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Changing Research Methods in Environmental Epidemiology

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Abstract. The recent report of the epidemiologic study in Woburn, Massachusetts has focussed renewed attention upon the methods used by epidemiologists and other public health professionals in evaluating the health impact of environmental exposures. Much attention has been given to the statistical methods by which the data gathered in epidemiologic studies, both observational and demographic, should be analyzed. Epidemiologic methods have not been accorded as much attention, although the development and validation of such techniques is vital to the progress of environmental epidemiology. An annual meeting at which recent epidemiologic and statistical methodologic advances would be discussed could greatly help the epidemiologic community in quickly assimilating such knowledge. Less emphasis has also been given to the means by which those data are collected during the study. Several approaches to dealing with the problems faced by environmental epidemiologists in collecting data are discussed, such as the development of national population-based disease registries. The use of such national data sets, such as the NHANES and NHDS data bases, are also noted. An audit of the national vital statistics system is suggested, insofar as it can serve as an indicator of sentinel health events. Similar assessments of other national statistics systems, such as those maintained by the Centers for Disease Control, are also needed.

Key words and phrases: Health outcomes, epidemiologic methods, environmental epidemiology, environmental health statistics, exposure assessment, disease registries.

1. INTRODUCTION

The domain of environmental epidemiology, both occupational and nonoccupational, has expanded greatly in the past decade. The results of environmental epidemiologic endeavors have had a marked impact on our society, to a degree unimagined by epidemiologists, statisticians and environmental engineers twenty years ago (Lilienfeld and Lilienfeld, 1977; Lilienfeld, 1980; Lilienfeld, 1983; Susser, 1973). Consider for a moment the importance of such work in the Mansville bankruptcy or in the banning of various chemical processes (Whorton, Krauss and Marshall, 1977; Whorton, Milby, Krauss and Stubbs, 1979; Taylor, Selhorst and Calabrese, 1980). Without environmental epidemiologic data, such events would not have occurred.

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It should be remembered that environmental epidemiology is an inherently interdisciplinary pursuit. It is difficult to imagine an environmental epidemiologic study that did not involve at least an epidemiologist, a biostatistician and an industrial hygienist. Of course, other areas of expertise are usually required in such a study. For instance, when studying the health outcomes of an environmental exposure to dioxins, a toxicologist is invaluable for focussing on the outcomes of interest and for constructing biologically plausible models of action.

Recently, several investigators at the Harvard School of Public Health reported the results of an investigation of the health effects associated with the consumption of water contaminated with trichloroethylene in Woburn, Massachusetts (Lagakos, Wessen and Zelen, 1986). The study was notable both for its findings, which included showing that a relationship existed between consumption of the contaminated water and leukemia, and for its methods, particularly the manner in which the investigators estimated the amount of trichloroethylene that an

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individual had consumed. Unfortunately, the data in the study were collected by individuals in the study population, which likely biased the data (MacMahon, 1986; Whittemore, 1986). There were other methodologic difficulties in this study, which have been addressed by MacMahon, Whittemore and other workers in a recent issue of. the *Journal of the American Statistical Association* (MacMahon, 1986; Whittemore, 1986; Rogan, 1986). Suffice it to say that one of the reasons that the Woburn study attracted much attention on the part of environmental epidemiologists was its investigator's method of estimating who had been exposed to what and when they were exposed. Indeed, it is the assessment of exposure that is the cornerstone of any environmental epidemiologic study (Walker and Blettner, 1985; Landrigan, Melius, Rinsky and Thun, 1985).

2. ADVANCES IN EXPOSURE ASSESSMENT

The most direct means of ascertaining exposure is through measurements of the chemicals of interest to which the individual is exposed (Blot and Fraumeni, 1986; Landrigan, 1983; National Academy of Sciences, 1985; Rinsky, Smith, Hornung, Filloon, Young, Okun and Landrigan, in press). For example, in the occupational environment, the epidemiologist usually must rely on an industrial hygienist for information on which jobs in a factory involve exposure to what chemicals and at what level. An example where such information was critical to the study design is the recent investigation of the relationship between benzene exposure and subsequent mortality from myelogenous leukemia in two plants in Ohio by Rinsky and his colleagues at the NIOSH (Rinsky, Smith, Hornung, Filloon, Young, Okun and Landrigan, 1987). They were able to locate industrial hygiene data for benzene exposure for all of the jobs at the plants. They were therefore able to relate the dose of benzene received with leukemia mortality among the plants' workers. Their major finding was that workers exposed to benzene at the upper limit of the current OSHA standard of 10 ppm had a Standardized Mortality Ratio of 4000. Without the industrial hygiene measurements, that finding would not have been made.

I should note that Rinsky and his colleagues had to manually locate each of the industrial hygiene measurements on their own. This was a time-consuming process, one that generally cuts down markedly on the productivity of the environmental epidemiologist. Frequently, these measurements are not even accessible by the epidemiologist some thirty or forty years (a typical latency period) after they had been made (Armenian and Lilienfeld, 1983). During the past decade, there have many advances in computer technology which may provide a cost-effective means by which such data can be used. Our colleagues in pharmacoepidemiology have made use of several prepaid medical care and statewide Medicaid data sets to examine the relationship between pharmaceutical use and subsequent disease occurrence (Strom, 1987). The pharmaceutical use, hospitalization discharge diagnosis and outpatient visit diagnosis data are routinely collected by these health care delivery systems as part of their billing systems. As these data are already on a computer, all that the pharmacoepidemiologist must do to collect his data to link the pharmaceutical use with subsequent outpatient diagnoses or hospitalization discharge diagnoses. There are, to be sure, many caveats to this approach, such as validating diagnoses, and so on (Shapiro, 1987). Nonetheless, there are many advantages to it, as well, such as the low cost and the fact that the data are not subject to the recall biases present in many epidemiologic studies (Avorn, 1987). Environmental epidemiologists can easily adopt this approach. For example, one major corporation, General Electric (GE), has placed its industrial hygiene data on a computer. The GE occupational epidemiologists plan to link these data with mortality data collected on an annual basis from the National Death Index (NDI) and Social Security Administration records. Several other corporations have similar efforts in linking industrial hygiene data which is maintained on a computer and mortality data from the NDI and Social Security Administration records. Indeed, the First International Workshop on Data Banks in Occupational Health was held in 1986 and a second meeting is planned for October 1988.

An alternative approach to the issue of determining exposure is the addition of occupational and residential information to the battery of data collected at the time of enrollment into a prepaid medical care system, such as Kaiser Permanente or other HMOs in the United States. At the time of annual renewal, these data could be updated. A standardized residential and occupational history form could be used for obtaining this data. An example of such a form has been developed by Swanson and her colleagues at the Michigan Cancer Foundation (Swanson, Schwartz and Brown, 1985). An advantage to such a data collection scheme would be the ability to examine the interaction between "environmental" exposures and pharmaceutical ones. The recent work of Shapiro and his colleagues in the International Aplastic Anemia Study, in which the association between dipyrone and aplastic anemia was found to be dependent upon the area of Europe in which the study was conducted, illustrates the importance of such a consideration (International

Agranulocytosis and Aplastic Anemia Study Team, 1986; Shapiro and Levy, 1986).

Another of the means used to assess exposure is the amount of the chemical of concern present in an individual's blood. Those individuals with higher concentrations of the chemical are presumed to have had a greater exposure to it than those with lower ones. Unfortunately, there are few data sets in which blood has been collected which is also available for use in an environmental epidemiologic study. However, one data set holds particular interest for the environmental epidemiologist: the National Health and Nutritional Examination Survey (NHANES), which collects information for a national sample of the United States population at a given point in time (Feinleib and Feldman, 1984; United States Public Health Service, 1978). This information includes serum levels of various chemicals. The potential uses of this data set by the environmental epidemiologist are seemingly endless. Of course, one of the big advantages of the NHANES data set is that the data have already been collected!

Recently, technology has been developed for the quick assessment of subclinical neurotoxicity (Letz and Baker, 1986). It will be used in the next cycle of NHANES (NHANES III) (personal communication, E. Baker). Similarly, new technology for exposure assessment should also be added to the NHANES. For example, during the past five years, x-ray fluorescence has been developed to the degree that if applied to the tibia, one can estimate the body burden of metals such as lead (Wielopolski, Ellis, Vaswani, et al., 1986; Somervaille, Chettle and Scott, 1985). Hence, rather than relying exclusively on such measures as the blood level of a given metal, which may reflect recent exposures, the environmental epidemiologist can use these estimates of metallic body burden to evaluate the effects of long-term exposures (Wielopolski, Ellis, Vaswani, Cohn, Greenberg, Puschett, Parkinson, Fetterolf and Landrigan, 1986). As other markers both of short- and long-term exposures and of various health outcomes are developed, they too should be incorporated into these surveys (Harris, Vahakangas, Autrup, Trivers, Shamsuddin, Trump, Boman and Mann, 1985; Wogan and Gorelick, 1985).

3. DEVELOPMENTS IN MEASURING HEALTH OUTCOMES

Much of what I have been discussing has concerned exposure. Health outcomes are also of interest to the environmental epidemiologist. The National Hospital Discharge Survey, also collected by the NCHS on an on-going basis, provides hospitalization rates for various diseases, ranging from pneumoconioses to aortic aneurysms (Feinleib and Feldman, 1984; U. S. Department of Health and Human Services, 1986). These data are descriptive in nature; they can provide a starting point for an epidemiologic discussion of such diseases as aortic aneurysms or idiopathic dilated cardiomyopathy that may be related to environmental exposures but which are otherwise extremely difficult to develop an epidemiologic profile for. The NHDS data set can also be used for examining secular trends in surgical procedure rates, which may reflect the incidence and prevalence of diseases which are environmentally related, although not currently thought of as such.

Another system for evaluating trends is afforded by the national vital statistics system. Mortality trends and differentials can provide much insight into the epidemiology of a given condition and suggest what agents may be worthwhile investigating (Perlman, Leaverton, Massé and Lafferty, 1982). Unfortunately, this particular data system is in need of a "tune-up." Audits are needed at both the state and the national level to determine what is the accuracy of death certificate cause-of-death statements and of other death certificate data, such as occupation. The latter need evaluation with regard to the demographic characteristics of the physician and funeral director who have completed the form. Analyses are also needed concerning trends and differentials at the state and national levels of disease-specific autopsy data. These audits and analyses are necessary to provide a base for the epidemiologic use of the national vital statistics system. In some cases, the last such analyses are at least thirty years old and are, therefore, in need of updating (U. S. Department of Health and Human Services, 1982). An example of the need for such updating is provided by our experience in Minnesota. At the Minnesota Department of Health, mortality statistics provide a basis for epidemiologic inquiry and public health action. In the case of asbestos, for instance, malignant mesothelioma mortality provides a low-cost means of evaluating which regions in the state may have had environmental exposures to asbestos (Lilienfeld and Gunderson, 1986a, 1986b). This information was important both in suggesting the possible sources of a presumed exposure and in pinpointing which regions of the state would be in need of increased health care as a result of that exposure (cancer screening programs, as well as treatment). We found that pleural malignant mesothelioma is miscoded as a cause of death; it is tabulated as lung cancer, or as cancer of the thorax, not otherwise specified, or as cancer, not otherwise specified. (This is the situation when a mesothelioma is listed on the death certificate.) It is doubtful that mesothelioma is the only entity that is undercounted in the nation's vital statistics register (Percy, Stanek and Gloeckler, 1981). The audits would pinpoint which diseases are undercounted and by how much and, similarly, for overcounted conditions, by how much. A similar call for an audit can be made for the data collection systems run by the Centers for Disease Control (Seta and Sundin, 1985). Environmental epidemiologists must know, for example, what the quality of the CDC congenital defects data is before such data can be properly interpreted.

The last methodologic suggestion that I have is for the epidemiologic community to call for the development of population-based disease registries. During the past six months, the value of the SEER cancer registries was seen when our symposium chairperson reviewed SEER incidence data (Bailar and Smith, 1986). He and Smith were able to infer that the "war on cancer" was not going well and needed some epidemiologic insights. Although the SEER program has its difficulties, which are beyond the scope of this discussion, it has also highlighted the importance of having an available pool of diagnostically-confirmed cases for retrospective studies. Unfortunately, case ascertainment is one of the most difficult and expensive tasks in an epidemiologic retrospective study. It is even more of a problem in prospective ones. Even though the start-up costs for such registries might be high, the epidemiologic community (environmental and nonenvironmental) will benefit greatly in the long run with the lower costs of conducting epidemiologic studies.

4. TRAINING INITIATIVES

Of course, with so many potential approaches to environmental epidemiologic research, a question that must be asked is: Who will do all of this work? Unfortunately, space does not allow for a complete discussion of the need for new training initiatives in environmental epidemiology, including the development of prebaccalaureate programs (Lilienfeld, Garagliano and Lilienfeld, 1978; Lilienfeld, 1979; Fraser, 1987). It would be useful to have some discussion of this need, both in terms of the demand and the new programs needed to meet it. Suffice it to say that the needed additional personnel are yet to be recruited and trained. A related area is the need for new forums for the presentation of research results and, perhaps more importantly, discussions of the current research directions in environmental health, generally, and environmental epidemiology, in particular. Such discussions should extend to the current programmatic priorities of the federal government, particularly the agencies of the Public Health Service. In this manner, advances can be incorporated into these programs and the impact of the programs themselves greatly increased.

5. THE SOCIAL CONTEXT OF ENVIRONMENTAL EPIDEMIOLOGY

Another area in environmental epidemiology that is changing is the interface between it and the general public. It is difficult to conduct an epidemiologic study without public co-operation and participation. Generally, the public has been willing to support and participate in epidemiologic studies. However, the epidemiologic community has been so successful in our research that the general public has come to expect answers from us that we simply cannot provide. Also, there is a movement afoot "in the land" for communities to conduct their own epidemiologic studies, using community members as interviewers, data clerks and so on (Legator, Harper and Scott, 1985). It is not too difficult to see many "mini-Woburn" studies being conducted in the not-too-distant future. Clearly, such studies could produce much information about the relationship between exposures and diseases that would be uninterpretable. But the general public has not been educated as to the reasons for this. I would propose that the epidemiologic community embark upon a concerned program of public education about epidemiology, epidemiologic studies and what the strengths and limitations are to the epidemiologic approach to examining the health effects associated with environmental exposures. A particular group for which such a program would be beneficial is the press. Environmental epidemiologists and the press are not always on the best of terms with each other. Frequently, I have found, this situation is the result of a lack of familiarity by some members of the press with epidemiology. The American Heart Association holds an annual meeting with the press to review the year's developments in cardiovascular disease. Perhaps we in epidemiology should do likewise.

Lastly, there is a need for marked reform in the federal Privacy Act. Recently, in Minnesota, several epidemiologists were informed that at the conclusion of 1986, their access to hospital records (even to identify a physician who can be contacted to obtain a patient's consent to participate in a study) would cease as a result of recent court rulings and increased liability insurance costs (Russell, Bartels, Kappel and Rhame, 1986). The interpretation of the current law by the courts poses a great danger to much of the epidemiologic enterprise in the United States and the environmental epidemiologist is not immune to these developments. As I had commented earlier when discussing disease registries, without access to cases, the environmental epidemiologist will have a great problem in conducting much research.

TABLE 1
Potential research resources in environmental epidemiology

1. Development of occupational and residential history components in current HMO data sets
2. Utilization of existing population-based data sets ("Piggyback")
NHANES
Corporate data sets, General Electric
3. Development of exposure assessment technology (tibial bone lead amounts)
4. Utilization of national vital (and other health) statistics system
Audit of national vital statistics system
Expansion of current set of data elements (occupation)
5. Development of disease registries
Population-based
National coverage

6. CONCLUSION

The areas of environmental epidemiologic endeavor that I have discussed are summarized in Table 1. They cover a wide variety of statistical data types. Mortality and morbidity statistics, existing and future data sets and traditional and newly developed techniques of exposure assessment are all part of the changing landscape of methods used in environmental epidemiology. In some instances, such as the development of disease registries, the opportunity for implementing these techniques is present. In a decade or two, legal and financial restraints may not allow for such a development. As for the addition of occupational and residential histories to other health data set components, the time for such action is *now*. The data will then be available when needed during the next decade or two. Considering the methodologic advances that have attended environmental epidemiology during the past two decades, however, I am confident that many of these research resources will be developed and exploited by the epidemiologic and biostatistical communities.

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