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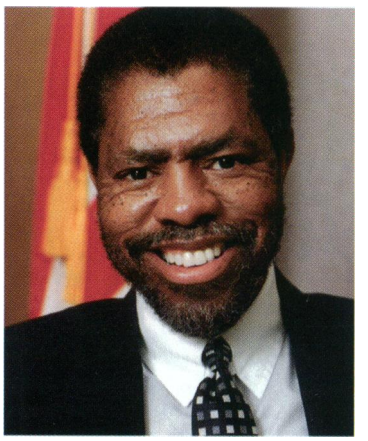

Editorial

Thinking Big: Four Ways to Advance Environmental Health Research to Answer the Needs of Public Policy

Environmental health research has reached a juncture where tremendous opportunities lie ahead, if we but have the leadership to move our many disciplines forward—and the vision and courage to think big. The hard work of the past 30 years has developed our skills and our tools to a point where we can advance the very concept of what environmental research is all about—if we but dare to commit to the adventure—if we have the sense and seize the resources to make what we imagine real.

I envision four major efforts: 1) to map the "environmental genome," to analyze the blood of enough Americans to determine the variations in some 200 susceptibility genes; 2) to determine, in a large-scale survey with testing, what major chemicals a large representative sampling of Americans have been exposed to and carry around in their blood; 3) to address, at last, the problem of mixtures—the problems of the real world; and 4) to develop and put in place faster, better testing using transgenic mice and other innovative methods.

We know that, in the past, Congress and the American people have been rightly critical of a process in which costly environmental health regulatory policies have had to be developed without adequate information. Too often, there is too little scientifically sound information on which to base many decisions. When there is too little information, there are opportunities for lobbyists on one side to posit that further regulation will end outdoor barbecues and campfires, while the other side paints an apocalypse if regulations are not immediately put into place. Indeed, without more basic data there can be no satisfactory solution to the complex issues surrounding human exposure to environmental pollutants and health outcomes. We may find ourselves overregulating, at a cost to our economy, to avoid risking underregulation, with potential harm to health. But without better information, we cannot make the best decisions—ones that provide full health protection at the most reasonable cost.

This problem of too little information is highlighted in the news media almost on a daily basis. The most current example is the Gulf War veterans illness—a situation in which there is too little information about individual differences in susceptibility, too little information about the health effects of mixtures, and too little information about multiple chemical sensitivity, chronic fatigue syndrome, and fibromyalgia.

Likewise, there is too little information on the health effects of exposure to environmental estrogens to develop public policy in which the American people can have confidence. Both the EPA and industry groups acknowledge that more research is needed on the health effects of human exposure to ozone and particulate matter in the air we breathe.

To compensate for lack of scientific information, environmental health protection policy is often based on broad and expensive programs of environmental remediation, controls, regulations, and public education. This question of cost of intervention versus benefit leaves both Congress and the public in the uncomfortable position, particularly in times of scarce resources, of having to decide whether to relax environmental controls and appear uncaring or to continue to spend large sums of money on programs whose impact on public health is uncertain.

In the face of considerable challenge and public criticism, one can either dig in and defend the status quo or one can face the facts and lead and embrace the change. My belief is that the status quo is no longer defensible and that, since we now have the tools and the skills, we should vigorously lead an effort to ensure that the research is done to improve environmental health decision making.

I envision investment in four critical areas of science where major information gaps exist, areas where reasonable research questions can be formulated, areas where technologies are available, areas where understanding offers the potential to significantly improve public health and regulatory policy.

First, research is urgently needed to determine the basis for the wide variation in individual responsiveness to exposures to environmental toxicants. There are differences in responsiveness, or susceptibility, differences in past and present exposures to related and unrelated toxicants, and differences related to age, gender, lifestyle, or genetic predisposition; yet these are rarely taken into consideration in assessing human risk because the database is not available. To address this problem, the NIEHS proposes to expand its molecular genetics research to identify susceptibility genes for environmentally induced diseases through a new Environmental Genome Project.

This genome project will be a broad multicenter effort to obtain information about DNA sequence diversity for the U.S. population on all of the environmental disease susceptibility genes now recognized (more than 200).

Second, there is an urgent need to develop new approaches to toxicological testing to cut costs and increase timeliness. Using the current methodologies, it takes approximately five years to evaluate a chemical for carcinogenicity at a cost of two to six million dollars. If we are going to work our way through the thousands of chemicals to which humans are exposed, we must develop bold new screening strategies. There are new high-throughput screening assays that promise to be less costly, more relevant to predicting human risks, and timelier in generating the information (in a year or less).

Third, investigation of the mechanisms and health effects of mixtures is another area where lack of information is a serious problem.

The current toxicologic databases were developed using single chemicals in animal bioassays.

As we all know, humans are exposed to a variety of chemicals, either concurrently or sequentially at different doses via multiple pathways. The problem of mixtures is not limited to interactions between chemicals because health outcomes of exposure to chemical agents can also be influenced by the simultaneous exposure to physical and biological agents.

For example, the risk of radon-induced lung cancer is increased in cigarette smokers, and people infected with hepatitis B virus are more susceptible to aflatoxin-induced liver cancer. Thus, our inability to say whether agents act in an additive, synergistic, or antagonistic fashion creates real problems in health risk assessment.

Depending on the assumptions made regarding the nature of the interaction between components, risk may be seriously over- or underestimated with dire economic or public health consequences, respectively.

Fourth and last is the major challenge of strengthening the links between fundamental science, toxicology, epidemiology, and public health. We can make environmental health research findings more applicable to human risk assessment by determining the actual range of human exposure to specific chemicals.

We can now measure many of these chemicals in body tissues such as blood and urine. As a top priority, using improved and highly sensitive analytical procedures, we should expand the National Health and Nutrition Exposures Survey coordinated by the National Center for Health Statistics to monitor the exposure of the U.S. population to the chemicals listed in the National Toxicology Program's Biennial Report on Carcinogens.

Such "real world" exposure assessment would be far more useful than estimation of exposure based on the EPA toxic release and production information, as is currently done. Also, the current approach does not take into account the biologically effective dose and individual or species/group differences in the uptake and metabolism of various chemicals.

Estimation of exposure based on toxic release and production information is, at best, only a reflection of the potential for human exposure.

The public health component of the above goals can best be achieved through NIEHS partnerships with the CDC and the EPA. Our ongoing partnership with the CDC on exposure assessment could be expanded, and new ones with the EPA are under discussion.

Progress in the four areas of research offers "real world" answers to the quagmire of indecision and discontent that is a consequence of having too little information. And, best of all, our vision of a more science-based environmental health regulatory decision-making system is achievable, given today's technologies.

Let's put the uncertainties and public debates about environmental health policies to rest with science. Let's join the chorus calling for "sound science," and let's insist on the resources to do the job. We can pull together and focus some resources ourselves, but we must also insist that policy makers who call for "sound science" appropriate the resources to generate the science.

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