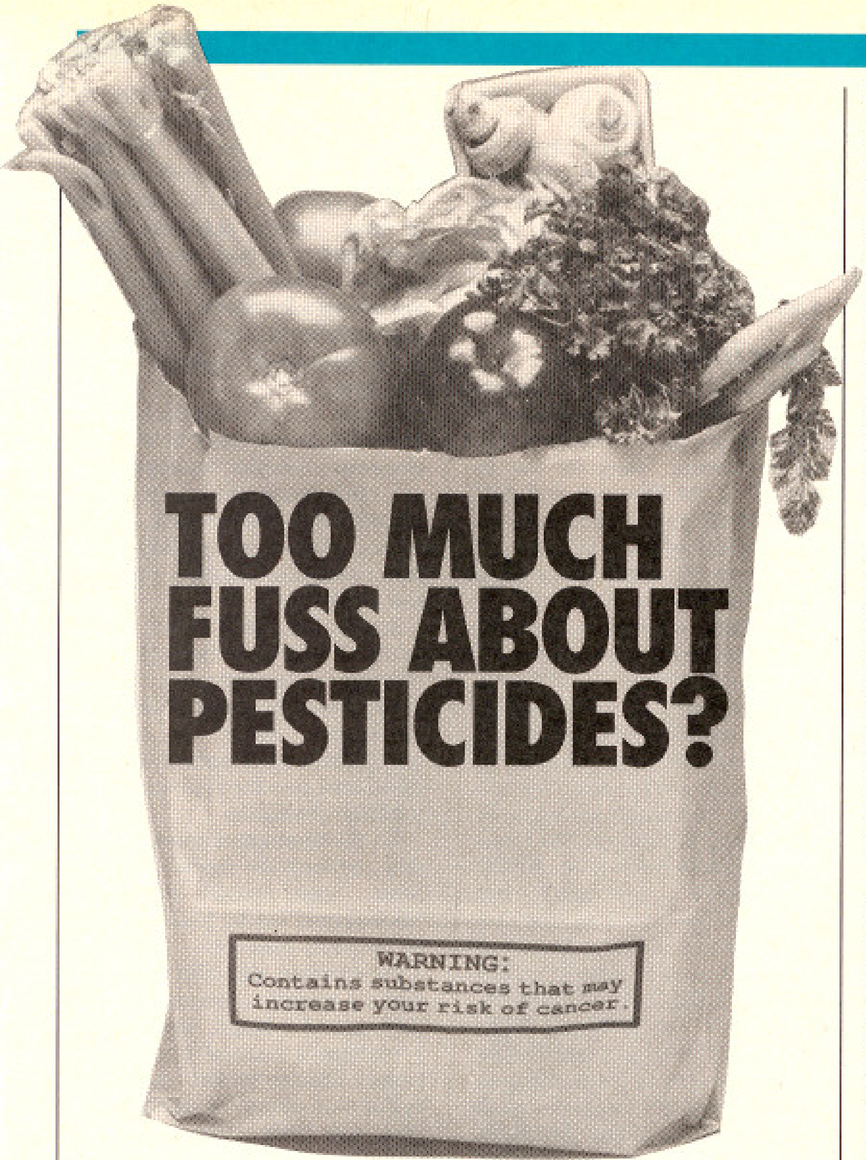
TOO MUCH FUSS ABOUT PESTICIDES?

Why worry about low levels of pesticides in the diet when many foods contain high levels of natural carcinogens? An interesting question—but is its premise right?



In the wake of the controversy over *Alar* in apple products (see CONSUMER REPORTS, May 1989), an old argument against strict regulation of pesticides has gained new currency. Pesticides in the diet, the argument goes, pose only trivial cancer risks. Thousands of natural carcinogens in foods pose risks vastly greater than the tiny hazards of synthetic pesticides.

Even so, the argument continues, no significant fraction of human cancer has been positively linked to "nature's carcinogens." Therefore, health and safety officials should focus on "real" health hazards, like smoking and drinking, and worry less about pesticides in the food chain.

The demand for environmental protection has often come under attack from those who profit from pollution. What's new is the claim that there are convincing *scientific* grounds for putting food-safety concerns on a back burner.

The politics of pollution

The contention that controlling manufactured hazards is silly when natural ones are so much greater is founded not in science but in political philosophy. It's part of the mindset that distrusts most government intervention in the marketplace, even intervention to protect the public from environmental hazards or from unsafe products.

Political views are matters of opinion, and thus beyond proof. Science, on the other hand, is perceived as a discipline dealing in provable facts. In political disputes over environmental hazards, activists on all sides collect scientific data to buttress their case—as if science could "prove" an opinion correct. In that vein, those who would weaken environmental protection have long sought scientific justification for their view that controlling chemicals is unnecessary.

A classic example was Edith Efron's 1984 book, "The Apocalyptics," which attacked environmental advocates as political activists seeking government control of economic activity. Asserting that neither human health nor the environment was seriously threatened by chemical pollutants, Efron accused environmentalists of scaring the public with threats of cancer to attain political goals.

Efron attempted to prove her case with scientific "facts." As others had before her, she assailed animal testing as an unreliable measure of whether chemicals pose true risks of human cancer. She argued that synthetic chemicals have rarely been shown to cause cancer in people. And even if some pollutants *are* carcinogens, she asserted, the attention they receive is undeservedly great in light of the hazards nature hurls at us.

To hear Efron tell it, Americans were virtually swimming in a sea of natural carcinogens. Her list included a great many things never shown to be carcinogenic, like caffeine, proteins, corn oil, sugar, and salt, as well as some actual natural carcinogens, like aflatoxin, a byproduct of mold growth on peanuts and other crops. Since all these natural "carcinogens" had had no demonstrable impact on human cancer rates, Efron reasoned, why should anyone worry about traces of industrial chemicals that pose theoretical hazards?

It was fairly easy for experts in carcinogenic-risk assessment to dismiss Efron's viewpoint as ideological wishful thinking. The data she cited did not prove that most substances she listed were carcinogens. No respected scientists advocated her view.

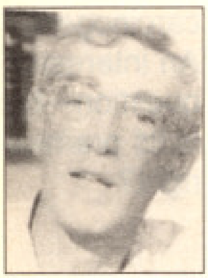
That has now changed.

Ammunition arrives

In April 1987, an article titled "Ranking Possible Carcinogenic Hazards" appeared in Science, the preeminent U.S. scientific journal. The paper's lead author was Bruce N. Ames, chairman of the Biochemistry Department at the University of California at Berkeley and widely known for his research on methods for assessing potential hazards of chemicals. In the early 1970s Ames invented what has become a stan-

dard measure of a chemical's propensity to cause genetic changes in bacteria. It's one of many tests used to assess a substance's possible toxic effects.

In their Science article, Ames and his co-authors proposed an innovative method to rank the risk of possible carcinogens. They calculated an index of hazard for selected carcinogens from two key factors: potency of the carcinogen (as measured in animal tests) and the estimated human exposure to it. They called their index HERP, for Human Exposure/Rodent Potency, and proposed comparing HERP indexes of substances to sort the big hazards from the little ones.



"The pesticides we are eating are 99.99 percent all natural." That's the message biochemist Bruce Ames has been delivering on TV and elsewhere. The subtext: no need to worry about pesticides added to the food supply.

The Science article provoked debate among scientists and regulators, but not over the idea of ranking risks (something regulatory agencies have attempted to do in various ways for years). The most provocative aspect of the report was what it implied about the relative size of various carcinogenic hazards.

To illustrate their ranking system, the authors chose 14 examples of environmental pollutants, pesticides, and food additives, and 15 "natural carcinogens." According to the HERP indexes, most of the natural hazards were hundreds or thousands of times greater than the hazards from synthetic chemical pollutants.

Publication of the Science article provided an important morale-booster for the chemical industry and its political allies: An eminent biochemist, one who as a matter of principle does not serve as a paid consultant to industry, was lending scientific support to the contention that society should stop pursuing "zero risk" and learn to live with "trivial" chemical hazards.

While other scientists began the long, slow process of assessing Ames's approach, data, and assumptions to see whether they were valid, political advocates rushed to incorporate Ames and his views into their propaganda.

A star is born

For anyone following the recent public debate over pesticides in foods, Bruce Ames seemed to turn up everywhere. There he was on CBS TV's "60 Minutes" and ABC TV's "20/20," arguing that there are natural carcinogens in all foods and that people shouldn't worry about pesticides. Dozens of readers sent us a widely syndicated column he wrote making the same points.

The National Agricultural Chemical Association, an industry trade group, has referred journalists to Ames, and a videotaped lecture he gave on comparative cancer hazards has been circulating among pesticide users. This summer, the American Council on Science and Health, an advocacy group largely supported by the chemical, food, and agricultural industries (but self-described as a consumer group), released a film called "Big Fears, Little Risks." The ACSH paid Walter Cronkite $25,000 to narrate the film, which stars Bruce Ames expounding his message. California grape and fruit growers have distributed the ACSH film as their response to concerns about pesticide residues in their produce. Now when environmentalists complain about pesticide residues in foods, their opponents are sure to cite the "Ames argument."

Ames's paper in Science recognized the tentative nature of the HERP approach and its rankings. In recent interviews and columns, though, he has presented the HERP rankings as scientifically proven facts. A whole world view about regulating chemicals now hangs by the slender thread of Ames's interesting but unproven ideas.

Carcinogens everywhere?

With Ames's entry into the debate, Edith Efron's argument—that we are surrounded by carcinogens and that eliminating a few chemical residues won't do much to reduce risk—has gained a new twist. Ames has refined the message by referring to what he calls "nature's pesticides," his term for substances evolved by plants to repel plant-eating fungi, insects, and animals. Ames writes that "The pesticides we are eating are 99.99 percent all natural…tens of thousands of these natural pesticides have been discovered, and every species of plant contains its own set of toxins, usually a few dozen.…It is probable that almost every plant product in the supermarket contains natural carcinogens."

Among the commonplace foods Ames lists as containing natural carcinogens are apples, bananas, broccoli, cabbage, carrots, celery, cocoa, grapefruit juice, horseradish, mushrooms, mustard, orange juice, pepper, pineapples, radishes, turnips, and many others.

Ames, of course, does not intend to set off a panic in the pantry. His message is that since we haven't been harmed by a diet of naturally carcinogenic foods, we needn't worry about small additional doses introduced into the food supply by synthetic chemicals.

But do we consume a diet of naturally carcinogenic foods? In many cases, Ames brands substances "carcinogens" on the basis of flimsy or equivocal evidence.

For example, take allyl isothiocyanate, a natural substance found in cabbage and mustard. Ames calls it a carcinogen because it produced benign bladder tumors (not clear evidence of cancer) in one study in male rats. Tests of the same compound produced negative or equivocal evidence in female rats and in both male and female mice. Few toxicologists would label allyl isothiocyanate a carcinogen on the basis of such limited and generally negative results.

Or take hydrazines. A few members of this chemical family (which includes UDMH, the breakdown product of *Alar*) are proven carcinogens. A number of other hydrazines occur naturally in mushrooms. Mushrooms rank fairly high on Ames's HERP index because of the "mixture of hydrazines, and so forth" that he says they contain. But no hydrazine found in mushrooms has to date been convincingly shown to be an animal carcinogen.

Or take ethyl alcohol. Consumption of alcoholic beverages is associated with an increased cancer risk in humans. A variety of known or likely carcinogens are found in whisky, beer, and wine. But there is no evidence that ethyl alcohol itself is a carcinogen; alcohol per se does not induce tumors in animal tests. Yet Ames labels ethyl alcohol a carcinogen, and estimates the risk of drinking beer, wine, and even orange juice according to the amount of alcohol each contains.

It might be scientifically accurate to refer to allyl isothiocyanate, the hydrazines in mushrooms, and other substances on Ames's list as *suspected* carcinogens, in need of further tests. But a flat statement that these compounds are "carcinogens" perverts the term.

Ames strays even further from scientific precision when he suggests that thousands of his "natural pesticides" are probably carcinogens. He reaches that conclusion by extrapolating what's known about a few compounds to thousands of others. According to Ames, only a few dozen of those natural substances have been tested even partially for carcinogenicity. Somewhat less than half of those tested, about 20 in all, have shown any evidence of carcinogenic activity.

Ames says it's reasonable to assume that a large fraction of other "natural pesticides" would turn out to be carcinogens *if they were tested.*

But that's unlikely. Since it's not possible to test all natural and synthetic substances for cancer-causing potential, those chosen for testing are usually chosen because other evidence suggests they may be carcinogens. It makes little sense to assume that a similar fraction of all *untested* substances, including substances thus far unsuspicious, would turn out to be problems. Ames's suggestion that there are thousands of natural carcinogens in foods is simply speculation.

Are natural hazards worse?

According to Ames's index, natural substances in beer, wine, mushrooms, basil, and herb tea had HERP scores roughly 100 to 20,000 times higher than pesticide residues. Ames also stresses that since natural pesticides are present at levels "enormously higher than the amounts of man-made pesticide residues in plant foods," natural risks are much larger.

But does Ames's work really prove that? Certain weaknesses in the study suggest not. Here are some obvious ones:

Highly selective examples. The 14 synthetic chemicals and 15 natural substances in Ames's HERP chart do not provide a representative picture of either category. For instance, only two synthetic pesticides were included. There are some 300 food-use pesticides, more than 60 of which are at least suspected carcinogens. There is no conceivable way Ames can draw valid conclusions about the aggregate cancer risk from pesticides by looking at two examples.

Inappropriate examples. The two pesticides Ames did include—DDT and EDB—have both been banned. DDT, in particular, has not been used legally for almost 20 years. Yet Ames based his exposure estimates (and thus his HERP indexes) on the most recent available residue data. It's hardly surprising that trace amounts of a banned pesticide remaining in the environment present a very low risk. Far from demonstrating that pesticides needn't be regulated, Ames's analysis can be taken as evidence of the benefits of controls on DDT.

Misclassification of hazards. Some of the carcinogens Ames calls "natural" are largely man-made. Nitrosamines in bacon, for instance, are byproducts of using nitrite as a food additive. Nitrosamine contamination in beer came from combustion products introduced into malt during drying. Not only are nitrosamines not natural to beer, they were eliminated from its manufacture more than a decade ago, in response to public-health concerns.

Unrealistic assumptions. To estimate dietary risks, one must know the concentration of the carcinogen in various foods, the amounts of those foods people eat, and the number of people who eat them. It doesn't make much sense to contrast a risk from a substance in foods eaten in large quantities by everyone to a risk from something consumed by only a few people. But several of Ames's "natural carcinogens" are found in items like dried squid and comfrey tea, not exactly dietary staples.

Ames's analysis also overstates the likely intake of several natural carcinogens. Two of his larger HERP scores were for the popular herb basil (containing the suspected carcinogen estragole) and for mushrooms. Ames assumed a daily dose of one gram of dried basil leaf, a hefty intake even for a marinara lover. He assumed that people eat a half-ounce of mushrooms a day, which is about 10 times the average intake, according to USDA surveys.

By contrast, Ames used average U.S. daily intake estimates to calculate exposure to environmental pollutants and pesticides. When "worst case" high intakes of natural substances are compared with average intakes of pollutants, natural hazards seem far worse. But that's hardly a fair comparison.

Ames also vastly oversimplifies the world by looking at one substance at a time. Most foods contain many different substances that can either increase or reduce potential cancer risks. More than 20 suspected carcinogenic pesticides may be used on apples and tomatoes, for instance. And just to complicate matters, many foods contain natural "anti-carcinogens." For example, when broccoli is fed to animals, it inhibits tumor induction by other carcinogens.

In a 1988 report in the Journal of the National Cancer Institute, Frederica Perera and Paolo Boffetta of the Columbia University School of Public Health critically examined Ames's HERP approach. They included additional examples and used consistent exposure measures. Their analysis concludes, in striking contrast to Ames's own, that there are large and small risks within both the "natural" and "synthetic" categories. They estimated that many manufactured carcinogenic hazards in the diet were at least as large as many natural ones.

Perera and Boffetta's study demonstrates that the results of such comparisons depend almost entirely on the assumptions, choices of examples, and biases of the analysts. They conclude that the causes of cancer are too complex and the uncertainties too massive for the simplistic HERP approach to be a credible tool for setting public-health priorities.

Don't worry, be happy

Those who argue that Ames's work does justify changes in public policies on, say, pesticide residues, assume that consumers are intensely concerned about synthetic chemicals in foods but are not at all concerned about natural carcinogens. Actually, consumers care about any *avoidable* risk in the food supply, natural or man-made. Public concern about aflatoxin in peanut butter, for example, has been very high. Indeed, aflatoxin has been tightly regulated for many years, partly in response to vigorous demands from consumer groups in the early 1970s. Natural root beer, containing the carcinogen safrole,

was banned years ago. If the public becomes aware of other natural cancer hazards that regulation could reduce, it's likely to demand protection from them as well.

In one respect, however, there is a difference between natural and man-made risks that makes some people more willing to tolerate nature's hazards. The difference is usually an ethical distinction, quite independent of the relative size of the risks.

Pesticide residues, for instance, are in foods because someone made an economic decision to use those chemicals. Those whose businesses prosper from the use of pesticides usually assert that the benefits of use outweigh the risks. Consumers are not consulted on such matters. The risks are simply imposed on them. Small wonder that consumers are far more upset about pesticides than they are likely to be about a natural hazard. Nature may not be benign, but it is blameless.

Are small doses harmless?

A major theme of Ames's argument is that small doses of carcinogens are harmless. Creatures have been exposed to natural carcinogens throughout evolutionary history, Ames argues, and the human body has numerous defenses to protect itself from such toxins, whether natural or synthetic.

The body does have some defenses against exposure to toxic substances, but whether those defenses are effective against a lifetime of low-level exposure to a cancer-causing agent is uncertain. When millions of people are repeatedly exposed to even small doses of a wide variety of carcinogenic chemicals, the risk of an increase in cancer cases becomes a significant public-health concern.

Debate has raged among toxicologists for decades over the existence of thresholds for carcinogenic effects—dose levels below which no risk exists. There are several theoretical reasons why thresholds might exist. But there is no practical way to demonstrate the existence of thresholds within the genetically diverse human population. People are exposed over a lifespan to many different substances that might cause or promote cancer. No one knows how those many small risks add up.

Regulatory agencies have long taken the position that, in the face of uncertainty, it is prudent to assume no threshold for carcinogenic risks. That's an ethical choice, and it has economic consequences. Many people may disagree with the choice or dislike the economic costs of current regulatory practice. But that's a far cry from asserting that carcinogens are harmless at low doses, a position with no provable basis in science.

Of mice and men

Another prominent argument heard since the FDA tried to ban saccharin in the 1970's is that regulatory decisions about carcinogens should not be based on animal tests. Ames has raised anew some long-familiar problems in relying on animal data, such as differences among species in the way carcinogens are broken down by the body. (Even so, he was willing to rely on rodent data for the potency factors in his HERP index.)

Other advocates have taken an extreme position, arguing that rodent tests are an unacceptable basis for policy. They urge that carcinogens be regulated only after they have been proved to cause cancer in human beings.

In a news release and full-page newspaper ads last spring, for example, the American Council on Science and Health attacked the U.S. Environmental Protection Agency for proposing to ban *Alar* on the basis of test results in mice. A chemical-industry trade association has gone so far as to sue the U.S. National Toxicology Program in an effort to prevent it from classifying substances as carcinogens solely on the basis of animal tests.

Government regulators and scientific advisory bodies such as the National Academy of Sciences have explicitly recognized the limitations of animal tests for at least two decades. The question is not whether animal data are perfect, but whether they are useful in making prudent public-health decisions.

The overwhelming consensus among experts is that animal data are useful. Regulatory decisions are based on human data when such data exist, but that's a rarity. Human cancer may not manifest itself for many years after exposure to a carcinogen—or not until years of chronic exposure have taken place. Even then, it's often impossible to tell which of several cancer-causing agents may have done the damage, or whether some combination of factors led eventually to the disease.

Thus, animal data are used as a reasonable basis for inference that a risk to humans exists. Because most known human carcinogens have also been shown to cause cancer in certain animal species, it's prudent to assume that the reverse is also true.

Those who support using animal data for risk assessment believe that consumers are best protected when action is taken to *prevent* harm—by relying on imperfect animal data—rather than postponing action until widespread human harm is apparent.

Those who believe that health has been overprotected, and that costs to industry should be given more weight, should make that argument directly rather than attack the value of useful animal data.

Political animals

The debate over regulating pesticides in foods is inherently a political one, a battle over how society should manage risks and allocate limited cancer-prevention resources. In using and misusing the HERP approach pioneered by Ames, political activists and Ames himself have stretched science out of shape, in CU's judgment.

Some improved variation of the HERP index may ultimately prove useful for comparing carcinogenic hazards. But the conclusions Ames has drawn from this uncertain instrument depend almost entirely on the examples and assumptions he has fed into it. Because many of those are wrong or debatable, the conclusions are suspect. Treating them as "scientific facts" undermines the role of science and lends its own form of pollution to public debate. ■