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Changing Policy Roles of Environmental Epidemiology

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Abstract. This paper discusses the evolving interdependent relationship between environmental sciences (such as epidemiology) and environmental law and regulation. Societal needs for expert evaluations of the potential hazards of toxic chemicals have tremendously influenced the development of toxicology and epidemiology. In this regard, much recent environmental law reflects its "shotgun wedding" with environmental science; these science-forcing laws require that regulatory agencies take action based on findings that may be at or, very often beyond, the frontiers of environmental science.

Recent developments in environmental law and the growth of the animal protection movement have independently contributed to renewed interest in and heightened expectations for the role of epidemiology in developing environmental standards and actions. Those who oppose animal experimentation often argue that data on humans are required to estimate human effects; some recent laws, such as Superfund, mandate consideration of human health assessments as one of the bases for deciding whether and how best to clean up abandoned hazardous waste sites.

Requiring epidemiologic confirmation of hazards would make evidence of human harm a prerequisite for regulatory action. Because the animal models and statistical tests on which much environmental regulation now rests are models designed to anticipate human and environmental effects, their statistical validation and development remain crucial to the development and application of environmental law. For the most part, epidemiology is best suited for confirming past risks and not for predicting and preventing future risks.

Key words and phrases: Epidemiology, animal models, environmental law, toxicology, risk assessment, paradigm.

This paper reviews briefly the relationship of environmental science and law and discusses judicial reviews of lead regulation as an illustration of the basic science-forcing nature of recent environmental policy and laws. It also discusses the historic shift from a research paradigm based on pharmacology to one based on toxicology and recent factors that encourage the use of epidemiology to estimate likely human risk and develop environmental standards. Finally, it concludes that regulatory policies that require epidemiologic confirmation of hazards exact a double-edged penalty: they impede the development of policies that anticipate and prevent risks; and they restrict agencies to reactive policies deriving from the confirmation of human harm.

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SHOTGUN WEDDING OF EPIDEMIOLOGY AND ENVIRONMENTAL POLICY

Epidemiology and environmental law evolved independently and only recently were forced to co-develop. The relationship of environmental law and science may be characterized as an uneasy partnership. When courts have reviewed agency decisions based on risk assessments, the term "shotgun wedding" has been used to describe the enforced intimacy between science and law (Davis, 1985).

BASIC SCIENCE-FORCING LAWS

During its environmental heyday in the 1970s, Congress passed several laws that may be thought of as

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"basic science-forcing." Laws such as the Clean Air Act Amendments of 1970 and the Toxic Substances Control Act laws authorized agencies to act when it can be demonstrated that a given compound poses or may pose an unreasonable risk of causing significant adverse health effects. Such laws may be based on agency findings made at or beyond the frontiers of scientific inquiry. (See, e.g., 33 USC §§1251(d), 1252, 1254, 1361 (1982); 42 USC §§7403(b), 7404(b), 7407(C), 7408, 7601 (1982). For a summary of provisions in the major environmental statutes that authorize agencies to regulate at the frontiers of scientific knowledge, see Appendix I, U. S. Environmental Protection Agency (EPA), Chemical Substances Designation (1981).) To make such findings, public administrators increasingly rely on a variety of scientific techniques for assessing risks to human health. (The agencies' use of risk assessment in regulatory decision making has been the subject of considerable commentary by scientists and legal scholars. See Risk Assessment in the Federal Government: Managing the Process, National Research Council, 1983.)

Many risk-assessment techniques are highly speculative, and almost all rely upon multiple assumptions of fact, some of which may be entirely untestable (National Research Council, 1983; 1986). In this regard, preventing or reducing exposure to toxic chemicals can be viewed as a form of preventive medicine and environmental management. For effects of interest, such as neurologic diseases, no methods are generally agreed for evaluating this potential. For others, such as cancer, statistically validated animal models of human hazard have been generally accepted, but are not without critics as to their direct and universal relevance to humans.

Given the anticipatory, preventive thrust of these basic science-forcing environmental laws, toxicology and related experimental techniques for estimating risks were expected to play an important role in identifying priority problems and establishing environmental standards. In early stages of environmental law, courts tended to interpret experimental and theoretical evidence liberally that a given exposure constituted an unreasonable risk. Environmental regulatory needs pushed and prodded science to devise methods for anticipating and predicting harm to public health and environment. As a retrospective science, epidemiology probably was not expected to play a major role in the development of preventive regulatory policy, except insofar as new exposures could be expected to be similar to previously documented ones.

ANTICIPATORY POLICIES

Some early U. S. case law developed when courts reviewed agency actions and should be reviewed when considering anticipatory policies. In *Ethyl Corporation v U.S. Environmental Protection Agency*, [541 F2d at 13; cert. denied, 426 US 941 1976], the D. C. Circuit Court of Appeals found that the level of proof required under the Clean Air Act for a finding of endangerment did not require proof of actual harm to humans, but only proof of a "significant risk of harm." Indeed, the agency was not even required to prove that harm was "probable," but rather that there was a rational basis for inferring harm. In this case, the inferred harm was presumed to affect the intellectual growth and development of inner city children. Later studies showed that all children are at risk. EPA based its decision on three types of evidence: theoretical modeling of lead dust, epidemiologic and clinical studies of exposed populations and laboratory studies of animals. The court argued that where the risk averted was of major consequence, conclusive proof was not required. In a later case on the same issue [*Lead Industries Association v U.S. Environmental Protection Agency* (647 F.2d 1130 (D.C. Cir. 1980), cert denied, 449 U.S. 1042 (1982)], the D. C. Circuit Court of Appeals upheld EPA's air quality standards for lead, commenting that conflicting evidence did not undermine agency action. As long as EPA could show a rational (and reviewable) basis for its actions, it could rely on evidence on the frontiers of science.

PARADIGMS OF THE USE OF EPIDEMIOLOGY IN ENVIRONMENTAL POLICY

Some science historians consider that science evolves through paradigms or periods, which may be characterized by a typical, shared approach to problem solving and objects of study.

> "[S]ome accepted examples of actual scientific practice provide models from which spring particular coherent traditions of scientific research .... The study of paradigms ... is what mainly prepares the student for membership in the particular scientific community in which he will later practice. Because he there joins persons who learned the bases of their field from the same concrete models, his subsequent practice will seldom evoke overt disagreement over fundamentals. Those whose research is based on shared paradigms are committed to the same rules and standards for scientific practice. That commitment and the apparent consensus it produces are prerequisites for normal science, i.e., for the genesis and continuation of a particular research tradition. These periods are marked by the dominance of certain rules for what constitutes the normal practice or paradigm of science." (Kuhn, 1973)

The advantage of "normal science" is that it provides uniformity and consensus; however, when some new problems do not fit prevailing paradigms, challenges arise. These challenges may be bitter and protracted disputes, but they ultimately produce paradigmatic change. Kuhn and others refer to extraordinary episodes in which changes of scientific commitment and practice occur as scientific revolutions, marked by paradigm shifts. Thus, the dominant paradigm of science shifted from Galilean to Copernican cosmology and from the physics of Newton to those of Einstein (for most applications).

This concept of paradigms in science is rooted in the study of science as science and not so much in science as a social institution. However, science exists, thrives or suffers along with the society in which it is undertaken. In the case of environmental sciences, societal needs for expert evaluations of potential hazards of toxic chemicals have tremendously influenced the development of pharmacology, toxicology and epidemiology, and the shift of public interest in these respective fields.

THE PARADIGM OF PHARMACOLOGY

Twenty five years ago, no graduate degrees in toxicology were granted, and environmental epidemiology existed as a footnote. Pharmacology, with its emphasis on developing therapeutic drugs, offered the chief research relevant to the development of environmental standards. Prevailing rules and methods of pharmacologic research derive from classic medical research and the writings of Claude Bernard (Cranefield, 1976). Early studies are characterized by detailed case histories of the responses of a few animals or people. The study subjects were sometimes volunteers or medical pioneers (Richardson, 1970) and often were those with limited freedom, such as prisoners and prostitutes; seldom were control subjects used.

Thus, some of the earliest published DDT research involves single subjects who were observed for periods ranging from 1 day to several weeks to determine whether gross or acute effects occurred (Cameron and Burgess, 1945; Haag, Finnegan, Larson, Dreyfuss, Main and Riese, 1948). According to the prevailing pharmacologic approach, such case studies constituted a reasonable basis to conclude that DDT was a safe chemical, when used as directed. This approach did not consider that chemical effects could occur twenty or thirty years after exposures, and that worse things than immediate- and short-term skin rashes or stomach-aches might be involved. Rarely were statistical evaluations undertaken of those small numbers of subjects studied.

This pharmacologic approach to screening chemicals advocated the careful study of a few animals to assess potentially acute effects of pesticides. Two factors began to challenge this pharmacologic approach to testing. First it was realized that within animals and between species, severity of effects could vary several hundred times. Second, the public health risks of chronic diseases with long latencies, such as cancer and heart disease, became more widely known, along with the need for longer term studies with statistical power (Davis, Mandula and Van Ryzin, 1985).

THE TOXICOLOGIC PARADIGM

Other circumstances have also bolstered the growth of toxicologic studies of chemicals. Where previously, acute effects ranging from skin irritation through death were noted, now subtle chronic effects, ranging from behavioral and reproductive hazards through complex, chronic degenerative diseases such as atherosclerosis and cancer are now studied.

The toxicologic approach considers that, given the heterogeneity of species and within species, statistical samplings of sufficiently large numbers of animals are necessary to assess the relative risks of a substance. Case studies of a single organism are valuable but cannot provide the basis for assessing and extrapolating the risk or safety of a substance for a population. Rather, toxicology protocols require the long-term, two-year evaluation of different dose levels in sufficient numbers of test animals to determine statistical significance.

EARLY APPLICATIONS OF EPIDEMIOLOGY TO ENVIRONMENTAL EXPOSURES

Some of the early epidemiologic studies of DDT were flawed in important ways reflecting the pharmacologic paradigm. Laws, Curley and Biros (1967) studied 35 men out of 1263 employees of Montrose Chemical Corporation. The major selection criterion was a work history of more than five years of relatively heavy occupational exposure to DDT. Exposure was determined subjectively by the men and their supervisors. Of 63 men who met this criterion, 35 were selected for study. It is possible that those not studied had significantly different pathologies than those that were ultimately examined. Even with this major flaw, the study found chronic disease problems. For instance, even this restricted study population of 35 men had an incidence of diabetes mellitus of 8.6% compared with about 2.5% in the general population, a greater than 3-fold increase in the crude relative risk of diabetes. The authors did not comment on this finding, although the earliest critics of DDT indicated disturbance of endocrinologic function and that diabetes might be associated with exposure. Blood disorders in the study populations were also not analyzed as to their significance.

This failure to consider the biologic importance of diabetes and blood disorders bespeaks the fact that early epidemiologic studies of environmental chemicals fell under the pharmacologic paradigm, with its emphasis on immediate, acute, gross problems, as opposed to chronic, long-term and less dramatic ones.

SOME RESERVATIONS ABOUT USE OF EPIDEMIOLOGY IN ENVIRONMENTAL POLICY TODAY

Recent basis science-forcing laws laid a framework and stimulated funding for research and development of toxicologic tests to predict and anticipate human risks. However, precisely because the animal models on which much environmental regulation rests are *models* designed to anticipate human and environmental effects, their validation and development remain the subject of intense debate.

Role of Animal Protection Movement

The growing movement of opposition to animal testing also adds to the pressures on in vivo toxicologic research on whole animals. Such groups argue that toxicologic tests are invalid predictors of human harm. They recommend that computer simulators be used, and an emerging consequence of this position is a resurgence of requests for direct human data.

Expanded Role for Epidemiology in Risk Assessment Activities

Questions about quantifying risks for humans based on the animal data often lead to calls for epidemiologic confirmation of most risk assessments. I want to suggest briefly why this is a mistaken notion.

First, many compounds of regulatory interest cannot be studied with the tools of epidemiology. Exposures may be erratic, records on exposures might not be able to be reconstructed or the exposed population may be too small to permit statistical evaluation of health status (Karstadt, Bobal and Selikoff, 1981; Karstadt and Bobal, 1982).

Second, where studies do exist on exposures to toxic chemicals, these commonly involve worker populations, which are generally healthy, working persons and not the typical U. S. population of young, old and ill persons, as well as the healthy working population (Halperin, Beaumont, Brown, Clapp, Haring, McCammon, Meinhardt, Okun, Reeve, Rinsky, Roscoe, Smith, Stayner, Stern, Ward and Bazas, 1986).

Finally, for many compounds of interest, such as ethylene oxide or the new generation of pesticides, chronic health effects with longer latencies may be involved. Production of many synthetic organic chemicals doubled in the 1970s from that of the 1960s (Davis, 1987). Chronic effects of these exposures may not be evident until the end of this century.

EXPANDED ROLE FOR EPIDEMIOLOGY UNDER SUPERFUND

Unlike many sciences that draw on statistics and are permitted relative obscurity, epidemiology captures much public attention. As one researcher put it, "if you ever want to be intensely peer reviewed, produce a study that has millions of dollars of regulatory consequences." Love Canal, Alsea, Times Beach and Woburn all have in common that they were places of well-publicized toxic pollution and subjects of multimillion dollar lawsuits. Objective information in these circumstances may be an oxymoron.

It is useful to think of two fundamentally distinct types of environmental policy—those that are reactive, with which we are all familiar, and those that are anticipatory. Anticipatory policies are designed to prevent environmental impacts before they occur. Of necessity, epidemiologic studies will provide reactive confirmation of past hazards; for the primary prevention of disease or other adverse impacts on humans, experimental techniques and models of human risk based on animal data remain essential.

Let me close with a warning about some new directions for epidemiology that may prove to be a new "catch 22" hidden in the latest Superfund law. In December 1980, in the wake of such incidents as Love Canal and the Valley of the Drums, Congress passed the Comprehensive Environmental Response, Compensation, and Liability Act—commonly known as Superfund. Superfund established a program to identify sites from which releases of hazardous substances into the environment might occur or have occurred, to ensure that sites are cleaned up by responsible parties or the government, to evaluate damages to natural resources and to create a claims procedure for parties who have cleaned up sites or spent money to restore natural resources. Recent amendments to Superfund call for health assessments of proposed sites for clean up. These health assessments can include epidemiologic studies of exposed persons. Conventional epidemiologic studies of many potential Superfund sites are likely to be problematic, despite their obvious promise for graduate student training programs. To be effective, such health assessments would need to rely heavily on experimental models of adverse health consequences, because the numbers of persons involved will often be too small to permit their statistical significance to be evaluated, and exposed populations will be difficult to ascertain. No amount of congressional wishing nor political jockeying will alter this: as in most other studies, epidemiologic studies in

these situations will confirm past damage but will do little to prevent or predict future harm. For the primary prevention of disease or other adverse impacts on humans, experimental techniques and models of human risk based on animal data remain essential (National Research Council, 1988).

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