THE SCIENTIST'S PERSPECTIVE ON RISK

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The Socio-Political Climate

Although life expectancy is currently at an all time high and our general health and well-being are better than at any time in our history, we in Western societies, especially in the United States, continue to worry about the risks in our lives. We worry a lot about the quality of our environment and, particularly in recent years, we worry a lot about our health and well-being. A great deal of concern in the last few years has been focused on the potential adverse effects on human health associated with traces of chemicals such as pesticides present in our food and water and, indeed, from time to time the level of concern has reached paranoic proportions. The Alar scare of 1989 was a prime example of this. Throughout the following discussion I will use the pesticide issue as a general case study to illustrate some of the points I wish to make.

As scientist writer Lewis Thomas has said, it sometimes appears that we are in danger of becoming "a nation of healthy hypochondriacs, living gingerly and worrying ourselves half to death."

The fear and worry that exist in a substantial portion of the public are very real. Unfortunately (or perhaps fortunately), most of this is not based on fact and most of it seems quite irrational. As a society we seem to have lost our ability to distinguish between serious threats and those of a quite trivial nature. We smoke billions of cigarettes and yet we worry ourselves ill over pesticide residues in food and water that, at very worst, constitute risks far lower than those most of us face travelling to work each day.

The reasons for all this worry are many and complex. They relate, in part, to the process by which information is communicated to the public (i.e., the media), in part to the characteristics of the receiver of the message (i.e., psychological factors that determine how we, as individuals, perceive and prioritize risks) and, in part, to the nature of the message itself (i.e., complex scientific and technical information often associated with a good deal of genuine uncertainty). These difficulties are exacerbated by the injection of a wide variety of political views and personal biases and, indeed, the issues tend to become so highly charged and the opposing views so polarized that it becomes

increasingly difficult, especially for nonscientists, to distinguish established fact from emotional fancy and political rhetoric.

For quite some time now, the U.S. public has been subjected to a constant barrage of generally bad news on pesticides through the popular written and electronic media. Much of this news is, of course, tailor-made to sell newspapers and TV; it is always bad and often sensational and emotional; there are victims and villains, poignant human interest stories combined with stories of corporate greed and government ineptness.

The only good news is the fact that the bad news is almost always highly exaggerated and frequently completely without foundation. To be sure, it is possible to find examples of situations in which, as a result of accident, gross misuse, or negligence, etc., people have been injured or even killed following excessive exposure to pesticides and other chemicals. Many pesticides are potentially hazardous to humans and they must always be used with caution. On the other hand, there is not one shred of scientific evidence to support claims to the effect that, in the general population, pesticide residues in food and water are responsible for a multitude of ills ranging from cancer, birth defects, reproductive effects and immune dysfunction (often referred to as chemical AIDS) to an increase in teenage suicides.

Quite predictably, this constant negative reinforcement has led to:

1. increased public fear and confusion over the health effects of pesticides and the development of strong antipesticide sentiments;
2. distrust in government regulatory efforts and increasingly strident demands for more protective regulation;
3. increased suspicion of the motives of the agrochemical industry.

This describes the general atmosphere in which many regulatory decisions on pesticides are currently being made at both the federal and state levels. As a result of intense public pressure, regulators continually find themselves "under the gun" to take further action to obviate or minimize the perceived health or environmental threats associated with a pesticide, irrespective of whether action is justified by the scientific evidence available. Care must be taken to avoid taking overly hasty action based on incomplete, misleading or erroneous information. Such actions will not only fail to have the desired health-related effects but may well have serious negative impacts on the agrochemical and agricultural industries.

To the scientists charged with assessing risks and attempting to provide advice and recommendations on regulatory issues, it is saddening to realize that the public's perception of the nature and magnitude of the health risks associated with pesticides and other chemicals is frequently quite at odds with the available facts. It is also frustrating for scientists to see that many important legislative initiatives and regulatory decisions relating to pesticides are based, not on science, but on a variety of political or other nonscientific factors. It often seems

that science is becoming increasingly less important in the regulatory process.

To understand more clearly some of the frustrations of scientists over the use, misuse and abuse of science in the regulatory process, we need to look more carefully at the state-of-the-art of the science of risk assessment and the role of science in the regulatory decision-making process.

The Regulatory Process

According to the National Academy of Sciences (NAS), the regulatory process can be divided into two distinct elements, risk assessment and risk management. Risk assessment is considered to be a scientific process that characterizes the nature of a risk and assesses the probability of its occurrence. Risk management is the process whereby an appropriate regulatory decision is reached on how a given risk can be obviated, minimized or otherwise managed. Risk management per se is not a scientific process. Obviously, it requires science; but it also involves a series of value judgments through which the regulator balances the risks against a variety of other factors (costs, benefits, alternatives, social and political considerations) that depend on the statute under which regulatory action is being contemplated.

Unfortunately, as we will see, there is often a very fuzzy dividing line between the processes of risk assessment and risk management and the policy issues associated with the latter often have a powerful influence over the scientific input into the process.

Toxicologic Risk

Risk is defined simply as the probability that an adverse effect of some kind will occur. In the case of a chemical such as a pesticide, the potential risk to human health is a function of the toxicity of the material (i.e., its intrinsic capacity to cause an adverse effect such as neurotoxicity, cancer, etc.) and the level (intensity and/or duration) of exposure.

Risk = Toxicity x Exposure

The importance of the level of exposure cannot be overstated and, of course, the fact that the response to any chemical is always related to the dose, is central to the discipline of toxicology. For many, the very fact that a pesticide (or pesticide metabolite) is present in food or water, *at any concentration*, is a cause for immediate concern. It must be realized, however, that such pesticide residues are present in extraordinarily low concentrations, ususally measured in parts per million (ppm) or parts per billion (ppb).

A few years ago we had great difficulty in measuring 1 ppm of anything. Now we routinely measure ppm and ppb and occasionally we can measure ppt (parts per trillion) and ppq (parts per quadrillion). Our current analytical chemical capabilities are truly amazing and they

allow us to find the smallest traces of almost anything we choose to look for. This has tended to heighten public fears about the risks of pesticides in our food and water because it gives many the impression that we are wallowing in a sea of potentially dangerous chemicals. What we must remember is that we no longer live in a pristine environment. If we choose to use pesticides and release them into our environment and our food supply, we will always be able to measure traces of these materials in our food and water.

The major problem, of course, is not in detecting and measuring pesticide residues in food and water (that's easy and will no doubt get easier) but in determining what, if any, significance such residues might have in terms of adverse effects on human health. We seem to have developed the unfortunate habit of making lists of materials present in food and water without considering the levels. Regulatory action cannot be justified simply on the basis of the presence of a given pesticide in food or water but only after carefully evaluating whether the chemical represents a potential health threat.

A careful exposure assessment is a critical component of any good risk assessment.

Risk Assessment

The assessment of toxicological risk is the concern of the toxicologist. The commonly accepted definition of toxicology — the science that studies the adverse effects of chemicals on living organisms and assesses the probability of their occurrence — clearly indicates risk assessment and prediction as integral components of the discipline.

There are two ways in which we can evaluate the potential adverse effects of chemicals on human health:

1. We can conduct prospective studies on various surrogate species (rabbits, mice, etc.) in the laboratory and hope that we can extrapolate the results to predict the effects likely to occur in man.
2. We can conduct retrospective epidemiological studies in which we compare the health of populations exposed to a given chemical against that of similar unexposed populations.

There are, of course, a great many difficulties associated with both methods and consequently there is always a lot of genuine scientific uncertainty in predicting the effect of chemicals on human health.

Unfortunately, this uncertainty is widely misunderstood. Most non-scientists believe we know a lot more about toxicology than we really do and have very precise and accurate risk assessment capabilities. Consequently, many feel that there is no excuse for not rapidly identifying chemicals that pose a threat to human health. The media and the public are also at a loss to understand why the "experts" frequently disagree over what appear to be relatively straightforward issues and tend to view this dissension with alarm, suspicion and mistrust. These general misperceptions have tended to alienate the public from science and have

led to a good deal of public skepticism with regard to the views expressed by many scientists.

While there is no question that the science of toxicology is rapidly advancing our state of knowledge and understanding of the interactions of chemicals with living organisms, it must be emphasized that evaluating human health risks will always be an uncertain process.

Acute Versus Chronic Effects

Toxic effects are usually described as being either acute or chronic. Acute effects usually occur within a relatively short time (up to 24 hours) after exposure while the onset of chronic effects such as cancer or birth defects may be delayed for years or extend to future generations.

The evaluation of acute toxic effects seldom causes serious problems. The main reason for this is that, for chemicals causing acute toxic effects, it is generally agreed that there exists a threshold dose below which an effect will not occur. Furthermore, this threshold can be determined experimentally in laboratory animals. In practice, a "no observed effect level" (NOEL) can be measured; it is simply the highest dose tested at which no adverse effect was observed. The NOEL is a useful benchmark from which a number of regulatory guidelines, health advisories, etc. can be derived. While there is still some uncertainty associated with the extrapolation of acute animal NOELs to humans, this is usually acceptable to all concerned including the public.

The situation with respect to assessing chronic health effects such as cancer is quite different in all respects and is beset by a good deal more uncertainty and controversy. In evaluating acute toxic effects the objective is to measure the severity of specific adverse effects in individual animals; the emphasis is on effects resulting from high doses for short periods of time. In contrast, cancer risk assessment seeks to measure increases in the frequency of occurrence of a low probability event (formation of a tumor) in a population exposed to low doses of the chemical over a long period of time.

For statistical reasons it is simply not possible to obtain direct laboratory measures of the low levels of cancer resulting from long-term exposure of animals to the traces of pesticides to which humans are typically exposed in the real world. Two ways in which the power of the test can be improved is:

1. to increase the number of animals used in the test and
2. to increase the dose of the test chemical.

There are, of course, limitations to the number of animals that can be used in routine lifetime bioassays. Most tests employ about 600 animals and even with this number the cost is close to $1 million.

The dose is more amenable to change and, as a result, the doses employed in most animal bioassays for carcinogenicity are high. Indeed,

current EPA testing guidelines require that the high doses used should approach the so-called "maximum tolerated dose" (MTD), the maximum dose the animal can withstand. It is assumed that any effects observed at these high doses can be used to predict those likely to occur at the much lower doses (often ten or one hundred thousand times lower) of interest with respect to human exposure. This assumption is highly questionable as are the mathematical models used in the extrapolation process.

It is important to recognize that the quantitative estimation of human cancer risk of necessity involves the extrapolation of results obtained under one set of conditions in the laboratory (e.g., rodents exposed to very high doses for a lifetime) to predict those likely to occur under another completely different set of conditions in the real world (humans exposed intermittently to very low concentrations).

This extrapolation process across both dose and species is fraught with difficulty and uncertainty and involves many controversial assumptions of very doubtful scientific validity. This is the point at which the policy aspects of regulation impinge directly on the scientific input into the risk assessment process. Thus, many of the steps in cancer risk assessment as practiced by the U.S. Environmental Protection Agency (EPA), for example, are based entirely on assumptions and policy decisions that do not necessarily reflect the best science available. Wherever there exists an area of uncertainty the EPA steps in and establishes a guideline (policy assumption) that essentially says "since we really don't know how to do this we will agree to do it this way"; the guidelines provide convenient bridges by which regulators avoid areas of scientific uncertainty. Since, quite understandably, regulators wish to err only on the side of safety and prudence, the guideline assumptions invariably involve the use of highly conservative procedures. Unfortunately, regulators often try to bend scientific truth to justify and validate such assumptions.

An assumption with far reaching regulatory consequences is the one that holds that, in sharp contrast to the case with acute toxicants, there is no threshold for carcinogens. In other words, the only "safe" dose of a carcinogen is zero. This causes numerous problems, one of which is that, in the United States, carcinogens are regulated differently from chemicals causing other adverse effects. Since, as discussed earlier, modern analytical instrumentation allows us to find traces of any chemical we care to look for, we are constantly finding "carcinogens" that, by definition, constitute a finite level of risk. As a result, we have been trapped into playing a rather futile numbers game in which we are continually trying to decide what constitutes an acceptable level of risk.

The final risk estimates generated from cancer risk assessments usually appear as single very precise values — not, for example, 1 in a million or even 1.5 in a million, but often 1.53 in a million! It must be emphasized that these represent highly theoretical, super conser-

vative, worst case estimates that have little or nothing in common with the real world. Statistically, even the most frightening values might just as easily be zero. Furthermore, these risk estimates may vary by up to a millionfold (or more) depending on the assumptions used in the assessment. As indicated earlier, our obsession with generating what appear to be very precise estimates of cancer risk is unscientific and misleading. It causes the public to believe that we have exquisitely sensitive test methods and places pressure on regulatory agencies to adopt increasingly more stringent standards.

It is now accepted in the scientific community that cancer is a complex multistage disease that can occur through a number of different mechanisms. It is also widely accepted that in most, if not all, cases there are practical thresholds of exposure below which a carcinogenic response will not occur. Consequently, EPA guidelines for assessing carcinogenic risk are currently under review. It is of considerable concern to scientists that the guidelines are overly inflexible and unable to change sufficiently rapidly to accommodate new scientific advances.

It is also of fundamental importance to recognize that the very process we use to classify carcinogens is based almost entirely on the results of tests with laboratory animals. There is little, if any, evidence to suggest that many of the chemicals currently classified as "carcinogens" are likely to be "human carcinogens,"particularly under the conditions of human exposure. Here again, our apparent obsession for making lists of various things comes to the fore and our lists of "carcinogens" are always assumed by nonscientists to be lists of "human carcinogens."

Summary and Future Needs

The foregoing discussion indicates just some of the reasons why scientists often take a somewhat jaundiced view of current risk assessment procedures (as employed by regulatory agencies). Also, recognition of the unreasonably high level of conservatism built into the risk estimates explains, in part, why scientists frequently seem to take a somewhat cavalier attitude toward many of the "risky issues" that attain national prominence.

There is also a feeling among many in the scientific community that we are not able to distinguish between serious and trivial risks and that many of our current regulatory priorities are inappropriate. For example, Dr. Bruce Ames of the University of California in Berkeley continues to point out that, of the total human dietary intake of potential carcinogens, only about 0.01 percent are synthetic chemicals like pesticides. The rest are naturally occurring products from plants, fungi, etc. or materials that are formed during cooking (Ames and Gold). If Dr. Ames is correct — and he has widespread support in the scientific community — a large proportion of our current efforts to identify, evaluate and regulate the traces of synthetic "carcinogens" in our food supply will have little, if any, effect in reducing cancer incidence in the United States.

While, clearly, we must continue to be vigilant to identify and obviate situations that represent a significant level of risk, we must clearly recognize that we have limited resources available for this purpose. If these resources are squandered or misdirected along unimportant pathways there will be fewer left to apply to more serious issues. It is important that we direct these precious resources along avenues that provide the biggest return.

Looking into the future there are three major needs that will improve the process by which we identify and regulate toxicologic risk and that, importantly, will provide the public with reassurance that the regulatory system is indeed providing an appropriate level of "safety." These needs are:

- To continue to increase our understanding of the basic mechanisms through which chemicals exert their potentially adverse effects on living organisms;
- To ensure that regulatory decisions are based primarily on the total weight of scientific evidence available and are influenced as little as possible by emotion, sensationalism and media-hype;
- To establish health-based priorities as targets for risk assessment and possible regulatory activity;
- To improve the risk communication process to increase the public's level of understanding of risk and risk assessment.

REFERENCES

Ames, B.N., and L.S. Gold. "Too Many Rodent Carcinogens: Mitogenesis Increases Mutagenesis." *Science* 249 (1990): 970.

National Academy of Sciences. *Risk Assessment in the Federal Government: Managing the Process.* Washington DC: National Research Council, National Academy of Sciences, 1980.