INTRODUCTION

Medical geography and epidemiology share the common goal of understanding disease processes and improving methods of health interventions. While they share a common history, the fields have diverged and developed different, often complementary, approaches to the same types of problems. Medical geography differs from epidemiology in its underlying focus on applying the concepts and methods of geography to investigate health-related topics (1). Much like other subdisciplines within its field, medical geography attempts to integrate concepts and methods from various social, physical, and biological sciences to create a unique specialty. Throughout much of its development and continuing to the present, the focus of medical geography remains very much on an ecologic perspective of health. Its emphasis is on the interplay of the behavior of humans and the environment to generate observed health outcomes so that, in addition to the traditional issue of spatial variation in disease incidence or prevalence, research related to understanding variation in individual risk perception and movement patterns has come into play (2, 3). Coupled with this is the practical application of these research issues, such as the optimal structure and network design of health care delivery systems (4).

In contrast, epidemiology is purposive for health promotion and disease prevention, with a focus on providing paradigms for the investigation of specific health problems and providing etiologic explanations for these problems, especially from a biological perspective (5). From a medical geography perspective, epidemiology provides an additional rich source of methods, concepts, and information that can be incorporated to study problems of interest.

Although antecedent, individual studies in medical geography exist, Meade et al. (1) trace the emergence of systematic interest in the field to the early 1950s. The field developed over the subsequent decade before a substantial international focus was created. Much of this delay reflected technologic limitations rather than conceptual difficulties (6). Recently created analytic methods and technologic advances suggest that it may be appropriate to reevaluate the contributions of each field to the study of problems of disease and disease control and the identification of areas of research in which the two fields can more actively interact with one another. This review focuses on recent technologic and analytic developments in medical geography, especially where they apply to epidemiologic study.

Epidemiology has, historically, been rooted in dealing with acute public health phenomena and has investigated these problems from the perspective of implicating specific agents and/or exposures as the cause of disease. This has led to a significant focus on study design and analytic methods. In contrast, medical geography has maintained an ecologic perspective to study disease patterns, especially emphasizing the cultural-environmental interactions that lead to disease events (7). Thus, while each deals with aspects considered by the other, the primary difference appears to be the focus of medical geography on the spatial context of health-related issues—an aspect that epidemiology recognizes but rarely explicitly considers.

In recent years, environmental epidemiology has bridged the distinction between medical geography and epidemiology. This occurred especially when environmental epidemiology shifted its focus to exposure-centered rather than disease outcomes. This shift has occurred because of the increased attention on chronic, degenerative diseases; because of the recognition that their etiologies are often multifactorial and dose dependent; and because of substantial technologic improvement in measuring environmental contaminants (8). These factors, in combination, have created conditions favoring an integrated, environmental approach in which the spatial relations of features, such as populations at risk and environmental pollu-
tants, are key and methods to assess exposure for the populations require a spatially explicit modeling of environmental conditions. This approach fits quite comfortably within the medical geographic approach while avoiding many of the difficulties associated with strictly group-level analyses. However, issues of “ecologic bias” will probably need to be considered and evaluated on a study-by-study basis.

**ANALYTIC APPROACHES**

Two major areas of analytic study and application in medical geography have been developing methods to identify disease clusters and applying methods to estimate conditions or outcomes in places where measurements have not been obtained. The first of these reflects a formalization of the methods of earlier efforts but also characterizes the important methodological issue to identify environmental conditions associated with rare disease events, such as (potential) clusters of childhood leukemia cases (9, 10), or acute disease events, such as zoonotic disease outbreaks (11). Identification of significant clustering then serves as the starting point for further investigation and the creation of hypothesized relations between the environment and health outcomes.

The perspective of spatial clusters that has developed recognizes that clustering occurs at a variety of spatial scales from regional to local scales. Underlying these can be geographic changes in risk factors, which introduce a degree of spatial autocorrelation in the outcome. Spatial autocorrelation of cases can occur because there is a contagious nature to the underlying process, as with many infectious diseases, because of a single time and place of exposure, or because there is localized heterogeneity in the environmental covariates of risk (12). Identification of risk factors and the extent of their effects (see below) that are used to adjust the spatial analysis need to be explicit (13).

Commonly, the approach for cluster identification is to partition the study region into a large number of small areas and identify stratum-specific reference rates that can be coupled with counts of the population at risk for each small area (14). Under the null hypothesis, the number of cases in each small area has a nominally Poisson distribution with the expected number of cases equal to the mean of the Poisson process. Clustering occurs when the departure from the null hypothesis results in increased variability in the number of cases (14). When arbitrary partitions of the study region, such as political boundaries, are made under the null hypothesis, the case locations become a realization of a nonhomogeneous Poisson process whose intensity depends on the strata-specific population distribution and large-scale geographic factors, making identification of the null model more problematic. Similarly, the distribution of environmental covariates affects the underlying model. Approaches for estimating the effects of environmental covariates are a significant focus of research (see below).

Distance methods have been an especially useful method of identifying clusters (14) and correspond closely in design to epidemiologic studies. Both methods rely on using locations of cases and controls to specify the nuisance function associated with local population structure (14). The method compares the spatial distribution of cases relative to a random labeling of the combined case and control locations (13). No particular distribution is assumed for either the cases or controls.

An alternative approach that explicitly addresses the spatial scale of clusters is proposed by Diggle (15). In this approach, the second-moment properties of the process generating the disease are used. The mean number of cases within a specified distance of an arbitrarily selected case is determined relative to the local population density, with the same term defined for the control series. The statistic is the difference between the two values over all distances. Positive values of the statistic are indicative of clustering. In both approaches (13, 15), the spatial distribution of the local population is a nuisance parameter that requires a random sample of unaffected individuals or sites. As such, both fall closely within case-control study design methodology.

Identification of clusters, however, does not address issues related to identifying the environmental determinants of disease. The presence of spatial variation in the underlying environmental risk factors and the estimation of their effects remains a substantial area of further research. In part, this reflects the underlying effect of spatial autocorrelation of environmental conditions. One recent approach to estimate these effects and partition their impact as local or regional follows from methods proposed by Cressie (16). The purpose of these analyses is to identify a suite of environmental covariates associated with the outcome variables of interest and relies on hierarchical modeling in which risk, the variable of interest, is unknown but the outcome—counts or locations of individual cases—is observed. The outcome is modeled as a function of the risk, e.g., in the situation of counts, a Poisson function might be appropriate. Then risk is modeled as a function of the environmental factors, which explicitly consider that variances are location specific and the spatial autocorrelation is used as a measure of spatial dependence among sites (12). Parameterizations for the spatial covariances follow standard structures used in geostatistics (16), and parameter estimation is per-
formed using the Monte Carlo Newton Raphson method proposed by McMullough (17).

Estimating outcomes or conditions at unmeasured sites has been an area of special concern in geography because of the (usually positive) spatial correlation among sites that renders the assumption of independent observations in traditional statistical methods inappropriate (18). Various methods have been proposed in geostatistics to efficiently interpolate spatial data. Statistical methods such as kriging, which represents the best linear unbiased predictor procedure to estimate surfaces, however, have the practical difficulty of overestimating low values and underestimating high values. Such an approach represents a practical difficulty if the surface being generated is related to disease risk.

METHODOLOGICAL DEVELOPMENTS

Probably the key development in medical geography during the past 15 years has been the increase in the availability and power of computing systems and the development of software to deal with the relations of spatially explicit data. Moore and Carpenter (18) provide an excellent summary of recent key studies applying geographic information systems (GIS) to epidemiologic research, as well as a summary of various spatial analytic approaches. The ability to input, store, manipulate, and present the spatial relation of health events to other key features of interest is the critical characteristic of the field. As such, GIS, which have experienced explosive growth as an application tool, are likely to continue to impact the field (6, 19), especially as these tools are coupled with epidemiologic analyses (20–22). Several studies have demonstrated the feasibility of using mapped environmental features, stored in GIS, as predictor variables for outcomes of epidemiologic studies with a substantial degree of success (22, 23). More recently, Cubbin et al. (24) explored using mapped environmental features to develop qualitative tests of hypotheses for three different social hypotheses related to patterns of violence. A key feature of these studies is that GIS was able to calculate variables that were, from a practical perspective, nearly impossible to obtain from field studies. Thus, the approach uses the observed occurrence of disease to identify the risk factors, based on stored environmental information, and then uses the spatial distribution of the identified environmental risk factors to characterize the sizes and locations of risk areas. These results can then be presented as maps to identify regions of high or low risk for the outcome.

Historically, GIS has relied on its cartographic influences that have minimized the extent of statistical analysis. This is evident in the limited number and types of statistics that are resident on most software systems. Most of these statistics are simple, univariate, first- and second-order statistics. However, as epidemiology and medical geography have begun to interact in this area, we can anticipate that there will be substantial cross-fertilization of approaches.

One area that GIS has significantly impacted is applied medical geography. In particular, the design and development of health systems (4) and studies of the patterns of land use (25, 26) for planning have incorporated GIS technology and methodology heavily. This suggests that GIS might similarly impact several aspects of applied epidemiology, such as identification of study populations. For example, GIS was used to overlay environmental risk factors for Lyme disease with street address maps to recruit volunteers for a vaccine trial study (6). This stratification procedure produced a significant enrichment in the numbers of at-risk individuals relative to that obtained by other methods.

FUTURE DIRECTIONS

The conceptual framework of environmental epidemiology, especially when it focuses on exposures or the multifactorial nature of many chronic diseases, provides an excellent starting point for communication between epidemiologists and medical geographers. The most critical area for future development that would provide an area of common communication is spatial analysis. The appropriate methods for dealing with spatially autocorrelated health outcomes, either because they are by their nature autocorrelated or because of the spatial pattern of underlying environmental risk factors, remains an area that must be addressed. Substantial progress has been made in the past decade in dealing with spatially explicit data, but methods need to be developed to deal with estimation procedures and study design. For example, common study designs, such as matched case-control designs, are poorly characterized for spatially explicit situations (27). In unmatched designs, under the null hypothesis, the spatial distributions of cases and controls are assumed to be drawn from the same, underlying spatial pattern so that the expected difference in their distributions is zero. However, in matched designs, even under the null model using random relabeling of points, the expected difference in their distributions is no longer zero.

In applied and environmental epidemiology studies, we can anticipate an increased need for up-to-date, accurate measures of environmental conditions that extend over large geographic regions. Increasingly, remotely sensed data gathered from various platforms, such as satellites, provide real-time or near real-time
characterization of the environment that are used to interpret the dynamics of environmental conditions that could impact health outcomes. GIS provides an important methodology that bridges epidemiology and medical geography by providing the tools for explicit spatial characterization of data. However, a practical issue with these systems will be the substantial size of the environmental data generated (often reaching terabytes of data) at high repeat frequencies (days or weeks). Analyzing and interpreting results from these inputs will provide a substantial challenge that cannot be met by traditional data analytic and management approaches (28). Methods such as context-based data search and retrieval, which abstract the data with no loss of relevant information, will need to be developed further to deal with these issues (28).

Integration and analysis of distributed data sets will represent a serious issue in the near future as well, especially as they relate to data quality. Development of standards for data quality and the appropriate metadata needed for both efficient searching and documentation of quality are still being created. The Federal Geographic Data Committee and the National Spatial Data Infrastructure represent attempts to coordinate geographic data that would meet appropriate standards for data quality.

ACKNOWLEDGMENTS

Supported by an NASA Earth Sciences Enterprise program ESIP to IBM T. J. Watson Research Center NCC 5–305.

The author thanks Drs. A. Das, S. R. Lele, and N. Cressie for their discussion of the issues involved with spatial analyses.

REFERENCES