

HEALTH INTELLIGENCE FOR ENVIRONMENTAL PROTECTION: A DEMANDING CHALLENGE

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1. Health research goals

The health research program of the Environmental Protection Agency has three major goals. The first goal is to minimize the adverse effects of the environment upon human health by preventing exposure to harmful new environmental agents, by reducing exposures to existing pollutants and by predicting the adverse effects of proposed environmental control options. The second goal is to quantitate the health benefits of environmental controls and the third is to optimize the environment for man's health and well being. Progress is being made toward each of these goals but the pace must quicken.

A number of Federal programs, many well established and several newly proposed, serve interlocking functions in preventing exposure to harmful new agents; three new approaches are of special interest. The Toxic Substances Act, now being considered by the Congress, would fill an important gap in existing regulatory authority. Essentially, this Act would regulate synthetic organic chemicals, metallic compounds, and intermediary products from industrial processes that do not fall under existing legislation dealing with air pollution, water pollution, pesticides, radiation, noise, food, drugs and cosmetics. One such problem centers upon the polychlorinated biphenyl compounds whose value as heat mediators, plasticizers, and pesticide synergists led to widespread use prior to our understanding that such compounds are persistent environmental pollutants whose ecological and biological effects resemble those of DDT. Another example is the recent concern about the possible adverse health effects of exposure to optical brighteners which are exceedingly useful additives to plastics, textiles, paints and, most importantly, home laundry detergents. The second new approach is the National Center for Toxicological Research which is a joint effort of Food and Drug Administration of the Department of Health, Education and Welfare (DHEW) and the Environmental Protection Agency (EPA). This facility will conduct carefully controlled animal research on the carcinogenicity, mutagenicity and teratogenicity of environmental agents. Research on any one agent will involve large numbers of several species of animals and thus great expense. These research requirements led to the nick-

name "megamouse facility." Even this substantial effort will screen only a limited number of environmental agents. Clearly, the third approach, development of relatively simple laboratory methods to pre-screen environmental agents prior to animal toxicology studies, is an endeavor of critical importance. Such work is now underway in the National Institutes of Health. Even with progress in each of these areas our posture may still remain essentially reactive as environmental health considerations would have at best a minimal effect upon the early phases of developing technology.

Unfortunately, society lacked the wisdom to prevent exposures to many potentially harmful environmental agents and now such exposures must be reduced. Measures limiting emissions of pollutants from transportation and industrial sources, national ambient air and water quality standards, and cancellation proceedings for several persistent pesticides are current examples. Dose response studies of the health effects of pollutants are vital in executing environmental control because most regulatory legislation specifies that control actions be based upon protection of human health.

Man has seldom predicted the magnitude or subtlety of the adverse health effects of his efforts to control the environment. Failures may continue to occur but systematic prediction efforts are now mandatory. Only the existing pesticide legislation requires an assessment of the impact of proposed control actions. The adverse health consequences of control action may result in more frequent or more severe health impairments than the pollution which a control action is designed to prevent. An obvious example is the restriction of power generation during an acute air pollution episode which might cause voltage reductions and alter the functioning of patient monitoring equipment in intensive care units of hospitals. When such episodes are accompanied by hot weather, as was the case along the eastern seaboard in the summer of 1970, strict emission controls could limit electric power available for air conditioning and thus intensify the mortality peaks known to be associated with heat waves.

Environmental controls based on the need to protect human health should actually protect health and the benefits should be quantitated. Failure to achieve this goal will make it extremely difficult to evaluate the adequacy of environmental controls or the true social cost-benefit relationships. For example, restriction of selected persistent pesticides might be expected to alter tissue pesticide residue levels in biological monitors, including man. Similarly, control of heavy metal emissions into the environment might be accompanied by a reduction in the body burdens. Pollution controls designed to minimize the adverse health effects of the air environment should be accompanied by studies to quantitate improved lung function and decreased respiratory morbidity.

The environment should be optimized in the broadest ecological context for the health and well being of man. This represents an extension of the classic aims of public health that seem very easy to articulate but extremely difficult to pursue because of value conflicts in our society. Specific examples include adding essential trace substances like fluorides to municipal water supplies to help prevent dental caries and adding minerals and vitamins to foods. Sound

and light levels, housing, temperature and humidity are other factors in the physical environment which can be optimized. An even greater challenge is the social environment. Physical inactivity, faulty diet and damaging behavioral traits including drug abuse and cigarette smoking, have been repeatedly proved important risk factors for disabling and life threatening diseases. Optimization of the social environment is undoubtedly more difficult but in many respects inseparable from efforts to improve the physical environment.

2. The relationship between health research and environmental controls

The health intelligence needs for environmental controls must be met by the coordinated efforts of different research approaches including toxicology, clinical research and epidemiology. Coordination of Federal environmental health research programs is being fostered by the Office of Science and Technology. Major health research programs are supported by EPA, DHEW, the Atomic Energy Commission (AEC), the National Science Foundation (NSF), and the Department of Defense (DOD). Generally, the research projects of EPA focus upon the effects of pollutant exposure while those of DHEW explore the mechanisms of disease production.

Health effects research must be accompanied by adequate monitoring of environmental pollutants and appropriate covariates. This research should establish dose response relationships between pollutant exposures and adverse effects. Interactions between pollutants must be recognized and the more important ones quantitatively defined. The type and timing of obligated or contemplated environmental control actions are key factors in determining what health research and monitoring is necessary. For example, dose response studies of the acute and chronic effects of acute pollution exposure are necessary in setting standards that trigger emergency environmental control actions. Such studies often require assessment of the effects of dose rate upon some health indicator and thus may demand more intensive sophisticated and expensive environmental monitoring. Establishing a sound basis for long term standards is even more demanding. Different health indicators and a different environmental monitoring regimen are required to quantitate the relationship between long term, continuous or intermittent, low level pollutant exposures and subsequent acute or chronic adverse health effects. In the latter studies demographic and personal covariates are at times overwhelming problems. Despite these difficulties it is axiomatic that rational environmental controls can neither be established or evaluated without adequate health research and environmental monitoring programs.

3. Biological responses to pollutant exposure

Our society has not always considered the full range of biological responses when evaluating environmental pollution. A hierarchical ordering of biological responses may be helpful in relating health intelligence needs and applications.

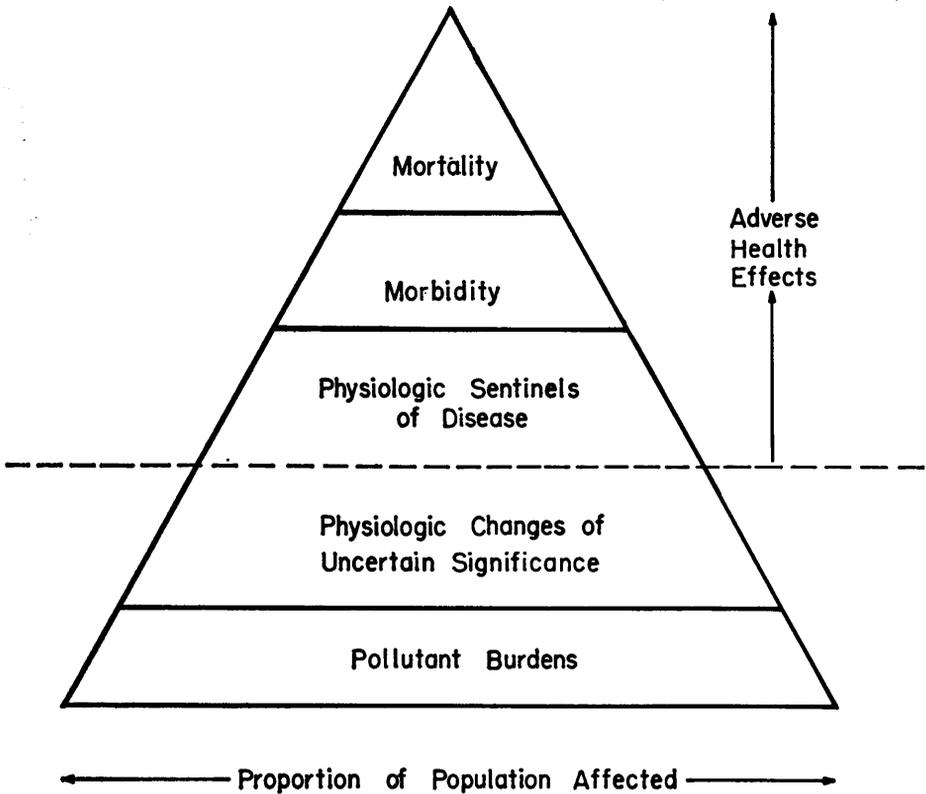


FIGURE 1

A biological response model for pollution exposure.

As shown in Figure 1, five stages of increasing severity may be considered. First, a pollutant burden not associated with any known measurable changes in function. Essentially, all of mankind is so affected. Second, a pollutant burden associated with measurable physiologic changes of uncertain significance. Third, a pollutant burden associated with physiologic changes that are sentinels of disease. Fourth, a pollutant burden associated with morbidity and fifth, one associated with mortality. Adverse health effects might then be defined as preclinical sentinels of disease, illness or death. Generally, health research techniques are adequate to study mortality and pollutant burdens; and better studies of pollutant effects upon morbidity are now underway. However, only limited progress has been made in measuring subtle changes in physiology which follow pollutant exposures and in separating those changes which are sentinels of disease from those of uncertain significance. Such research is extremely important if the present arbitrary rough safety factors are to be replaced by a quantitative appraisal of the risks actually present.

Environmental control actions based on the concept of "no health risk" and health effects defined in terms of "mortality risk" have been proposed. Such a philosophy ignores the spectrum of response and assumes some sort of effects threshold. Equally troublesome is the demand for avoidance of even minor insignificant alterations in physiology. Such "no risk" standards will in fact contain health risks either in terms of morbidity and physiologic changes or in terms of health costs of exceptionally strict environmental controls. An alternate more acceptable approach is to define a socially acceptable risk function in which health costs of pollution and pollution control are but two of many factors.

4. Relationship between selected approaches to health effects research

Laboratory and animal toxicology, clinical research and epidemiology each have unique capabilities for environmental health research; yet there are crosswalks between each approach. A health research program that does not consider each approach and appreciate the necessities of exploiting their biological crosswalks will certainly be wasteful and probably also inadequate. Health research planning has generally been opportunistic and limited to a single approach with only sporadic feeble efforts to exploit biological crosswalks.

The unique capabilities of toxicology include dose response studies where covariates can be carefully controlled, controlled studies of pollutant interactions, lifetime chronic exposure studies, toxicity evaluation prior to human population exposure, studies of sentinel animals, and controlled studies of carcinogenesis, mutagenesis and teratogenesis. Biological crosswalks to other approaches include effects of pollutants on animal models of human disease induced or aggravated by environmental pollution, definition of which physiologic changes are in fact disease sentinels, and the kinetics of absorption, distribution, metabolism and excretion of pollutants.

Clinical research usually involves intensive study of small numbers of normal or diseased human beings in a laboratory setting. Unique capabilities of clinical research include studies of absorption, distribution, metabolism and excretion after pollutant exposures and observation of the acute and chronic effects of accidental exposure to environmental agents. Biological crosswalks included controlled exposure studies limited to part of the dose response range in normal human volunteers, investigation of the benefits of pollutant removal and the effects of pollutant exposures in groups of patients afflicted with specified illnesses, and intensive study of a limited number of naturally exposed studies to identify new biological response indicators. Clinical research studies can verify and link toxicological and epidemiological findings.

Unique capabilities of the epidemiological approach include observation of the health of man in the most relevant, real life setting, studies of the effects of chronic pollution exposure on humans, ability to relate environmental distribution of pollutants and actual population exposures, and assessment of the

health benefits of pollution control. Crosswalks between epidemiology and other approaches include appraisal of the disease sentinels observed or predicted from toxicological and clinical studies, assessment of the interactions between pollutant exposures and diseased populations and identification of the acute effects of high level episodic exposure to a complicated mixture of pollutants.

5. Health research program planning for the environmental protection agency

Systematic appraisal of complex environmental control problems demands an overhaul in research program planning. The envisioned approach within EPA is depicted in Figure 2. Parts of this approach are already being imple-

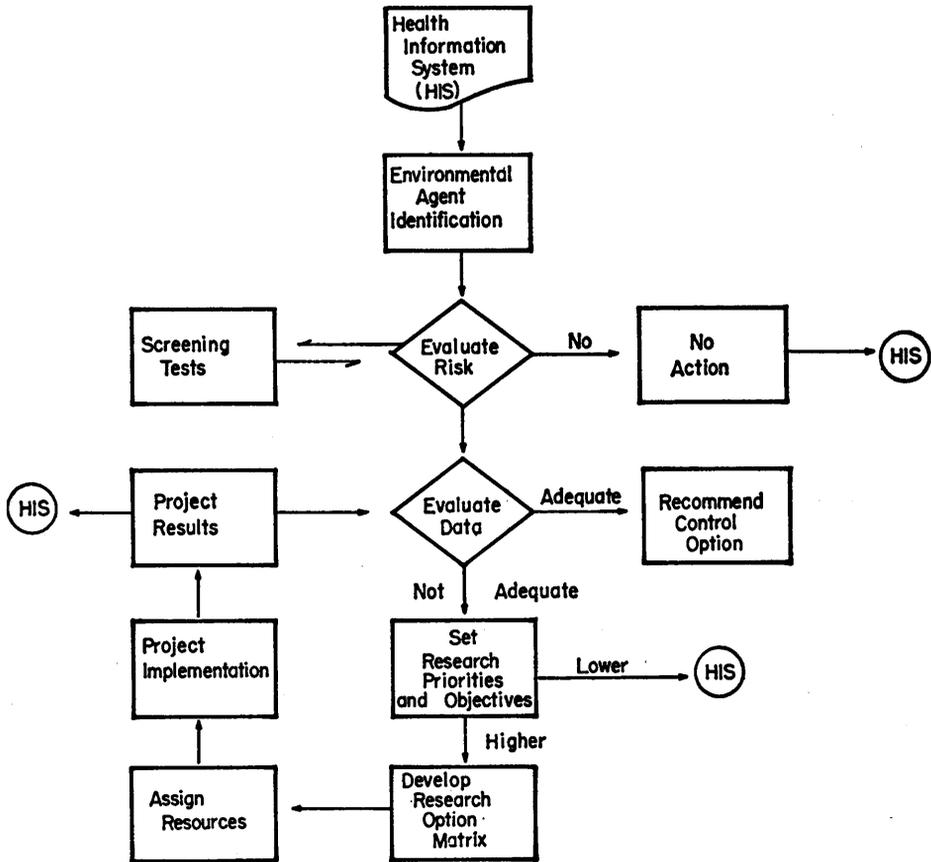


FIGURE 2

Envisioned approach to health research program planning within the Environmental Protection Agency.

mented. An environmental information system, which will include a health information component, must be structured so that potentially harmful environmental agents may be identified at the earliest possible point in time. A task group in the Office of Science and Technology is addressing this environmental information system problem. The potential health risk associated any environmental agent must undergo a preliminary evaluation. Factors involved in this evaluation include the predicted innate toxicity of the agent and assessment of the magnitude and characteristics of the predicted exposed population. Some agents will not be expected to entail any additional risk; thus no control action would be necessary and this decision would be an input for the health information system. Often, there would be so little information available that a series of rapid *in vitro* or *in vivo* screening tests would be necessary before initial evaluation.

The existing effects and exposure data would then be evaluated to ascertain whether an adequate information base existed to recommend an environmental control option. Often the information would be inadequate. In that case, the problem in question would become another member of a set of environmental problems requiring health effects research. Realistically, it is unlikely that all such problems can be a focus for detailed program planning. Decisions regarding research priorities and objects will dictate that no further action be taken on many problems. These decisions would be inputs into the environmental information system. Higher priority problems would be assigned to task force of investigators who would be charged with developing a research option matrix of possible projects. The matrix has dimensions representing research approach, biological response level, exposure level and exposure time. Available resources would be reviewed and assigned to the chosen group of projects. Results of such research would serve as inputs for the health information system and into the data base for decisions on recommended environmental controls.

The research planning mechanism just sketched provides several distinct advantages to the Agency. First, a smooth transition from the reactive posture of today to the needed predictive posture can be accomplished within the framework. Second, the plan could provide a close working relationship among field investigators now geographically dispersed. Third, the needs of the Agency will be real and relevant to the investigator rather than a distant, rather unpleasant imposition.

6. Expenditures for environmental health intelligence and environmental controls

Environmental control expenditures of future years will be based upon the health intelligence gathered by research programs of today. There can be little disagreement that the present health information base is inadequate. Health research expenditures for the units now comprising EPA, excluding environmental monitoring not directly related to health projects, amounted to just

TABLE I
EXPENDITURES FOR ENVIRONMENTAL HEALTH INTELLIGENCE
AND ENVIRONMENTAL CONTROL
Annual average fiscal year 1972-76.

	EPA health research expenditures (millions)	Per capita expenditures	
		For health intelligence	For environmental controls
Fiscal year 1971	12.3	6 cents	
Fiscal year 1972	18.0	9 cents	\$125

over \$12,000,000 in fiscal 1971 and \$18,000,000 in fiscal 1972 as seen in Table I. Equivalent per capita expenditures were six cents and nine cents. If additional expenditures by other Federal Agencies were considered, the total in fiscal 1971 might rise to 50 cents. Average yearly costs of scheduled environmental controls have been projected at about \$125 per capita per year from fiscal year 1972 through fiscal year 1976. The Environmental Protection Agency and other Federal Agencies intend to work within the framework of national priorities to supplement the environmental health research effort.

7. Summary

Rational environmental control actions must be based upon an adequate pool of health intelligence. Clearly defined health research goals and their relationship to controls have been defined. Appreciation of the spectrum of biological response following pollution exposure and the interlocking nature of different research approaches is mandatory. A systematic approach to setting health research priorities should allow smooth transition from our present "reactive" posture to a "predictive" posture. The challenge demands an accelerated research program within the framework of national priorities.

Discussion

John R. Goldsmith, Environmental Epidemiology, California Department of Public Health

Possibly Professor Neyman's question on experiments concerning interaction of radiation and pollutants can be illuminated by three sets of epidemiological studies. Studies in Great Britain (Reid), and to a lesser extent in the United States, of air pollution effects indicate an interacting role of cigarette smoking and community air pollution on chronic pulmonary disease. Studies of uranium miners have shown a potentiation of pulmonary carcinogenesis of cigarette smoking by radon exposures. They have also demonstrated, incidentally, the prognostic value of sputum cytology. Finally, from Selikoff's work we have

evidence of interaction of cigarette smoking and asbestos exposure on development of lung cancer.

R. J. Hickey, Institute for Environmental Studies, University of Pennsylvania, Philadelphia

Could you please clarify a point? You seem to have referred to (a) mutagenesis, (b) carcinogenesis, and (c) teratogenesis as though they were in fact separate and independent processes, though this was possibly not intended. Do you consider these as independent processes, or may they not all be considered properly as variations of mutagenic processes?

Reply: J. F. Finklea

When finally elucidated, the underlying molecular events leading to cancer, congenital abnormalities and mutations may very well be similar processes.

Emanuel Landau, Environmental Protection Agency, Washington, D.C.

The factorial design suggested by Professor Neyman need not be limited to combinations of pollutants. Socioeconomic characteristics may be significant variables inasmuch as there appears to be some evidence from Winkelstein's work that the population at the lowest socioeconomic status is most adversely affected by a given pollutant level. This seems to be observed by British experience, too.

In animal studies, stresses on the animal such as temperature and humidity changes and impairment may be significant in studying effects of specific pollutants or combinations of them.

Harold L. Rosenthal, School of Dentistry, Washington University

Although Professor Neyman's question concerning multivariate experiments is a valid one, it would seem to me that the number of variables is so great that good epidemiological and biostatistical approaches would be more succinct. It seems to me that we have already performed such experiments on this earth with the human and animal populations. This does not mean that animal experiments should not be done or that they can not yield very good information. It only means that many experiments have already been done with human populations—either inadvertently or by design.

T. Sterling, Department of Applied Mathematics and Computer Science, Washington University

Is there a programmatic effort to introduce knowledge of sophisticated statistical designs and data analysis techniques in this model of the Health Information System? (In the sense of a programmatic effort.)

Reply: J. F. Finklea

Yes, in the sense that the proposed health information system would cite the appropriate statistical literature and research involving techniques necessary for environmental health studies.