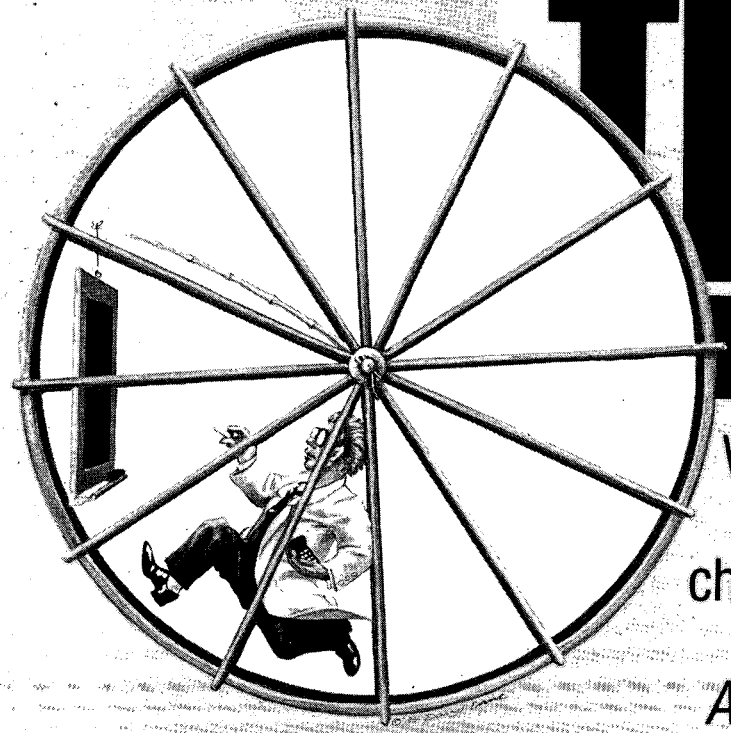
BEHIND THE CANCER TERROR



Why are Americans gripped by fear over the least trace of chemicals suspected of causing cancer? An excerpt from *The Apocalyptics: Politics, Science, and the Big Cancer Lie.**

By Edith Efron

In the course of five years of research and writing, I discovered a cultural crime which should not be possible in a free society: a complex corruption of science and a prolonged deception of the public. The crime emerged from the sciences of environmental cancer and cancer prevention, and it has all the superficial characteristics of "The Purloined Letter": It has been committed under our very eyes, its details are publicly recorded

in documents which are within hand's reach, and yet it remains invisible to most of the people of this country who are its victims. It is rendered invisible by one thing above all: the phenomenon of "the two cultures"—the dangerous barrier which separates the scientific and the humanist cultures and which may leave even the most educated layman incapable of differentiating between serious science and ideology in a white smock.

One of the realms in which one discovers this complex corruption of science is cancer prevention based exclusively on animal tests. The layman's understanding of this science is severely limited and is usually dominated by the approach to laboratory carcinogens adopted by the press. Shaped by the regulatory process, that approach is to present every announcement that a substance is "suspected" of causing cancer as high drama involving a battle between the regulators and an incriminated industry. My research into animal-man extrapolation, however, turned up an entirely different set of controversies—the extraordinarily large number of theoretical controversies in the academic world that lie concealed behind the regulatory facade. If one does not know these theoretical controversies, if one interprets the science of cancer prevention in purely economic-regulatory terms, one can never judge the nature of that science.

In the course of my investigation I found every reason to believe that the root of the many theoretical battles in the world of cancer research is politics—specifically, warring attitudes toward the American industrial system. One cannot put scientists into rigid boxes, but there do tend to be opposing factions that show up on one side or the other of every one of the specific and interlocking controversies in this field—and the sides are usually determined by whether the position enhances or diminishes the case for stringent regulatory action.

The most fundamental and most dramatic of these politicized academic controversies revolves, inevitably, around that theory in the cancer-prevention repertoire which justifies the most stringent regulatory action: the no-threshold, or no-safe-dose, or one-molecule theory. This theory holds that the most minute amount of a carcinogen, even a single molecule, might give someone cancer and, consequently, that the only safe dose or exposure is zero. The no-threshold theory is the premise of the process by which American citizens are sheltered from carcinogenic risk by American "regulatory" science, whose purpose, unlike that of basic science, is not to understand the biological mechanisms of cancer but to eliminate "suspected" substances from the environment whether biological understanding exists or not.

The no-threshold theory is a remarkable premise, however, for while it is the rock on which the temple of cancer prevention has been built, nobody has any idea if it is true. As Marvin Schneiderman of the National Cancer Institute (NCI) put it at hearings held by the Occupational Safety and Health Administration (OSHA) in 1978:

> *Another problem* and one which unfortunately is not amenable to scientific solution, *is the existence of a threshold. Is there a lower limit of exposure below which normal repair and recuperative processes will prevent cancer? This is perhaps one of the most pernicious questions that confront the regulatory agencies. It is the refuge of the apologist for industry and has support from traditional toxicology. [Emphasis added]*

A premise that "is not amenable to scientific solution" is a problem in a scientific endeavor, and it does generate hostility to regulators who impose it coercively—not only from "apologists for industry" but from "traditional toxicology," which is to say that a substantial number of "regulatory" scientists are as antagonized by the no-threshold theory as others are devoted to it. In fact, although regulators are loathe to inform citizens that anyone but industrialists condemns their policies, this is by far the most intense battle within the world of "regulatory" science itself.

The academic conflict over the no-threshold theory is so profound that it has caused certain institutions and people to adopt a position of cautious neutrality. In 1978, the Office of Science and Technology Policy circulated an early draft of its guidelines for the control of carcinogens. The draft was "widely" circulated among scientists, and responses were received from several dozen, including Joseph Fraumeni of the National Cancer Institute (NCI), Philip Handler of the National Academy of Sciences, David Rall of the National Institute of Environmental Health Sciences (NIEHS), Joseph Rodricks of the Food and Drug Administration (FDA), and Arthur Upton of the NCI and the NCI staff. On the basis of the response, the OSTP decided to leave the subject of thresholds out of its policy report: "Most comments made reference to lack of consensus among scientists regarding this issue. Since a full presentation of the debate is beyond the scope of this paper, we have elected to omit explicit reference to thresholds from the paper."

In the same year, Thomas Maugh of *Science* magazine, who

*This book reviews the first decade of cancer prevention in the United States and covers essential issues in carcinogen research, animal testing, and cancer epidemiology. The article here deals exclusively with an issue in animal-man extrapolation. Footnote references have been eliminated and, as in the book, scientists' professional affiliations have been "frozen" at the time of their statements.

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did try to review the debate, also preferred to remain neutral. Acknowledging the intensity of the conflict in the scientific world, Maugh, who is not normally given to hyperbole, said: "Debate between those who think carcinogens can be detoxified and those who do not has raged for years with all the intensity of a jihad. The analogy to religion is not inappropriate, moreover, since there is little hard scientific evidence to support either point of view. . . . Arguments on both sides of the question often seem to be little more than articles of faith, and it is exceptionally difficult for an impartial observer to decide which faith is more deserving of support."

If one examines the no-threshold/one-molecule debate by itself, one must inevitably end up perched on the fence, for "it is not amenable to scientific solution." If, however, one examines it within the context of the goal of cancer prevention, it becomes luminously clear that the "articles of faith" of one camp—the no-threshold camp—have necessarily been triumphant and that the dissenters against this position have necessarily been defeated in the battle.

The stated goal of the cancer prevention program in the United States is, quite simply, to protect—in advance—every one of the 226,000,000 citizens from the real or potential effects of carcinogens. The goal is stated in slightly different terms by different scientists, although they all mean the same thing. According to one group of scientists at the government's National Cancer Institute, including Charles C. Brown, Thomas R. Fears, and Marvin A. Schneiderman, "all members of a heterogeneous population must be protected at all times," and thus a regulatory agency "must consider the lowest threshold for an individual over his exposure period, as well as the lowest thresholds in the entire population." And Umberto Saffiotti of the NCI expresses the same idea more economically: "A prudent policy of cancer prevention requires protection of the most sensitive individuals in the population."

This goal is resonant with good intentions, but it poses very peculiar problems. On the face of it, it is obvious that no one can possibly know the identity of all the individuals in a nation of 226,000,000 or any random portion thereof who will be "most sensitive" to a disease that has not yet occurred as a response to a particular substance in question and that is not in general understood. All that can be known is that individual reactions are very different. Many scientists have testified to OSHA that, as OSHA puts it, there is a "wide variability in susceptibility to cancer within a population." Science is not presently capable of identifying the degree of "susceptibility" of every individual in the nation, particularly in a "heterogeneous" population.

The simplest way for the layman to understand the problem of varied susceptibility to cancer of a "heterogeneous" population is to consider the observation of David Rall of the government's NIEHS. "Man," he has observed, "is among the most heterogeneous systems on earth." In fact, "if sufficient effort were exerted, one could find that metabolically some man would exhibit a pattern like a rat, another man would exhibit a characteristic of a dog, and so forth." The "and so forth," however, is more important than the rest, because Rall only mentioned laboratory animals; but his statement, at a minimum, means that any given man may metabolize a carcinogen like any given *mammal*—that is, that somewhere a citizen of the United States may be metabolizing carcinogens like a gorilla, a leopard, a zebra, or an aardvark. The ultimate goal of cancer prevention in a heterogeneous species, then, is to protect that unknown susceptible citizen living somewhere on this gigantic continent who may, unknown to him or anyone else, metabolize carcinogens like an aardvark; and the aardvark, for all we know—since "sufficient effort" has not been exerted—may be helplessly vulnerable to carcinogens.

For the sheer pleasure of naming things, we will call this the Aardvark Principle. This "principle" is merely a symbolic restatement of the goal of cancer prevention as defined with greater solemnity by the above-quoted scientists at the NCI. Accordingly, OSHA, one of the government's leading regulators of environmental carcinogens, defines a threshold in the manner most appropriate to the Aardvark Principle:

> *For scientific or regulatory purposes,* threshold *would be a dosage level below which an effect (cancer)* could not *and* never would *occur, not merely a point below which an effect would be infrequent, no matter how very infrequent. [Emphasis in original]*

I found every reason to believe that the root of the theoretical battles in the world of cancer research is politics.

It must now be observed that the Aardvark Principle, all the more formal definitions of the goal of cancer prevention by NCI scientists, and OSHA's definition of a threshold as a dose that "*could not*" and "*never would*" cause a carcinogenic response in a single citizen have one unusual thing in common: To establish a threshold dose, all require the proof of a negative, which is impossible in logic. There is no way of demonstrating that an unknown individual in a population of 226,000,000 is *not* unusually susceptible to a disease whose mechanism is unknown; there is no way of demonstrating that an unknown individual does *not* metabolize carcinogens like an aardvark; there is no way to identify any metabolic response that "*could not*" and "*never would*" occur. The goal of cancer prevention may be resonant with good intentions, but a student of Logic I who presented a comparable proposition would receive a reso-

nant F. Assuming, however, that one accepts a public health goal that sets forth the need for a set of logically impossible calculations, one must thereafter conclude that one cannot perform those calculations—which is to say that one cannot calculate a threshold dose for man for any carcinogen.

In fact, a great many scientists have understood perfectly well that there is no way on earth to calculate a threshold dose for a population. Some scientists simply say forthrightly that the calculations cannot be performed and, short of challenging the logic of the goal, explain why. For example, Harold Stewart of the National Institutes of Health, chairman of the Ad Hoc Committee on Testing for Environmental Carcinogens, was quoted by OSHA as follows:

In the case of the human population, with the completely unknown variations in sensitivity to any chemical carcinogen and with the impossibility of knowledge of other variables that may affect responsiveness to these agents, attempts to establish threshold levels for carcinogenicity are unrealistic.

And William Nicholson of the Mt. Sinai School of Medicine was quoted by OSHA as follows:

Despite considerable research on the effects of carcinogenic substances. . . no data exist that would define a threshold for any carcinogen. The task confronting one who would define a level below which no carcinogenic risk exists for human populations is virtually an impossible one.

Other scientists, including representatives of regulatory agencies, prefer to make it sound as though the inability to determine threshold doses for a population are, rather, a function of a missing consensus which might one day make its appearance. Thus, in 1979, the Interagency Regulatory Liaison Group, Work Group of Risk Assessment, representing the Consumer Product Safety Commission, the Environmental Protection Agency, the Food and Drug Administration, and OSHA, said:

There is no presently acceptable way *to determine reliably a threshold for a carcinogen for an entire population. [Emphasis added]*

However they choose to formulate the problem, these scientists are simply expressing self-evident truth: No one can conceivably calculate the dose of a carcinogen that will be "safe" for the most sensitive individual in a population of 226 million people. The Aardvark Principle—the moral goal of cancer prevention—allows no such calculation.

In logic, this is all one needs to know about the threshold controversy. As long as one is determined to protect every human being in the Republic from a disease without having much human data and without knowing the mechanisms of the disease, no one can calculate safe or threshold doses in advance and there is nothing to argue about.

If there is nothing to argue about, however, what *are* the scientists arguing about—and why is the argument raging with the force of a "jihad"? Maugh, in *Science*, was satisfied to declare that the conflicting positions were "articles of faith." But there is a weird aspect of this battle that cannot be explained by clashing faiths. The curious fact is that none of the arguments purportedly offered in support of, or in repudiation of, thresholds are *relevant* to the concept of a threshold as it is defined by the goal of cancer prevention—that is, a *dose* of a carcinogen which "*could not*" and "*never would*" give anyone cancer. A rapid review of those arguments will illustrate the point.

The main arguments offered in support of the no-threshold theory are these (listed here without explanation and without attribution to specific sources):

1. Cancer may start with the transformation (possibly mutagenic) of a single cell.

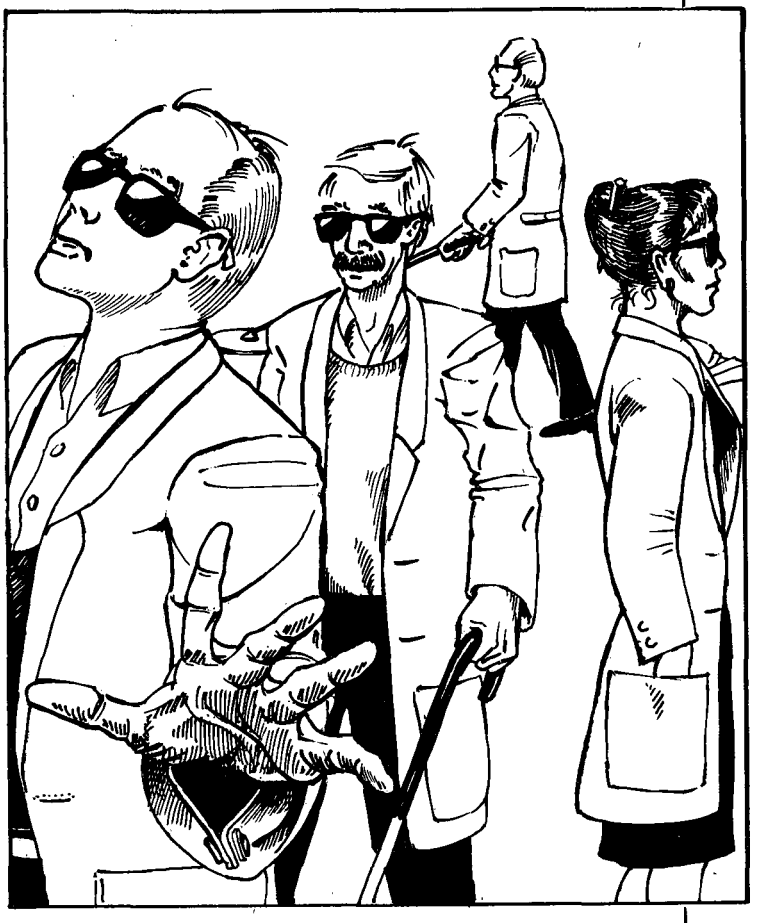
2. One molecule of a carcinogen or a mutagen may trigger cancer.

3. Cancerous cells are self-replicating, multiplying, proliferating entities.

4. The initiation of the process of carcinogenesis is irreversible.

5: Carcinogens interact with each other synergistically and "additively" or "incrementally" or "cumulatively"; thus, every minute dose of a carcinogen is added to a "background dose" which increases the risk of cancer.

These are the major ideas that, according to OSHA, represent the scientific consensus, and each of these ideas is mentioned



in literature reviews of the controversy as an argument for the probable nonexistence of thresholds. But these ideas are descriptions of a hypothetical process of carcinogenesis. They do *not* demonstrate that there is no *dose* of a carcinogen that "could not" and "never would" give anyone cancer; one can neither prove nor disprove such a proposition. These ideas are simply a collection of the most intimidating aspects of the various theories of carcinogenesis which are being brandished *as if* they were proof of the nonexistence of a safe or threshold dose.

And precisely the same thing is true, in reverse, of the critics of the no-threshold theory, who may not, as OSHA claims, represent the "consensus," but whose numbers are sufficient to have generated a "jihad." The alleged rebuttals to the no-threshold theory are exactly as irrelevant to the moral goal of

cancer prevention as are the defenses. Although most scientists do not make all of these arguments at once, taken collectively, they constitute the mirror opposites of the positions cited above and are listed in reviews of the literature as arguments against the no-threshold theory.

1. Exposure to very low levels of carcinogens—or to a single molecule of a mutagen or a carcinogen—may not necessarily be a significant threat, given the existence of a series of repair, recuperation, deactivation, and detoxification systems and other biological defense mechanisms in the total organism.

2. A minimum number of molecules in a cell must be affected before any biological reaction, including carcinogenesis, can take place.

3. Human beings are being pounded so consistently by so many carcinogens that nothing much happens at the target-cell level; the cells die and no carcinogenesis occurs. In addition, human cells are far more resistant both to radiation and to chemical carcinogenesis than are the cells of mice.

The no-threshold, or no-safe-dose, theory is the rock on which the temple of cancer prevention has been built.

4. The process of carcinogenesis is not necessarily an irreversible no-threshold phenomenon, for a great many metabolic variables (including high-dose testing itself) may inhibit or potentiate the carcinogenic response.

5. While examples of synergism do exist, there is no scientific evidence to support the idea that there are cumulative or incremental effects of carcinogens, that is, that minute doses of different combinations of carcinogens add up together to produce a cancer. In fact, certain combinations of carcinogens are *less* carcinogenic than the same carcinogens ingested individually. And, finally, there are anticarcinogens which act to prevent or inhibit carcinogenesis.

Even on the assumption that all these arguments are true, they too add up to a description of a hypothetical process of *resistance* to carcinogenesis. They do *not* constitute evidence that a dose of a carcinogen exists which "*could not*" and "*never would*" cause cancer in a single human being. Here, arguments are being brandished as if they constituted disproof of a population threshold, which is as impossible as a proof.

Even more curious, critics of the no-threshold theory are often arguing with a strawman, for many, if not most, of the defenders of the no-threshold theory are in full agreement that the second set of phenomena exist; they just argue that they cannot be measured—a proposition with which their opponents generally agree! Many of the defenders of the no-threshold theory also think, as do the critics of the theory, that the one-molecule theory of cancer is insignificant. Many of the defenders of the no-threshold theory are in full agreement that there may be individual thresholds. There is also full agreement that the human body has repair and other detoxification systems which protect it from a variety of toxic and carcinogenic effects, but here too the point is made that no one can calculate at what level these mechanisms fail to function. Finally, just as no critic of the no-threshold theory ever denies the phenomenon of synergism, no informed defender of the no-threshold theory denies the existence of anticarcinogens and inhibitory reactions.

When one examines this controversy carefully, therefore, one sees that this is not quite the "jihad" over thresholds that it is said to be. It is a complex, angry battle in which scientists tend to polarize around the most terrifying versus the most reassuring components of the various theories of carcinogenesis. In fact, there is no war over *population* thresholds at all, and there cannot be one. No opponent of the threshold theory has ever claimed to have set a safe dose of a carcinogen for the total population, including its most sensitive individuals. The scientists engaged in this "jihad" are clearly angry at each other about an unnamed something, but it cannot be about a set of ideas with which most of them agree.

One clue to this unnamed something is to be found in Marvin Schneiderman's comment, quoted earlier, that opposition to the no-threshold theory has won support from "traditional toxicology." It is clear that there is, then, a nontraditional toxicology and that the two kinds of toxicology are at war, in some fashion.

Toxicology is an old and complex science, and its history is, in effect, the history of man. Man was not born into a toxic-radioactive world with a copy of *Consumer Reports* in his hand. To preserve his own life, even primitive man became a toxicologist of sorts. Over the millennia, as he saw his fellow man die in agony after eating certain plants, berries, or fish, he learned to call those entities "poisons" and avoided them. In later stages of human development, when a vast lore on poisons had already been collected, men learned to kill others with natural toxic substances—for example, Socrates was killed with a cup of poison brewed from hemlock, and kings had human "tasters" who ate and drank first what was put before the king; if the tasters did not die in agony, the meal was deemed safe and the king ate and drank without fear.

This crude experimentation, however, protected man only from the most virulent, fast-acting poisons, where cause and effect could be quickly identified. By the sixteenth century, a far more subtle discovery was made by a German physician named Theophrastus Bombastus von Hohenheim, known as

Paracelsus. He had learned that every substance could be toxic, depending on the dose. His famous proposition, originally stated in German, was: "What is it that is not poison? All things are poison and none without poison. Only the dose determines that a thing is no poison." A Latin translation later reduced the idea to *Dosis sola facit venenum*—"Only the dose makes the poison." And on the frontispiece of a current text, *Toxicology: The Basic Science of Poisons*, edited by Louis J. Casarett and John Doull, yet another translation stands: "All substances are poisons; there is none which is not a poison. The right dose differentiates a poison and a remedy." The idea of Paracelsus is endlessly retranslated and reformulated because it is the fundamental principle of modern toxicology, the science of which Paracelsus is the recognized father. Libraries are stuffed, today, with studies of the toxicity of natural substances, and the knowledge is constantly growing. In 1979, the German toxicologist Schmähl reported: "Paracelsus' idea was recently confirmed by a case when a man in Germany died because he had drunk 17 liters of water within a very short time. He died from a cerebral edema and electrolyte disturbance. In this special case, even water acted as a fatal poison."

From this remarkable discovery that all substances at some dose could be poisons and that poisons were dose-related it was just a step—a long step—to the systematic use of laboratory animals as "tasters" for men. In a contemporary toxicology laboratory, animals are tested at different doses of a drug or an industrial substance, and their responses to each dose level are recorded. The lethal dose—LD50—is that dose at which 50 percent of the animals die, and the responses to a graded succession of doses are recorded to identify the "dose-response" curve. Traditionally, the safe or threshold dose for man has been calculated at a minute percentage of the dose which has no effect whatever on the animal.

Thus does the laboratory animal serve as a taster for man in the fields of pharmacology and industrial toxicity. If, today, most human beings are not poisoned in a highly toxic world, compounded by the highly toxic industrial revolution, one may conclude that the animal has served as a fairly efficient taster.

This does not imply, however, that the laboratory animal has rendered it unnecessary to study man directly. Errors have always been made, animals have not always predicted well for man, men have died from doses of drugs and toxicants which had been thought to be safe, and further knowledge was gained from these accidents. In the last analysis, however helpful the animal tasters, one still only knows with certainty what is dangerous to man by studying man. Conversely, one only knows what benefits man by studying man: penicillin, to cite the classic case, kills hamsters and guinea pigs, but it is a lifesaver for most men. As Casarett and Doull explain in their toxicology text, the standards set on the basis of animal dose-response curves are "provisional":

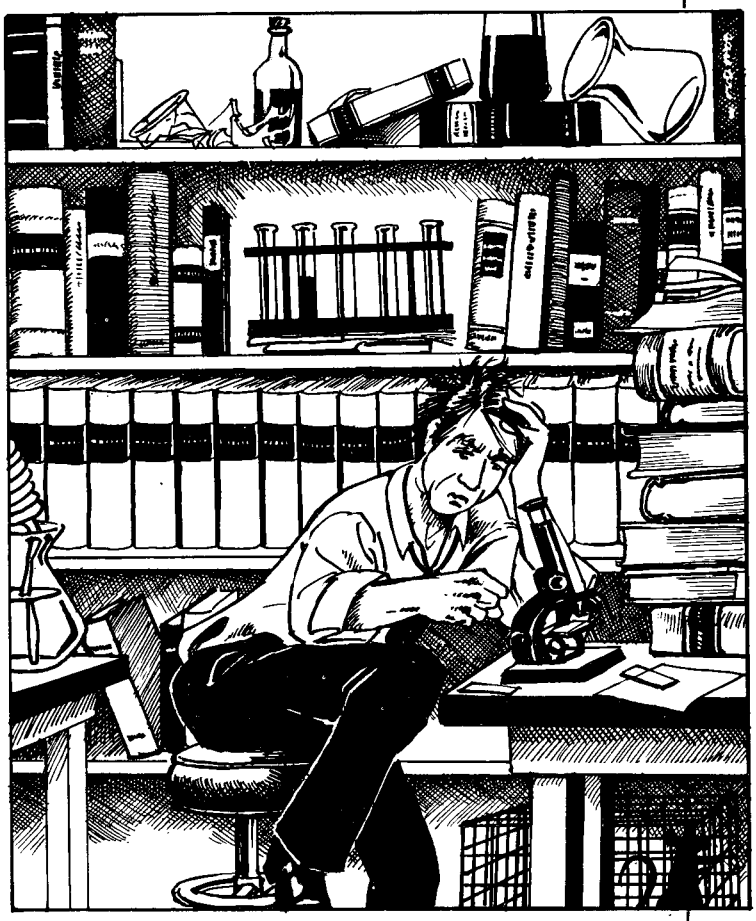
[They] are usually modified as more experience is gained with human exposure under conditions of use. Community standards are likewise developed and modified on the basis of current knowledge. Thus the "standards" set for safety in all circumstances are not firm, fixed, immutable figures. Rather, they represent the best judgment, at any given time, of the safety of a toxicant based on the sum total of all toxicologic information.

Direct human experimentation has been reduced to a minimum with the use of animal "tasters," but it is still necessary to engage in empirical studies of man himself. Man remains his own most reliable experimental animal.

So far, of course, we have just been discussing chemical toxicity. But carcinogenesis is a form of chemical toxicity, and Paracelsus is the father of this science as well. Indeed, the same toxicologists study both toxicity and carcinogenesis. And the fundamental discovery of Paracelsus, *Dosis sola facit venenum*—"Only the dose makes the poison"—and the modern study of dose-response curves are also applicable to carcinogenesis. Indeed, if any firm principle of carcinogenesis is known at all—a principle that applies both to animal and to man—it is Paracelsus' principle of dose-relatedness. Here is an explanation of the phenomenon as offered by William Lijinsky at OSHA hearings in 1978:

In the case of cigarette smoking there is a clear-cut response relationship; that is, the incidence of lung cancer is greater, the larger the number of cigarettes smoked per day and the longer the period for which they are smoked. Thus we can say that the higher the dose rate, or the longer the period of exposure, the higher is the risk of developing lung cancer. . . .

Exactly the same experience pertains to tests of chemical carcinogens in experimental animals. Those receiving higher dose rates, or the same dose rates for a longer period, have the highest risk of developing cancer. . . .



From the animal tests another aspect of dose-response can be deduced, namely that the higher the dose of carcinogen administered, the earlier the tumors appear. . . . Furthermore, only at the highest doses do all of a group of animals die of the tumors induced, and at lower doses the animals often live out their natural lifespan and die without any induced tumor.

When considering dose-response we have the two measures, time to death with induced tumors . . . and proportion of animals with induced tumors; the former decreases and the latter increases as the dose of carcinogen is increased.

Similarly, Jerzy Neyman, director of the Statistical Laboratories at the University of California at Berkeley, working with the reported carcinogen urethane, describes "a striking dif-

ference between crops of lung tumors in mice depending on the high or low dose-rate. With the high dose-rate, there are many more tumors."

Finally, carcinogenesis is dose-related in radiation carcinogenesis as well as in chemical carcinogenesis. As Henry Pitot of the University of Wisconsin sums it up: "As in the case of most agents producing effects in biological systems, the evidence is overwhelming that chemical and physical [radiation] induction of the neoplastic transformation is dependent on the dose of the carcinogenic agent." This is pure Paracelsus.

Where, then, is the conflict between "traditional" toxicology and "nontraditional" toxicology? We learn its essentials from Umberto Saffiotti of the NCI, who, in 1977, announced the birth of a "new toxicology." There was one primary difference in this "new toxicology" which led, in turn, to other differences. The primary difference was a rejection of what Saffiotti called the "traditional empirical approach" to man. One would use animal research in carcinogenesis just as one did in pharmacology and industrial toxicology—but, said Saffiotti, when it came to setting provisional safe doses based on that animal research and then assessing the effects of those doses in man, that "empirical approach" would not do for carcinogenic chemicals.

The reason, he said, lay in the mechanisms of carcinogenesis, which were uniquely different from the mechanisms of toxic substances in that they were characterized by "a trigger change in the target cell's regulatory mechanism, which determines a self-replicating cell lesion." That initial molecular damage, produced by exposure to a carcinogen, might be very restricted—"even to a few cells." Depending on the condition of the individual, it would then manifest itself in "the proliferation of the altered cell population." Such carcinogenic effects, he said, were different by nature from the effects of terminal toxicity. He called them "self-replicating toxic effects," and he observed that a "new toxicology" was evolving to control the carcinogens which induced such "self-replicating" toxic effects. That "new toxicology" was interdisciplinary, he said, and needed the participation of professions "ranging from chemistry and physics to biology and pathology, and from environmental sciences and sociology to law and economics."

Two aspects of that explanation are of particular interest. First, since no one, in 1977, knew the mechanisms of cancer, Saffiotti was not actually describing those mechanisms. He was simply using a good many words, including the postulate of the "single-cell" or "few-cell" theory, to describe what everyone already knew about cancer—that something unknown, whether inside or outside the individual or both, made cells proliferate. The conference title itself had described cancer more economically; it was a conference on "cell proliferation." Saffiotti was actually enunciating a new *moral* edict for toxicology: that while the "empirical approach" to man might be permissible for drugs and other toxic substances, it was impermissible for chemicals that might be "potential" carcinogens. Carcinogens in man must henceforth be studied without reference to man.

The second innovation of the "new toxicology," as Saffiotti explained it, was the invitation into the ranks of toxicology of a group of unusual new specialists who knew nothing whatever about biology, toxicity, or carcinogenicity: sociologists, lawyers, and economists. It is not difficult to see why sociologists, lawyers, and economists moved into the "new toxicology" just as empiricism was being evicted. In the very year that Saffiotti defined the "new toxicology" for his colleagues, he had also defined the professional ethics of animal testers in carcinogenesis as that of bearing witness to "suspected mass murder." With such a view of the function of the "new toxicology," the empirical approach to man was of little use—in fact, it was an obstacle; "suspicion" could not flourish in the atmosphere of empiricism. The "new toxicology," in sum, was a demand for a new moral-political approach to toxicology which would, with the aid of sociologists, lawyers, and economists, rationalize the pursuit of "suspected" industrial "mass murder" without any need for the empirical evidence of harm to man that is traditionally demanded by both science and the law.

The "new toxicology" was morally and politically triumphant, a triumph which was profoundly satisfactory to all those who imagined, as did an Ad Hoc Committee chaired by Saffiotti in 1970, that "the mass" of environmental cancer came from industry and that the disease could be virtually obliterated by law. But a strange price had been paid for that triumph. The study of carcinogenesis was still in its infancy, but the "new toxicology" had committed itself to cancer prevention—to the identification of "potential" carcinogens and to the assessment of carcinogenic risks to man—with only a sparse handful of human data available and a taboo against the "empirical approach." However one may applaud its morality, the "new toxicology" had actually paralyzed itself scientifically. Without the "traditional" empirical method in a disease that no one understood, it was left immobilized in a posture of moral probity—and was unable to learn anything that it did not already know about the exogenous causes of cancer in man. Above all, it could never begin to discover what chemicals or what *doses* of chemicals did or did not have effects, save in mice and rats. But the purpose of cancer preven-

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tion was not to protect mice and rats but to protect people. Thus, the "new toxicologists" could only declare, on *moral* grounds, that even the tiniest dose of an animal carcinogen, even a single molecule, had to be considered perilous for man. *The no-threshold theory was born of the abandonment of empiricism.*

The traditional toxicologists, however, cannot seem to grasp that with a "new toxicology" which morally forbids empirical studies of dose-response effects in man and with a moral goal of cancer prevention which forbids any calculations at all, there is no scientific argument to be made. They keep repeating the classical concepts of toxicology as if that science had not been eviscerated, and they stubbornly keep adapting its tenets to carcinogenesis—above all to the idea that there *must* be a threshold dose. But when they are challenged by the "new toxicologists" to prove a negative—to set a threshold for a given group of people which will *never, ever* give any one of them cancer, to set a threshold for the total population which will *never, ever* give anyone cancer...they fall still.

From that eerie stillness there emerge hostility and angry prophecies. Thus in August 1979, in an article in the science section of the *New York Times* entitled "How Tiny Chemical Traces are Found," Lawrence Garfinkle, vice-president and epidemiologist of the American Cancer Society, was quoted:"...one part per *billion* of anything seems just too small to worry about. Some of us think all instruments capable of detecting chemicals and concentrations lower than one part per million ought to be smashed before we drive ourselves crazy." At the very time when technology was doing the precise bidding of the theoreticians of cancer prevention who were committed to ridding the continent of every last trace of a carcinogenic molecule, talk of instrument-smashing was coming out of the mouths of prominent students of cancer.

That hostility to the very instruments on which the new science of cancer prevention relied was not new. It had simply become more intense among those who saw where the instruments were taking them. In 1976, when Alexander Schmidt was the FDA Commissioner, he complained that "we will be chasing a 'receding zero,' and some idiot in some lab will come up with something sensitive to parts per quintillion, and our policy says we will adopt it." Obviously, such scientists felt trapped, and Schmidt's irritable little prophecy tells us clearly that it was not the technology itself that was tormenting them but "our policy."

In the late 1970s, a fulfillment of Schmidt's prophecy occurred in a far more dramatic form than he could ever have dreamed. It involves a particular court case that demonstrates the ultimate implications of the no-threshold theory.

In 1973, it was found that acrylonitrile—a chemical that is now considered an "established" carcinogen—could migrate from plastic bottles and containers into the food and drink they contained, and the Food and Drug Administration (FDA) instituted proceedings to ban the use of acrylonitrile in the manufacturing of such containers. The manufacturer, the Monsanto Chemical Company, reported, however, that its technology had improved during this period and that with its new bottles no evidence of molecular migration could be detected. The company, consequently, demanded a new hearing and, with some difficulty, got one. One of the major issues that turned out to be at stake in the ensuing proceedings was the law of diffusion. Both the FDA and Richard Wilson of Harvard University, who had been asked to serve as consultant to the industry, found themselves discussing that law of physics, which governs the movement of all molecules of liquids, gases, and solids as they intermingle in nature.

To appreciate the oddity of this, one must know something about the law of diffusion. Here is a simple explanation of its meaning which has a reassuringly literary context. A 1977 paper by George B. Koelle of the Department of Pharmacology of the University of Pennsylvania began with this passage:

In a memorable scene from Samuel Butler's The Way of All Flesh, *old George Pontifex drops and breaks a pint bottle of Jordan water that he has been saving for many years for his first grandson's christening. The quick-thinking butler averts an impending crisis...by snatching up a sponge, recovering half the treasured liquid from the floor, and filtering it through a bit of blotting paper. On reflection, the same purpose would have been served by the simpler expedient of turning an adjacent tap and drawing a fresh pint from the local English water supply.*

However one may applaud its morality, the "new toxicology" had actually paralyzed itself scientifically.

Koelle explained that the Jordan poured 6.5 x 10^6 tons of water into the Dead Sea every day and, when the outpouring of one day had intermingled with all the waters of the world—an amount of water estimated at 1.5 x 10^{18} tons—an intermingling which could be expected to occur over a huge expanse of time, "a pint of water sampled from any source will contain 3.7 x 10^{12} molecules of Jordan water."

He then distilled the calculation into its simplest terms:

...if a pint of water is poured into the sea and allowed to mix completely with all the water on the surface of the earth, over 5,000 molecules of the original sample will be present in any

pint taken subsequently. The general conclusion to be drawn from these calculations is that nothing is completely uncontaminated by anything else.

This "general conclusion," without the technical reasons, is the law of diffusion.

The reason for which the FDA and Richard Wilson, for Monsanto, were discussing the law of diffusion was quite simple. The FDA had declared that it didn't matter whether one could no longer *measure* the migrating molecules in Monsanto's new bottles. What mattered, said the FDA, was that according to diffusion theory, molecules of acrylonitrile *were* migrating and could be so legally described. Richard Wilson responded that application of the theory of diffusion indicated that the migration was so infinitely small (a few parts per billion) as to be toxicologically insignificant. To this the FDA replied, consistent with the no-threshold theory, that no amount of a carcinogen was toxicologically insignificant. Monsanto appealed the case.

A summary of the court's findings was published by Peter Barton Hutt, former legal counsel to the FDA and later a partner in the law firm involved in the case. A number of different issues were involved, but we restrict ourselves here exclusively to what the court had to say on the subject of diffusion theory. Hutt's summary of the legal opinion, written for the legal profession, is accurate, succinct, and has the additional merit of being funny. Here is the essence of it:

. . . the court remanded to FDA its decision that any use of acrylonitrile, at any level and under any circumstances, could potentially result in migration. To the extent that FDA's "diffusion principle" amounted to nothing more than a restatement of the second law of thermodynamics, the court explicitly rejected it. . . .

. . . the court held that Congress did not intend that reasonable expectation of migration would be satisfied merely by a simple recitation of the diffusion principle. In short, the court agreed with the industry contention that Congress did not enact, as part of the definition of "food additive," the second law of thermodynamics.

There was no implication here that the court found limitless migration of molecules of acrylonitrile tolerable. In fact, the first bottle, which did have detectable amounts of acrylonitrile leaching into the food, was found unacceptable by the court—the improved bottle was found acceptable. As Hutt put it, "this is one of those rare cases where both sides won." The layman, of course, can make no assessment either of the safety of Monsanto's bottle or of the carcinogenicity of acrylonitrile. What he can assess is the linkage of the no-threshold theory with the law of diffusion. Although the judges in this case did not say so—it was doubtless irrelevant to the legal-administrative considerations they are required to consider—they had actually come face to face with the true significance of the no-threshold/one-molecule theory: the fact that that theory, with the number of increasingly sensitive measuring instruments, inexorably skids into the dimension of reality governed by the law of diffusion—and that there is no way to arrest that skid.

It was this problem of the "receding zero" that in 1979 led Lawrence Garfinkle, an eminently civilized scientist at the American Cancer Society, to ventilate his fantasies and those of other cancer researchers about smashing the new instruments before they all drove themselves "crazy." It was an expression of violent frustration by scientists who have found themselves in an obviously bizarre trap and cannot think their way out of it. In a situation like this, a layman who has no professional vested interests, no professional responsibility, and no concern for peer judgment—who, in a word, has nothing to lose—may be able to see the nature of the trap more clearly. It is, in fact, a rather simple trap, but it must be set forth in five steps:

1. If, *on moral grounds*, one expels the "empirical approach" from toxicology and one is left with an infant science that lacks both theory and human dose data;
2. If, *on moral grounds*, one establishes a goal of cancer prevention based on a logical fallacy which requires that one prove a negative;
3. If, *on moral grounds*, one tolerates that logical fallacy, which leaves one with no calculation for thresholds other than the calculation that no calculation can be made and that the only safe exposure is a zero exposure;
4. And if the instruments keep growing so much more sensitive that the zero goal keeps receding at a breathtaking rate;
5. Then one finds oneself in an extraordinary trap in which one realizes that one is driving oneself and others "crazy" and starts having fantasies about smashing instruments.

Such a fantasy, however, simply means that one has only thought oneself back from Step 5 to Step 4 but has not pursued the reasoning further. What would keep intelligent scientists from thinking themselves back to Steps 3, 2, and 1? The answer stands out clearly, particularly since I have obligingly italicized it three times. To think back one step further than Step 4, where the mischief can be blamed on instruments, the scientists would have to challenge the core of the "new toxicology"—the prevailing concept of morality, of goodness, that is held by his colleagues and by the regulatory agencies and that has now been taught to the Congress, the press, and the public and is enshrined in the law. For reasons that pertain to cultural matters outside the realm of this discussion, one of the last things on earth that most respectable people—scientists and nonscientists alike—will do is challenge the conventional moral beliefs of their peers, however irrational they may be. It is psychologically easier for such men, even when highly educated, to express the fantasies of primitives—knowing that they are the fantasies of primitives—than to stand up and say aloud: "What is really 'driving us crazy' is our notion of morality." And that may well be at least one of the unnamed—or unnamable—*somethings* that all these scientists are really fighting about.

The plain truth is that there *is* something "crazy" about the moral standards of the "new toxicology" and "regulatory" science which have culminated in the Aardvark Principle and the law of diffusion. This mixture of morality and logical fallacy as a substitute for data is unmistakable folly, and it has caught both the scientists and their science in a trap. Nothing demonstrates it more vividly than the sight of the "new toxicology" falling like a stone into a bottomless abyss—falling into that invisible dimension of nature in which single molecules of every substance on earth endlessly intermingle, falling with *no scientific concepts at all* to break its fall because they have been *morally* disallowed. Whatever else may be said about the no-threshold/one-molecule theory, it is its suicidal inability to differentiate itself from the law of diffusion that tells us it is intellectually bankrupt.

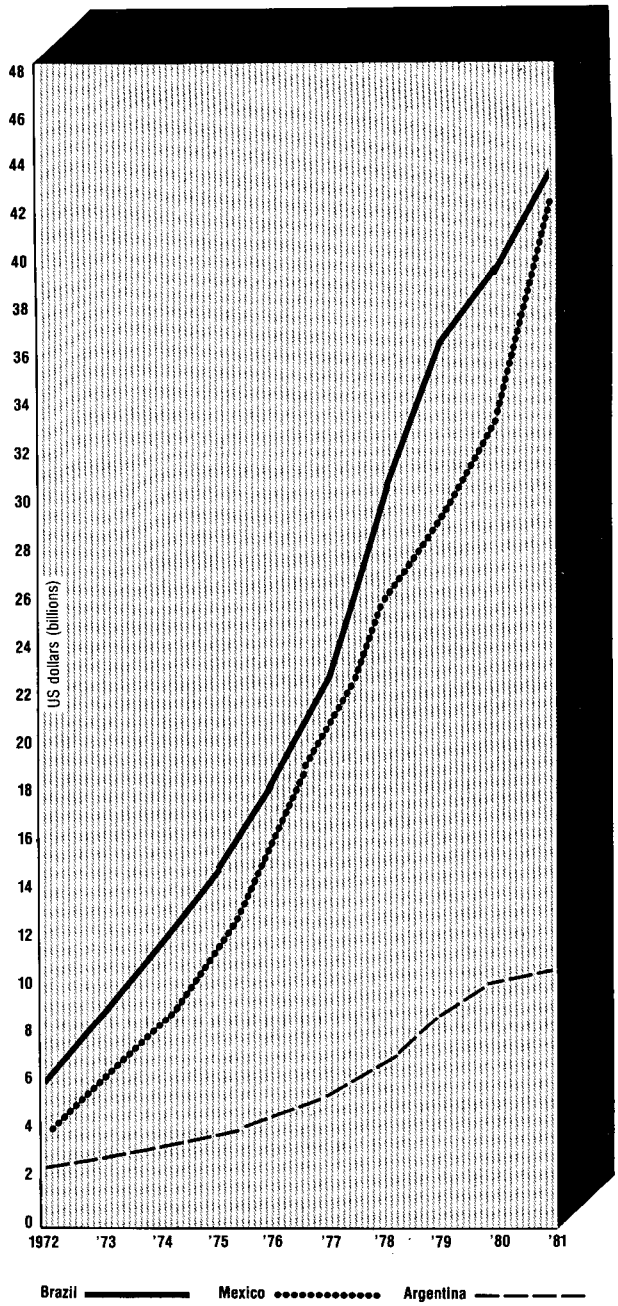
It is on this bankrupt premise that the entire regulatory process, that cancer prevention is based. And this is merely *one* of a series of astonishing irrationalities that I discovered at the heart of the "science" of cancer prevention by animal-man extrapolation, irrationalities of which the American public is still unaware—irrationalities so numerous, so ideological at root, so implacably hostile to science itself that they add up to a cultural crime. ◻

Edith Efron is the author of The News Twisters *and collaborated with William Simon on his* A Time for Truth. *This article is adapted, by permission of the author, from her forthcoming book,* The Apocalyptics: Politics, Science, and the Big Cancer Lie *(Simon and Schuster).*

Paper Crisis

We didn't really have an international debt crisis before, but Congress is doing its best to create one.

By Jon Osborne



1
Public and publicly guaranteed debt

In *nominal* terms, the growth of Argentina's, Brazil's, and Mexico's debt is staggering.

We face global financial ruin from an "international debt crisis," the authors of countless recent books and articles warn us. They tell us why the crisis exists and, typically, how to avoid the disaster that it is ushering in. But a close examination of both the logic behind the crisis prediction and the evidence submitted to support it reveals the forecast to be, at best, premature, and at worst, a convenient fiction popularized by those now benefitting from the political results of its general acceptance.

Weak arguments and scarce evidence have, of course, never discouraged government action, so in November 1983 Congress approved an administration plan to grant the International Monetary Fund (IMF) an additional $8.4 billion, if not to actually solve the anticipated crisis, to at least frighten the bogeyman away for the time being. The sad irony of this tale is that the very measures that Congress has just taken to remedy this doubtful crisis will only make its advent more likely.

First to warn us of the possibility of an international debt crisis were the banks that made loans to foreign governments—loans now thought to be vulnerable to default—and the various governments that received those loans. And those same parties are also the principal beneficiaries of present government efforts here and abroad to insure this debt by subsidizing its repayment. Their authoritative voices warned of a financial collapse, and a press ever eager to exaggerate disaster echoed the doomful pronouncements. Thus egged on, governments of net lender countries moved to shield indirectly, by way of IMF subsidies, their domestic banks from the risks naturally associated with international debt. The international banks want the subsidies as a means of costlessly increasing the security of their international loans. The debtor governments want the subsidies as a new source of income. Both benefit from these subsidies and therefore both claim that a crisis exists; but what is the basis of this assertion and how have these various interests been able to convince so many of its validity?

The mechanics of the crisis, as foreseen by its "victims" and their unwitting allies in the press, are deceptively simple: As a debtor government progressively borrows more money, the cost of servicing its debt rises proportionately. Because the borrowed funds are not always invested in productive ways, however, they frequently do not generate sufficient income to cover the interest

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