shigella* (Gordon et al., 1962c), or the significance of carriers in epidemic spread (Weiss, 1965), the laboratory dominates activities, with the field responsible mainly for proper selection and collection of specimens. Under other circumstances, as in community outbreaks of staphylococcal disease

with an origin in hospitals, both laboratory and field must make their full contribution (Nahmias & Eickhoff, 1961).

Several epidemiologic procedures of great merit have originated in the laboratory. The recognition of type differences within species of infectious agents permits sources of infection to be identified and aids in tracing lines of spread (Aycock & Foley, 1946). Through identification of antibodies in blood from representative fractions of a population (Paul, 1952), serologic methods demonstrate frequency of past infection and the limits of geographic areas involved (Tigertt et al., 1962). Differences in age distribution indicate when former epidemics occurred. Measurement of genetic markers, such as blood groups, certain enzymes, and abnormal proteins, helps in understanding hereditary influences (Blumberg, 1961). Comparison of successive samples of serum taken at short intervals from the same person establishes the occurrence of an active infection. Microscopic pathology serves similar purposes (Soper et al., 1934)—for example, suspicion of yellow fever or leishmaniasis may be confirmed by examination of punch biopsy specimens of liver tissue. Micro-analytical examination of the blood is used to determine nutrients in the field investigation of nutritional disorders (Arroyave, 1962).

Reference laboratories under the auspices of the World Health Organization are an application of laboratory epidemiology on a global scale. Located in various parts of the world are centers for influenza, salmonellosis, leptospirosis, and poliomyelitis. The purpose is to determine geographic distributions, the movement of communicable disease, and the nature of the prevailing infectious agent. Type determination and the demonstration of antibodies are made from specimens transmitted by regional laboratories.

The principle of associated laboratory and field investigation in epidemiology derives chiefly from the acute communicable diseases. Although it is not so widely employed in non-infectious diseases, its advantages have been demonstrated in chronic degenerative processes (Scrimshaw et al., 1957b), malnutrition (Béhar et al., 1960), lead poisoning (Ingalls et al., 1961), congenital anomalies (Ingalls, 1956), and injuries (Haddon et al., 1961). The laboratory contribution is no less important because the techniques are physiologic, biochemical, or enzymologic rather than microbiologic. Field investigation in these newer spheres of population pathology often fails to realize its full potential because of lack of laboratory support.

Geographic pathology

One of the oldest approaches to epidemiologic understanding is to compare the incidence and character of a disease in different places. Hippocrates (Adams, 1849) stated the principles of geographic pathology more than two thousand years ago; August Hirsch (1883-1886) crystallized them in his three-volume work of 1860; and the Second World War brought renewed

appreciation of the practical value of geographic pathology (Simmons et al., 1944). Modern travel (Lafontaine, 1964) has made the health problems of individual countries the problems of the world, with a resulting resurgence of interest in the geography of disease (May, 1958, 1961), at national (United States, National Academy of Sciences, 1962) and international (Doll, 1959) levels.

Although infectious disease has been the chief concern, other mass diseases and injuries are studied advantageously in this way. To determine what diseases occur where, geographic pathology uses clinical methods, gross and microscopic pathology, and, for the infectious diseases, microbiologic techniques. When the question is why the observed differences occur, in time and person as well as in place, the effort becomes specifically epidemiologic.

Early work in geographic pathology was concerned mainly with disease in relation to the physical features of the environmental complex. To determine causality, epidemiologists have to consider the biologic surroundings, especially food and food resources, and also the social environment. Both enter into cause and behavior of disease. The epidemiologist, unlike the geographic pathologist, commonly studies disease in a limited area and within a fixed population. He shares a global interest with the pathologist when he extends his observations to the broader reaches of time and place. Current studies such as the inter-American atherosclerosis project (Tejada et al., 1958), a major concern with cancer (Council for the Coordination of International Congresses of Medical Sciences, 1950), continuing efforts with communicable disease (Philip et al., 1949) and, more recently, with accidental injuries (Gordon et al, 1962b) illustrate some of the more common interests.

Serious difficulties in interpretation arise when results of independent workers are assembled in an endeavor to compare the behavior of a specified disease in separate localities. Differences in host and environment expectedly produce variations in morbidity, mortality, and other characteristics. Equally significant inequalities commonly derive from dissimilar criteria for diagnosis of the disease itself and for measurement of the observed characteristics. Differences in training and methods of approach of investigators also contribute to the difficulties of interpretation. The only reasonable solution is adoption of common criteria and techniques by workers in a specified field (Acheson, 1965).

Clinical epidemiology

A clinical understanding of disease or injury is fundamental to all epidemiology, for disease can scarcely be studied in its group manifestations unless properly identified in individuals. One novel use of clinical methods is in the control of threatening or expected epidemics. In the European Theater of Operations during the Second World War, isolated and restricted

outbreaks of an unusually acute respiratory disease were noted by Gordon (1949) in August 1943. Middleton (1947) established clinical listening posts in selected localities throughout the command, assigning experienced physicians to report changes in the prevailing clinical nature of respiratory disease among patients admitted to hospitals. The epidemic of influenza that came in November 1943 was no surprise; adequate facilities for medical care and administrative control were ready. This principle, often complemented by laboratory procedures, has been adapted to worldwide control of many diseases. The results have proved its worth.

Clinical epidemiology has another and special connotation. As epidemiologic interests have extended from large-scale epidemics to sporadic and isolated foci of infection, to behavior of the individual patient in relation to his family, his environment, and close associates, an intermediate activity has developed, which may be termed "small-group" epidemiology. Here investigation is by the clinician, commonly the pediatrician, rather than by the epidemiologic specialist. This is a natural outgrowth of the interest of practitioners in preventive as well as curative medicine.

Spence (1950), in Newcastle-on-Tyne, has expressed the need for the clinician to extend his observations by research in family practice and by field survey of random samples of the population. John Paul (1958) has presented methods, principles, and sound examples of how to do it.

Statistical epidemiology

Irrespective of method or technique of investigation, all epidemiologic procedure involves mathematics, sometimes no more than simple arithmetic, in other instances intricate statistical methods to establish true correlations. In research epidemiology, statistical procedure desirably runs throughout the study, having a part in early design, during observations, and ultimately in the interpretation of results.

Statistical method is often the main epidemiologic tool and is applied to data from many sources. Trends in frequency over time, in rates of occurrence according to place, and in differences in kinds of persons affected are sought (Hamer, 1906; Segi, 1960). Statistical epidemiology also considers changes in the character of a disease and the resulting fatality, a method used by Chapin & Smith (1932) to prove that smallpox breeds true in two lines, the mild alastrim and the classical variola.

The sources of data include official reports of deaths and illnesses in a community, clinical case histories, and the records of autopsies, as well as a variety of supplementary information. Some data are collected for a specific purpose; more are derived from periodic reports of official, voluntary, or industrial health agencies. Sometimes they come from sources not connected with the particular project, and commonly they have inherent deficiencies.

A statistical approach is fruitful so long as the limitations and biases of the original data are recognized. Witts (1964) and MacMahon, Pugh & Ipsen (1960), among others, have discussed these obstacles in detail. They include differences in diagnostic standards, medical practices, and methods of reporting, from place to place and among observers. Information may not exist for specific population fractions; sources are generally inadequate for common illnesses such as acute respiratory disease, the diarrheas and the dysenteries, and the acute communicable diseases of childhood. All too often the result is a presentation with all of the statistical niceties applied to unreliable and inadequate data. On the other hand, solid observations from laboratory or field have suffered from deficiencies in statistical interpretation.

Statistical epidemiology has contributed to theoretical epidemiology through statistical models that explain epidemiologic phenomena, develop new concepts, or confirm others arising from experiment or observation. This feature was first brought to prominence by Ross & Hudson (1931) in their work on malaria, based on earlier contributions by Brownlee (1919) and by Greenwood & Yule (1914). Recent contributions include Muench's work (1959) on catalytic models and Bartlett's (1960) use of stochastic procedure. The characterization of these activities as arm-chair epidemiology is not always justified. Many contributors are themselves qualified field investigators using field data.

Field survey

An accumulating knowledge of epidemiologic theory and the introduction of quantitative methods have led eventually from descriptive procedure to an analytic discipline. Considerations of how disease originates in a population and why it behaves as it does are now among the chief concerns of epidemiology.

The field survey is a cross-sectional study seeking to determine the number of cases of disease, or of persons with some other attribute, present at a particular time and in relation to the size of the population from which they are drawn. Technically it is a prevalence study, and in its simplest form a determination of point prevalence, prevalence at a specified time. The objectives are various: to assess the health of a community under normal conditions (U.S. Department of Health, Education and Welfare, 1962), to determine occurrence of a particular disease (Fleck et al., 1960), or to measure the nutritional state of a population (Jelliffe & Jelliffe, 1961; Jelliffe et al., 1961).

The main approach in a field survey can be clinical, laboratory, or the traditional field investigation. Usually the three combine to advantage, adding precision to the study. Each has its special usefulness and, even if functioning alone, is epidemiologic so long as the information gained represents a specific field situation (Winslow et al., 1952).

Although outside its specific purposes, the field survey often leads to factors in causality, which sometimes are confirmed by subsequent laboratory study, or justify a long-term incidence study. The field survey is less exacting in time and expense than the incidence study, but the frequent attempt to use it as a shortcut is much overdone. Repeated surveys at established intervals, the determination of periodic prevalence, increase the potentiality of determining causative factors.

Field incidence study

The prospective long-term field study concentrates upon incidence rather than prevalence, and its usual objective is causality rather than distributions and behavior of a disease. When experimental principle is introduced into field study, data are collected according to a preformed plan, with conditions defined, constants established, and controls provided. The Baltimore studies on syphilis of Clark & Turner (1942) illustrate method and principle for chronic infection; the Washington studies of Rowe and co-workers (1957), for acute respiratory disease; those of Reinhard (1963) in the western Arctic, for enteroviruses; and the Cleveland family studies of Dingle and associates (1965), for the general trend of several diseases in an open community, all with an emphasis on causality. The method finds increasing application as chronic diseases and injuries replace acute infections as the dominant epidemiologic interests in industrialized countries. The inherent prolonged nature of these conditions makes long-term observation essential. The Framingham heart study (Dawber et al., 1951) is projected over 25 years. The INCAP study of the synergistic action of nutrition and infection in Guatemala (Béhar et al., 1958b; Scrimshaw et al., 1967b) covered a ten-year period. Ultimate understanding of rheumatoid arthritis, cancer, and other currently prominent problems in population pathology would seem to rest in this approach (Reed, 1949).

Experimental epidemiology

The purposeful attempt to explore general laws and principles of mass disease by direct experiment with populations of animals was a natural evolution of field study of humans. Infectious agents peculiar to the species permit study of isolated factors in epidemic causation. Despite the important results of initial studies by Greenwood and associates (1936) and by Webster (1946), this method has had little recent attention except for Schneider's work on nutrition and salmonellosis (1951) and that of Fenner (1959) with myxomatosis of rabbits.

A Concept of Epidemiology

These several approaches to epidemiology have a single purpose: to improve understanding of disease as manifested in groups of people. But they differ in specific objectives and the kind of problems they seek to solve. Each attracts both persons primarily concerned with population pathology and investigators with a primary interest in some other science. Each worker tends to see his special world most clearly and, understandably, develops at times a fragmented idea of the scope of epidemiology. And yet, all of these approaches are "epidemiology", an opinion that the roster of the American Epidemiological Society amply supports.

The unit of observation, a human population, is the common denominator. Therefore, epidemiology deals with population pathology, not clinical pathology (disease of the single person), nor microscopic pathology (disease of the cell or tissue). All population pathology relates back to the field as the source of materials for investigation, and results are interpreted in terms of the group, not the individual. If the circumstance is otherwise, the work can be medical statistics, biochemical or microbiologic research, or clinical investigation, tangential and often contributing importantly to the broad base of knowledge upon which epidemiology rests; but it is not epidemiology.

Although many workers in epidemiology are familiar enough with the broad field to be classed as epidemiologic generalists, specialization is inevitable in a field that extends through the whole of medicine and public health. Competence is often limited by interest and by training to a skill in one general activity, occasionally in several, rarely in all.

Of the nine field activities just distinguished, the first two, the search for origin and source and for administrative control of disease, are grouped as *operational* epidemiology, their main function being to support the practical work of public health agencies. The next four, the identification of disease agents, geographic pathology, and the clinical and statistical approaches, may be characterized as *descriptive* epidemiology, primarily dependent on observational methods, concerned with disease behavior, and directed toward an improved prevention. Field survey, incidence study, and experimental epidemiology constitute *analytical* epidemiology and are research procedures pertaining to the origin and behavior of community disease.

These are neat categories, but far from rigid. Alert observation during routine operational activities has resulted repeatedly in important contributions to causality. The descriptive approach frequently uncovers leads that permit specific investigations, and statistical and laboratory epidemiology have important and independent functions in theoretical epidemiology.

Epidemiology thus has many interlocking interests, and multiple and sometimes devious approaches. It brings together a variety of scientific disciplines and a diversity of skills and techniques. Still, the one dominant

feature, the central theme from which there is no departure, is the relation of a disease process to a population living or working in a natural environment.

For years epidemiology has recognized the potential of some unifying discipline to provide a common ground for interpretation of the biological, social, and psychological characteristics of groups of people as they relate to health and disease. Ecology, its province being the relationships of living organisms to their animate and inanimate surroundings, finds increasing application in this capacity. As a part of human ecology, medical ecology supplies the principles for understanding disease as it affects aggregates of people (Winslow et al., 1952). Because ecology is a branch of knowledge both social and biological, it serves epidemiology well, for epidemiology is an applied science (Francis et al., 1955), at times requiring such divergent skills as those of physician, mathematician, anthropologist, biochemist, or meteorologist.

Conduct of Epidemiologic Field Studies

Nature of field investigation

The essence of epidemiologic analysis is work in the field. Even with a main stress on clinical, laboratory, or statistical procedure, someone must collect the material for examination; and the integrity and completeness with which that is done determine whether the results reflect population pathology or are a contribution to some one of many allied disciplines.

Field study of disease has no special individuality, whether operational and applied, or investigative and research. It is the scientific method applied to a particular circumstance. To speak of epidemiologic method is thus as justifiable and convenient as to speak of clinical or chemical method. Although reinforced with refined clinical procedures and laboratory techniques, the everyday, house-to-house observation of earlier years continues as the fundamental feature.

Field study begins with inferences and construction of hypotheses drawn from established facts about the behavior of disease. The information is from many sources, partly from other field investigations, but more often from the broad base of knowledge that exists in the biological and social sciences. Success requires the same planning essential to any experiment or other careful observation, including statistical considerations as to frequency of event, the necessary length of observations, and the size of population required.

Field research these days is usually a team effort, employing a variety of ancillary skills in support of a principal investigator. The community is the laboratory and, in contrast to some other approaches to population pathology, has the advantage of first-hand familiarity with the people and their

environment, and a knowledge of the strengths and weaknesses of the data collected. Modern methods of machine tabulation, computer analysis, and statistical manipulation have obvious value in dealing with long-term projects with much data, but the interpretation of results remains rooted in the value judgments of the worker in the field.

The limitation of field study to communicable disease has disappeared, although adherence to that restriction persists to an extent in clinical and basic science circles. In contrast to the lively and divergent views on scope and method, the techniques of field study have had less attention, although they are a critical and common factor. One explanation is the lack of practical experience in field operations during courses of instruction in epidemiology, of a specific effort to provide a training comparable to that of the clerkship in clinical medicine or the laboratory apprenticeship in the biological sciences. The academic epidemiologic laboratory does present principles of data collection (Anderson et al., 1962) and provides training in the analysis and interpretation of raw data, but little or no first-hand experience in the accumulation of that material. Skill in these matters usually is empirically acquired through service in a working organization. The recent establishment of a few fellowships for field training indicates the need for a more orderly development. Only too often field work is not in the best tradition of bench research, because of inadequate attention to method and materials. An all too frequent attitude is that little is demanded beyond visiting homes and talking to people, activities that require no particular skill.

Epidemiology demands more than this haphazard approach. A definite pattern is believed to permeate field endeavor, whether operational or investigative, whether a simple epidemiologic case study or an investigation of an epidemic, whether the complex prevalence survey or the still more intricate incidence investigation.

The conceptual idea

The decision to initiate a case study or to investigate an epidemic raises few questions of what to do or how to go about it. The operational procedures are a normal obligation of official health agencies, and the incentive is prescribed by regulations. In the ordinary situation, experience and tried procedures guide activities, and the objective—to institute prompt control—is definite. Occasionally, the decision for action is elective: an unusual local circumstance of no emergency nature attracts the interest of the investigator.

Help is sometimes demanded by other jurisdictions or even a foreign country when control is beyond existing resources, as in the recent cholera epidemic (SEATO, 1960) in Thailand and the Far East. Procedure is not always so simple in these situations. The cause of the trouble may be obscure, the circumstances or the size of the problem, overwhelming.

Hundreds of deformed infants were born before thalidomide was recognized as the inciting agent (Ingalls, 1962; Lenz & Knapp, 1962) and the situation remedied.

The research endeavor, the field survey or the incidence study, is of another order. Unlike operational ventures, these are voluntary undertakings, without predefined obligations. The urge is for a logical answer within the confines of practicality. Both the conceptual idea and its orderly development are important features, to be expressed finally as a hypothesis capable of test.

There are many compulsions to research, some of which lead to ideas for field study. An insistent need for better methods of prevention and control is a common incentive (Beck et al., 1962). Motivation also stems from less material things, such as a conviction that medicine should right the ecologic imbalance resulting from its success in controlling deaths by an attention to control of births. Plain academic interest, the need to know why things happen, is just as reasonable a stimulus; for the value of an established fact is not necessarily allied to its immediate usefulness. Many times the investigation is an intermediate, yet crucial, step in realizing a broader objective; the whole field of yellow fever research opened up once the rhesus monkey was established as a satisfactory laboratory animal in Lagos, Africa (Stokes et al., 1928). Occasionally, the simple challenge of the difficult provides the impetus, the sort of thing that sends men to the top of Mount Everest. Epidemiology has many such challenges (Kurland, 1958; Kurland & Westlund, 1954; Plunkett et al., 1960).

No formula exists for acquiring the critical idea. Likely ingredients are inspiration, chance, and genius, in combination or alone. As for chance, a famous dictum says that chance favors the prepared mind; and the prepared mind depends on experience and explicit knowledge in the same or a related field, searching always for analogies. Familiarity with procedures others have tried and discarded proves useful. A spirit of creativity is what really is needed, but that cannot be called up at will. In its absence, speculation may have to serve as a necessary but weak substitute.

Few ideas are born in their maturity. Studied reflection, or a period of allowing the idea to lie fallow for a time, may aid in the initial effort to form a concept. And after that, there is still work to be done in its evaluation, organization, and refinement before turning to the practical means for an answer.

First comes a statement of objectives and of the exact questions to be answered by the investigation in relation to long-term demands of the problem. This defines the dimensions of the contemplated study, its significance, and its relation to the general field of interest. Relative urgency is a consideration: whether the study must be done now to take advantage of a unique situation, or can be done equally well within the foreseeable future, or even postponed indefinitely without loss.

Finally, with objectives established and procedural methods projected, it is time to consider practical questions. Is there a suitable population available; can requirements in time, staff, and materials be met in relation to existing or potential resources? Attention turns seriously to the prospects of success in accomplishing the purpose of the proposed investigation. Scope and direction are reviewed in detail. This requires background information; to an extent it merges into preliminary planning; and this, in turn, leads to the formal design of experiment. An afternoon in the library may suffice for these purposes, or months may be necessary. The time depends on the problem, whether it is relatively familiar or a step into the unknown.

A review of the literature on what has been done tells of successes and failures, in relation to the particular problems and to the general field. Consultation with colleagues is in the normal course of events; the most valuable help often comes from a seasoned investigator, not necessarily expert in the particular field, but able to view the project with an objectivity derived from long experience in biologic research. Visits to places where similar studies are in progress are helpful.

Primarily, however, this is a time for independence of thought and action. More time than is profitable can be spent in accumulating background. Excessive delay often arises from unjustified doubts or the stifling of good ideas by conflicting opinions. There comes a time for decision. If there are serious reservations, the idea should be put aside for another day. With reasonable assurance that the argument is logical and that the operations are feasible, a hypothesis or hypotheses are formulated for test. The field study is on its way, with no uncertainty now about the next step.

Field reconnaissance

Preliminary assessment of the particular locality where the work is to be done is one principle in field investigation that should never be violated. There is no substitute for personal observation. The time necessary for reconnaissance varies with the problem, yet it is as much a part of case study and epidemic control as in the more pretentious field research of long duration.

In operational procedures, the initial survey is brief, because the investigation is of limited scope, the course of action, conventional, and the objective, definite: prompt control. An hour may suffice for a preliminary survey of poliomyelitis in a boys' camp (Rubenstein et al., 1948) and perhaps a day in scattered outbreaks, such as that of Eastern equine encephalomyelitis in Massachusetts (Farber et al., 1940). The first obligation is to establish working relations with local health and administrative authorities and, through their aid, to consult with physicians who have been seeing most of the cases.

Taking precedence over all else is a visit to the last reported patient. In a communicable disease, the object is to learn the nature of the infection, to obtain leads on lines of transmission and modes of transfer, and, if a chronic, non-infectious condition is involved, to establish clinical familiarity and to probe for possible sources of origin, which may involve anything from the habits of bus drivers to why children eat paint. Nothing must interfere with this visit, because it is there that the scent is freshest. What is found more or less establishes the plan for action.

The long-term research activities, field survey and incidence study, require more detailed reconnaissance. Since the proposed investigations will extend over appreciable periods, sometimes several years, working arrangements have to be established on a fairly permanent basis. Many such studies are in foreign countries, which multiplies the need for detailed preliminary information. A week of reconnaissance is little enough, and a month or so may be necessary. Technically, now is the time to start a field diary. Details escape, especially names, titles, and addresses—information of much value in the eventual planning of the study.

Good working arrangements with local authorities are so important that the principle is to neglect no one; omissions have been the source of future difficulties or even failure of a project. It is just good sense to start with national or state health authorities and, through them, with administrative departments, but not to the neglect of local officials. There is where the work is to be done, and it is a sound investment to establish solid understanding of what is proposed, to enlist the desired co-operation, and to assure appreciation of the importance attached to the community contribution.

In regions unfamiliar to the investigator, and especially in a country other than his own, personal knowledge of people, language, terrain, and facilities within the study area enters strongly into planning. Professional colleagues are helpful but, being themselves of the culture of the country, scarcely can reflect the reactions to strangers, or the effect of customs, habits, and traditions on the results. In rural India, Gordon and Taylor (Gordon & Wyon, 1960) pitched a tent against a village wall and lived in the community for a week, spending the days in the fields with farmers or in hunting trips with villagers as guides. In the evenings, scores of men gathered around their open fire to discuss the problems of the universe. In that atmosphere, one important item was settled: work in these simple communities was feasible.

Locating a place for field headquarters is an important job because residence within the study area, whether it is rural or urban, contributes to the success of this type of study. Local transportation almost always poses a greater problem than expected. When the study area is rural with a relatively large population, substations are needed on a village basis. Residence in the more comfortable quarters of a nearby city and visits to the natives do not compensate for the advantage of becoming an accepted part of the community.

Other considerations include the available numbers, competence, and reliability of local recruits to the technical staff, with bilingual ability sometimes a feature. Local records of reported births and deaths warrant scrutiny to determine their probable reliability and completeness and the extent to which they are representative of the more readily available data for larger political units. In underdeveloped countries, the lack of large-scale maps and census data for local communities is frequently a practical problem. In such ways reconnaissance seeks to determine the probable size of the job, the critical points of attack, the needs for staff and equipment, and the special skills demanded. This preliminary information determines just how feasible is a realistic design of experiment.

Experimental design

Whether a field study is operational or analytical, emergency or long-term, the differences in people, in terrain, and in time and rate of occurrence of the events to be observed are such that field investigations differ in plan of action, even with regard to the same disease.

The several planning stages in a proposed investigation are (*a*) organization, including selection of staff, equipment, and supplies; (*b*) field test of materials and methods, to determine suitability to the immediate problem; (*c*) pilot study under controlled conditions for presumptive determination of expected results; (*d*) definitive investigation; (*e*) analysis and interpretation of the findings; and (*f*) the suggested or defined direction that subsequent investigations should take in further development of the problem. All steps may not appear to enter directly into every study plan, but only because the procedures involved are implicit, and through long experience accepted as standard operating procedure.

The construction of an ecologic model, a theoretical illustration of the relationships between host, agent, and environment, is a major feature in developing the study plan. The model's purpose is to facilitate an answer to the formulated hypothesis, through definition of the several procedural stages just presented. The plan of a field study includes technical methods and materials to be used, and statistical assurance that the answers obtained will have significance, whether positive or negative. The facts accumulated when hypotheses were formed and during field reconnaissance are the basic materials. The plan is the guide to action—the what, when, where, and how to proceed.

Epidemiologic case study, as the day-to-day work of official health agencies, has through long experience evolved a standard operating procedure, originating nevertheless in the principles just stated. The plan is thus prefabricated, and the concern is more with choice of techniques than general procedure. It is extemporaneous and follows directly from the findings of the preliminary reconnaissance.

In epidemic control, preliminary reconnaissance has determined whether the disease is familiar or obscure, whether the outbreak is large or small, of sharp evolution or protracted course. Under any circumstance, prompt decision is required on the course of action, and much depends on proper appraisal. Errors in judgment have resulted in putting up an umbrella to stop a flood or, conversely, starting to build a dam in the face of a first sprinkle. In essence, control of an epidemic involves assembling a series of case studies and determining the connection of disease in one family unit with that in another and whether the infection relates to a common or a propagated source. The investigation may end in a day or two, the situation being little more than an enlargement of a case study to be completed by the principal investigator alone; or it may last weeks and require marshalling special laboratory facilities and an appreciable field staff. Planning, therefore, centers on an assessment of the situation. The objective is clear-cut: to identify the origin of the outbreak and institute prevention and control. The urgency of the situation necessarily puts reliance on previous experience and established procedure.

Like all research endeavors, the field survey is an elective undertaking with a studied course of action. Requirements for staff and materials are complex because of longer duration and the individual nature of the study. Technical methods frequently must be tested for suitability to the particular problem and to field conditions, or new ones may have to be developed. Statistical computations, based on expected rates of occurrence, are necessary to set the length of observations and the size of population needed (Fellingham, 1966). Because interpretation is usually through comparison, either of findings determined in other regions or of behavior at other times and under different environmental circumstances, the survey is without organized controls.

The prospective incidence study, in its customary form as a true field experiment, involves a major planning endeavor. Since controls are an inherent feature, it is necessary to build the experiment on an adequate mathematical and ecologic model. Most of such studies are long-term investigations and therefore require extensive attention to staff and materials. Many are in countries foreign to the investigator, so chosen because of special conditions favoring the investigation or the wish to compare known findings in one region with those in other places. The required methods are often original, or at least untested for the purpose, or must be modified to a new situation. Consequently, few shortcuts are possible in constructing the broad plan for action. This is no place for magpie methods, for the indiscriminate collection of information.

Because of its duration, the incidence study normally functions best through an established field headquarters, with the staff living and working in the study area under more or less permanent conditions. Housekeeping as well as technical operations thus enter into planning procedure. Most

other field studies are conducted advantageously from a central base of operations or from temporary headquarters in the local area.

The completed design almost invariably incorporates plans for exploratory study, a pilot investigation, and the main endeavor. The principles governing each are given in the discussion to follow. If the definitive study is of short duration (a year or so), observations sometimes proceed directly from exploratory study to that objective. Today, many studies are projected over several years, and decision for a pilot study with controls, under the general conditions of the main experiment, is usually wise.

Since so much data will accumulate during the proposed investigations, a noteworthy technical consideration is to prescribe methods of assembling and recording data in a form that permits mechanical sorting and tabulation. The fundamental need in experimental design is for epidemiologic sense and experience. As Greenwood (1935) once warned, a proposed line of investigation may be logically unassailable, statistically impeccable, and biologically ridiculous.

Field organization

Aside from reconnaissance, properly a part of planning, the first step in active field operations is to institute administrative procedures, select a staff, and assemble the necessary supplies and equipment. This is the technical aspect of field study.

Little is demanded in organization of resources for case study or epidemic control because the official health agency ordinarily responsible for such activities keeps the essential equipment and supplies in readiness. Case study is a one-man endeavor; and, except for co-operation of local health personnel, so is epidemic control. If assistants are needed in large outbreaks, trained and experienced workers are available in the central agency. Beyond what is needed for clinical examination, not much field equipment is necessary. A camera is a useful item; but, in general, satisfaction and accomplishment are inversely proportional to the number of kilograms of baggage.

Preparation for the field survey or the incidence study is more detailed. In contrast to operational epidemiology, organization usually starts from scratch, requires appreciable time, and is of studied character. The base of operations ordinarily is a university, a hospital, a research institute, or an official health agency, and has several functions. It provides administrative support, is the source of staff and supplies, and furnishes central laboratory and statistical services.

Sound policy, however, separates a research study from general activities by establishing a field headquarters. The distances involved may make this necessary, especially if the study area is rural, as it so often is. But even if the research activities and administrative headquarters of a central

program for the health problem concerned are in the same city, a separate field office for the research is highly desirable.

In many situations, the field station is both the focus of working activities and the residence for staff. If operations involve relatively large numbers of people and observations are continuous and repetitive over appreciable periods, as in incidence studies, substations or local centers are established in strategic sites, either in villages of a rural region or according to census divisions of an urban population. In general, the substations accommodate local workers responsible for populations of perhaps 2000 people. The staff at field headquarters is then restricted to supervisory personnel and to specialists concerned with the project as a whole.

Requirements for field staff are obviously a function of the problem under study, and are further influenced by the volume and complexity of the data to be collected. The field director, ordinarily a physician and epidemiologist, usually needs at least three key staff members. Large-scale projects, especially those in foreign countries, require an assistant director, usually designated from among these three, who assures satisfactory direction of the project during vacations and other anticipated absences of the director.

The key assistants are the following:

1. A laboratory worker with qualifications suited to the problem at hand is a primary member of the staff, since few sizable field studies function to capacity without local as well as base laboratory facilities. This is appreciated for infectious and nutritional diseases; its importance in field study of other disease processes is increasingly recognized.
2. The statistician of a field study group departs to an extent from his usual role as an office worker. He may be stationed wholly in the field or divide his time between base and field station; but, under either arrangement, he should participate in active field work sufficiently to evaluate the quality of record-keeping, completeness of the collected information, and the methods used.
3. The supervisor of field workers has the task of directing the work of the day in data collection. This is a most responsible position; and, in the authors' experience, the public health nurse is likely to be best qualified for it.

Recruiting general field workers for duties not requiring a physician is often a problem. The first choice is, again, the public health nurse with field experience; but often such nurses are not available in foreign countries. A command of the country's language and a familiarity with the environment, aims, and outlook of the people make persons of local origin highly desirable. Auxiliary nurses and social workers have been successful in this work, as have school teachers or young college graduates once they have

had suitable on-the-job training. For some problems and cultures, both male and female workers are required in order to uncover the needed information.

The administrative and professional acquaintances made during reconnaissance are renewed and put on a working basis. The field laboratory and the field statistical office are established, with a clear definition of responsibilities. Some laboratory examinations can only be carried out satisfactorily in the field; others are far better accomplished at the base laboratory. Thus, the isolation and tentative identification of infectious agents commonly are done in the field, and confirmation and typing, at the base laboratory. Similarly, the statistician must supervise the recording of data and make periodic trial analyses of results in direct conference with field workers, although machine analyses and the more technical procedures are done at base headquarters.

Supplies and equipment for field operations depend on the study. When the authors' field station was in Egedesminde, Greenland, and the base laboratory in Copenhagen, Denmark (Gordon & Babbott, 1959), field facilities were necessarily elaborate. When the base was a few miles away, as in the Guatemalan studies (Scrimshaw et al., 1962), much of the work otherwise done in the field could be accomplished centrally. The guiding principle is to emphasize the practical rather than the theoretical, to add facilities as need is demonstrated, and to respect the admonition to travel lightly.

Equipment for home visits in the field is relatively simple. Large-scale maps locating all households of the study area are a primary requirement. Governmental sources occasionally have such maps, but usually the field staff prepares them. In surveys, the official census often suffices. For long-term incidence studies, however, the study group makes its own census in the course of preparing standard family folders for household visits. Record forms comply with individual features of the investigation, with special attention to exactness in terminology (Payne, 1951), to such an extent that an explanatory code stating what information is wanted and defining technical terms is required for each item of all forms put into field use.

Where house-to-house visiting is the basic procedure and the population is urban or centered in villages, as in many rural parts of the world, travel is by foot. If roads are good, there is no difficulty in getting from field headquarters to local study areas or substations; but in many places the monsoons and other seasonal difficulties require a rugged vehicle, able to travel over difficult terrain. Under certain primitive conditions, bicycle, oxcart, dog sled, and river boats have been used. Another consideration is transport of staff and supplies between field station and operating base. Provision for staff travel to conferences and for meetings of consultants in the field also becomes significant when field work is abroad or done under isolated conditions.

The time required to set up a going organization varies with the project and the plan of operations. A month may suffice; three to six months are more likely, especially in a country foreign to the investigator. It is a peculiar and yet almost invariable circumstance that this phase in the development of a field study seems to take longer than anticipated. Still, the future flow of operations and the satisfaction with the eventual results are strongly influenced by the time given to preliminary preparation.

Exploratory study

The purpose of this first activity in the actual collection of data is to test record forms and techniques prescribed in the experimental design. A second objective is to train staff members new to field work and, often, to research method and principle. When the project represents new or unfamiliar ground, even a seasoned staff requires specific experience.

The exploratory study ordinarily is not a feature of case study or epidemic control. Standardized procedure has developed; data forms and other materials have had previous testing through long use, and special provision commonly exists for recurring conditions such as typhoid fever or lead-poisoning. The field investigator is presumably experienced or has the guidance of those who are. The preliminary reconnaissance is the common substitute. What is elemental is to recognize the unusual epidemic, with respect to clinical behavior, causative agent, or mode of transmission. If that is the situation, individual lines of inquiry and perhaps a tentative form for recording data may be tried out on a few initial cases before proceeding with the general investigation.

In field research, a preliminary test of methods and procedures and an evaluation of staff members are close to imperative. How comprehensive this should be depends on the familiarity of the staff with the problem and their previous experience. If this is the first study in the particular area of interest, new techniques must be learned from start to finish. Certain health conditions are particularly difficult. Alcoholism, drug addiction, and behavioral abnormalities all touch intimately on the sensitivities and sympathies of the study population. Field workers familiar with organic diseases frequently have a substantial adjustment to make in accommodating to these situations. To an extent, these considerations enter into all field epidemiology. Food habits are often difficult to elicit because they are so revealing of social and economic status. The venereal diseases are an especially sensitive subject.

In major projects involving a considerable staff, it is profitable for the eventual supervisors to do this initial work themselves. In the authors' Indian studies on population dynamics in Khanna (Gordon & Wyon, 1960), the field director himself served as the local village worker in the exploratory study, with the future supervisor of village workers as his assistant. Through

personal familiarity with existing difficulties, the leaders develop an ability to direct others effectively and sympathetically.

The exploratory study may last a month. Three months are more likely, and the work may demand as much as six months. The results must be sufficiently certain to establish necessary revision of forms, procedures, techniques, and, especially, the reliability of units of measurement. Identifying errors of omission is as significant as recognizing those of commission. A further obligation is to screen the staff for competence and ability to adapt to field life.

Pilot study

A pilot study, the full-dress rehearsal of the main investigation, may not be necessary in a well-defined or familiar field, particularly if the investigator or others have made previous studies. A pilot study is advisable when the problem is obscure, when epidemiologic constants are ill-defined or when methods are new. A material saving in time and money often results.

The pilot study differs from the exploratory study in being an experiment with adequate controls, designed to support the validity of a concept and an experimental design. It has the advantage of a proven and experienced staff, derived from the preceding exploratory investigation. As a small edition of the projected major research, in size of population examined and in duration, it usually lasts for several months—a year if the seasonal variations in the condition studied are important.

The pilot study may identify enough flaws or difficulties to determine that the experiment is unlikely to produce a clear-cut answer; it may uncover new evidence suggesting a second pilot study from a fresh approach. It may demonstrate revisions or alterations essential to making the original investigation possible or, better still, give assurance that the plan works and can be put into operation in the definitive study as formulated. On rare occasions, the pilot study gives an answer sufficiently conclusive to obviate the need for the larger investigation.

Definitive study

Two factors conceivably enter into the results derived from the pilot study and the decision to continue: first, the inherent value of the plan and the methods used, and, second, the technical competence with which the work was done. More than one good plan has failed because of its implementation. At any rate, a formal revision of the experimental design, including all modifications and additions suggested by the pilot study, is the first obligation in beginning the definitive investigation. The document itself will be consulted many times, because in every lengthy investigation deviations intrude, recognizable only by reference to the recorded plan of action.

Since the definitive study covers more area and a larger population than the pilot study, the staff is necessarily increased, and recruits must be trained. This process is now much simplified since the needs of the study are more definite and an experienced nucleus of workers exists. With a judicious mixture of old and new members, field operations usually start with little delay—a desirable objective in order to avoid missing time trends in data already collected. At the beginning, efficiency may not match that of the pilot study, since some members of the original staff are commonly appointed subsequently to supervisory duties.

Once adopted, the operating procedure laid down in the revised plan should be followed scrupulously, but not pedantically. In any research, fresh leads occur that are capable of development with little added effort. Yet there is need to limit additions suggested by interests of individual staff members or, more likely, by outsiders who know the expense of such long-term investigations and realize that many field studies devoted to other purposes have the capacity to accumulate kinds of information not warranting the effort or expense of an independent study.

Commonly, interest diminishes in long-term field studies, as the same kind of data is collected over a period of years. Sometimes quality and completeness also suffer from "working for the statistician and his statistical significance when the answer is before your eyes", as one youngster protested in frustration. Assigning such a worker the task of concurrent evaluation of results best relieves his boredom. Permission to undertake some small ancillary investigation originating with the worker himself is also good for morale. However, alterations in the general design of the study are another matter, and permissible only after strict evaluation of findings by periodic test analyses. The established goal of a definitive answer to the stated problem is not to be lost.

Staff changes are unavoidable in a study of several years' duration. The advantages of continuous direction are so great that strong effort is warranted to maintain key personnel for the duration of active field work. This is difficult when the site is remote or isolated, as it so often is. One experienced field investigator has said that today a study group can be delivered anywhere in the world and retrieved; the trouble comes in keeping the group there. Numerous long-term field studies have suffered from a policy of short terms of service of one or two years. The need for a concern with living accommodations as well as working conditions, of opportunity for renewed professional associations, of periodic consultations, and of academic recognition and advancement during the study, stems from the considerations just stated.

Analysis and interpretation of results

The case study is ordinarily a one-day field operation, its purpose being to institute administrative measures for control. The report, therefore, is

descriptive and the language, non-technical. It should be submitted promptly. The report combines clinical and laboratory results with field observations. Its essential considerations are origin of the disease, specific etiology, causative factors other than the agent, and, if an infectious process, the mode of transmission. Recommendations for prevention and control and the recognition of actual or potential involvement of other family units are main requirements.

The report of an epidemic has the same primary features, but is necessarily more extensive. The report does not await completion of the study. There must be a prompt and decisive preliminary statement to inform the public and to direct control measures. A final report gives recommendations for long-term control and measures to prevent recurrence; it contains tabulated information on the size of the epidemic, its duration, and the classes of people affected; and it emphasizes causative factors. It is a transcript of what happened, along with a succinct summary.

To use an epidemiologic expression, the handling of data in long-term field research follows the principle of medical asepsis as opposed to terminal disinfection. Periodic trial tests of the findings are essential to a productive investigation. The futility of a last grand clean-up, to find out what has been discovered, has often been demonstrated. Analysis of results is more than an obligation of the statistician; in varying degree it is a responsibility of all staff members. Analysis is at three levels: the first is a concurrent function of regular field activities; the second is a periodic examination of results; and the third is the definitive analysis.

The village workers at field stations and the unit statistician at headquarters assess both records and results as they accumulate. Field records require review to ensure completeness and accuracy; once a week coincides with usual needs. Under the leadership of the director and nurse supervisor, a conference of all field workers at least once a month provides an opportunity to compare results, pool difficulties and successes, and evaluate methods of collecting data. This is desirably a technical conference, independent of administrative meetings.

To stimulate interest and facilitate the daily work, pertinent items of the study should be charted by time and place and kept current at each field station. A pin map can mark geographic distributions. A permanent records of the local health authorities. Summaries of current events likely to have influenced results require a co-operative staff effort. Ordinarily made on a monthly basis, they substitute for the daily diary recommended for the reconnaissance and organizational stages of the study, when events moved at a faster tempo.

In this part of the work, the statistician spends a prescribed time at each field station, making home visits with the field worker, and reviewing methods of collecting and recording data. Another obligation is to check, in appropriate circumstances, observations made by the study group against official

records of the local health authorities. Summaries of current events likely to have influenced results require a co-operative staff effort. Ordinarily made on a monthly basis, they substitute for the daily diary recommended for the reconnaissance and organizational stages of the study, when events moved at a faster tempo.

In any long-term study, a periodic review of accomplishment is indispensable. Depending upon the size and nature of the project, this may be an annual report or one made at shorter intervals in the briefer field survey. The report assesses deficiencies in the collection of data and defects in experimental design, and identifies unproductive types of investigation. Perhaps the most important endeavor of all is the search by staff and advisory committee for new lines of inquiry, suggested by the data and developing in the course of the study.

The accumulated periodic reviews and reports set the pattern of final analysis. The first concern lies with the requirements of the stated hypothesis and the experimental design. Thereafter, the search is for ancillary information through unusual correlations to assure maximum yield from the data. Occasionally, these associated findings have equal significance with the direct objective. The work of bringing together the results of a long field study is little appreciated; in some instances, years have elapsed before it was finished. This makes formal publication of the plan of study, with major findings in preliminary form, an early obligation.

Direction of future research

The field study has now turned full circle, back to the point at which it began; the need is again for conceptual ideas. As the final obligation, the thoughts, the possibilities, and the suggestions for future research that have come from the study are set down in orderly fashion to ensure that subjects for future investigation are not forgotten with time.

The INCAP Field Study of Nutrition and Infection

The usual published report of a field experiment presents in orderly sequence an introduction, a list of materials and methods, the results attained, a discussion of the findings, and the conclusions reached. It tells little of the original incentive, the criteria for choice of method or of materials. Results follow in such logical order as to make one lose sight of dead ends, pauses for elaboration of necessary detail, or changes in emphasis as the investigation proceeded. The strategy can be traced, but the tactical development is obscure.

The purpose of this presentation would remain unfulfilled without brief consideration of these features. The illustration now presented is from

current practice; its aim is to show how principle was applied, how ecologic theory guided practice, and how action proceeded. Of necessity, this is drawn from personal experience. The choice is the field studies, at the Institute of Nutrition of Central America and Panama (INCAP), of the synergistic interaction of nutrition and infection, because these studies illustrate the long-term investigations now so much favored in field epidemiology and because the contribution of team effort in these larger endeavors becomes evident.

As so commonly happens, the conceptual idea originated from clinical observation. In this instance, independent and widely divergent sources eventually merged. Many years ago, when infectious diseases were more common, two communicable diseases frequently occurred concurrently in the same patient, usually as a result of a single exposure, their appearance being spaced by differences in incubation time. Complications in such instances were more frequent and fatality greater than the sum of expected effect from the two diseases when they occurred alone. Gordon (1932) applied the term "synergism" to this relationship, in analogy with the microbiologic designation of concerted action of two infectious agents.

Further clinical experience demonstrated a less frequent situation where concomitant infectious diseases produced the opposite effect of lower fatality, milder clinical course, and fewer complications. This was termed "antagonism"; multiple diseases sometimes seemed to hinder each other's progress. It was a far less common result than synergism. As would be anticipated, in some instances no modifying effect in either direction could be discerned.

The original concept related to infectious diseases, but the principle proved to be of broader application. A non-infectious disease with an infectious disease could induce a similar result, as could combinations of diseases unrelated to infection.

After comprehensive clinical experience in India, where coexisting diseases are commonplace, Taylor explored both the synergistic and antagonistic mass effect of concomitant diseases on general populations (Taylor & Gordon, 1953). Taylor extended these observations by laboratory experiments on the action of two associated viruses in tissue culture.

Later, in the course of field studies on population dynamics in the Punjab, Gordon, Taylor & Wyon established a prevailing synergism between acute diarrheal disease and the nutritional deficiencies of early childhood associated with weaning, and this came to be known as weanling diarrhea (Gordon et al., 1963).

Meanwhile, in Guatemala, and wholly independently, investigation of nutritional disorders among young children was taking the same direction. The Institute of Nutrition of Central America and Panama, under Scrimshaw's impetus, had long emphasized field observation in conjunction with laboratory and clinical research. The vital statistics of the country showed

a high death rate among children one to four years old, in addition to high infant mortality (Pan American Sanitary Bureau, 1964), but the recorded causes of death were suspect. Dietary surveys and clinical studies (Béhar et al., 1960) in the Guatemalan highlands established a high degree of malnutrition among rural children, especially protein deficiencies in pre-school children (Scrimshaw, 1959).

A survey of causes of death (Béhar et al., 1958a) showed that acute diarrheal disease and other infections were more often fatal in malnourished children aged one to four years than in well-nourished children (Scrimshaw, 1963). Furthermore, an infectious disease (Jelliffe, 1955), especially an acute diarrheal disorder, commonly preceded the appearance of the severe protein deficiency, kwashiorkor, by three to six weeks.

The association of malnutrition and intestinal infection was sufficiently regular to compel intensive study of diarrheal disease and its nature. Completed in 1957, these studies demonstrated that, although *Shigella* was frequently present in healthy rural children (Beck et al., 1957), clinical diarrheal disease was not regularly associated with the ordinary intestinal pathogens (Pierce et al., 1962), nor wholly dependent on environmental influences of sanitation and medical care (Scrimshaw et al., 1962; Bruch et al., 1963).

In 1958, chance brought Scrimshaw, Taylor, and Gordon together; and, in a year of common effort, they reviewed in detail the evidence on synergism and antagonism in its specific relation to nutrition and infection (Scrimshaw et al., 1959). With the help of several experienced consultants to INCAP in the fields of diarrheal disease and pathology, plans followed for a field investigation in Guatemala.

Field operations began in February 1959, with a pilot study to perfect methods and procedure. This phase was brief since much of the desired information about people and living conditions had accumulated during the exploratory studies, which were more numerous and extensive than usual. The experience of the pilot study was reviewed in May, and a revised plan was put into action that month as the definitive investigation. Field operations continued during the next five years, ending in 1964.

The experimental design called for children less than five years old in one rural village to live on the customary diet of the community, which was recognized as deficient. A medical clinic was established in the community, and provision was made for the home care of illnesses. A comprehensive program of preventive medicine was introduced, including immunization against preventable diseases, control of water and food supplies, fly control, and environmental sanitation through construction of privies and attention to wastes. A second child population of a distant village was provided with supplemental foods sufficient to give an optimal diet if consumed in the quantities provided. Medical care and environmental sanitation remained that of the usual village. A third population served as a control, with medical care, preventive medicine, and nutrition remaining unchanged.

In all three populations, resident village workers made regular home visits twice a month to learn of illnesses and to promote the particular program of that village. Bacteriologic surveys of the prevailing intestinal infectious agents were made every three months. All patients with acute diarrheal disease were studied as the disease developed, and bacteriological examinations were made. The nutritional status of childhood populations was measured quantitatively at suitable intervals by determinations of height, weight, skinfold thickness, and the presence or absence of a variety of classical signs and symptoms. Cases and deaths during outbreaks of communicable disease were plotted as a function of time, place, and person.

Some of the observations on acute diarrheal disease are presented in Chapter 6. They support and extend earlier studies in India and in the Arctic. The regularity with which the syndrome was again intimately related to nutritional practices reaffirmed its earlier characterization as "weanling diarrhea". The second-year death rate has proved as useful an index of the nutritional state of pre-school children as the better known infant mortality rate for general health practices (Gordon et al., 1967). A series of outbreaks of measles (Gordon et al., 1965b; Scrimshaw et al., 1966) and chickenpox (Salomón et al., 1966) in the rural villages and scattered cases of other common communicable diseases of childhood (Salomón et al., 1968) provided a further opportunity to compare the effects of nutrition on still other infectious diseases.

The more fundamental information derives from the almost daily records of illnesses, large and small; their number and their frequency; and the effect these illnesses have on growth and development, as determined by periodic measurements of height, weight, and bone maturation. These indices of the human ecology active in the formative years of early childhood portend the human resources of the future and therefore the economy and development of the region (Scrimshaw et al., 1967a, b, c, 1968; Ascoli et al., 1967; Gordon et al., 1968; Guzmán et al., 1968).

Comment

The study of disease as it occurs in nature, with the unit of observation a human population, is the basic concept of epidemiology. Its concern is population pathology. The observational unit distinguishes this approach from investigation of disease in the individual person (clinical pathology) and from disease of cells, tissues, or organs (microscopic pathology). The study of disease in groups of people takes different forms, through laboratory experiment, clinical investigation, or field study. If the findings relate directly to a specified population, or to representative fractions thereof, all are epidemiologic. The techniques, too, are from divergent sources: microbiology, genetics, sociology, statistics, and natural history.

The work of field epidemiology takes two directions: first, the practical service rendered by physicians in health departments and clinics in tracking down communicable and non-communicable disease, which constitutes operational epidemiology; and, second, the planned investigation in search of causes, origins, and distributions of a community disease or a physiologic state which is classed as analytical epidemiology.

The broad principles of ecology govern field study. Field method is no more than fundamental scientific method, based originally, as it is, on Baconian principles, refined by Claude Bernard, and turned to a special purpose. With its fundamental concepts of the significance of time, place, and person, field epidemiology naturally involves a sophisticated understanding of disease behavior under highly different situations.

Inevitably, field investigation ranges widely in order to recognize disease in the varied environments in which it occurs; it is more than geographic pathology and includes far more than what happens under the artificial conditions of crowded metropolitan communities. In temperate zones, diphtheria is a faucial disease; in the tropics, it is a skin disorder. The unusual behavior of a disease in exotic places often contributes fundamentally to knowledge, yet the quality of available data frequently is as incredible as the places from which the information comes. There is no substitute for first-hand observations.

A community of people serves as the field laboratory. The necessity for field investigation rests in the futility of attempting to divorce the study of what happens to man from what happens to his biological, social, and physical environment. Clinical entities as distinct as scarlet fever, erysipelas, and puerperal fever have a single infectious agent and constitute an epidemiologic entity. Other epidemiologic entities, such as aseptic meningitis and acute bacterial conjunctivitis, result from a variety of infectious agents, but the diseases they produce are clinically indistinguishable. Tularemia is a specific infectious disease, produced by a single infectious agent; yet it exhibits several epidemiologic patterns, each with its characteristic distributions by season, age, sex, and geography, as determined by deer-fly, tick, and rabbit.

The opportunities for serendipity are an attraction of field work. Investigation of almost any situation brings discovery of indirectly related or even unrelated phenomena, sometimes as important as the original study itself. A study of population dynamics in India gave insight into deaths from weaning diarrhea, later to be recognized as an epidemiologic entity.

This presentation has traced field method in principle from an original conceptual idea to construction of a hypothesis, then the plan for research and the process of fulfilling that plan, and, eventually, the interpretation of results and recognition of the next objective. The development of hypotheses is the crucial part of any investigation; the soundness of the research design is the main determinant of success. For these reasons, the emphasis

here has been on principle; and, as intriguing as it is, only minor attention has been accorded technical procedure.

Epidemiology takes many turns. Its modern development brings into play an imposing variety of scientific disciplines, both biological and sociological, so that it loses something of its original connotation. The laboratory now goes to the field, as does clinical medicine; and the field turns to the laboratory for confirmation and support of findings. Activities in office and laboratory sometimes dominate the work, with the result that the investigator misses the finest part of epidemiology—the personal and intimate familiarity with people in their natural environment.
