# Letters

## Alar in Apples

Daniel E. Koshland, Jr.'s editorial "Scare of the week" (7 Apr., p. 9) decries public "overreaction" to Alar in apples and cyanide in Chilean grapes. While it is understandable in light of recent media attention to food safety, Koshland's posture seems itself an emotional overreaction to too much bad news. His "shoot the messenger" attack on the Natural Resources Defense Council (NRDC) misconstrues both the reasons public interest groups sound such alarms and the public's reasons for responding as it does. And the editorial contains important errors of fact that may add to public confusion on the Alar issue.

Koshland uncritically accepts as "facts" two claims by the Food and Drug Administration (FDA) and the U.S. Department of Agriculture about the extent and seriousness of the Alar problem. Both agencies have tried harder to calm public fears than to inform the public about the risks Alar may pose. Their estimate that "only 5% of apples are treated with Alar" is sharply contradicted by several recent surveys of apples for Alar residues that found from 22 to 55% treated. The data come from sources as diverse as the FDA and New York and California state agencies, the Los Angeles *Times, Consumer Reports* magazine, and a private testing company (Nutri Clean). The largest sample (FDA's 1988 residue testing) found Alar in 38% of tested apples (*1*). Even assuming that 60% of the total apple harvest goes to processors (and is presumably not treated with Alar), the residue data cannot be reconciled with the "5%" figure. Far more than 5% of apples now on the market have been treated.

Koshland makes a much more serious error in asserting that Alar residues are "well below conservative Environmental Protection Agency [EPA] tolerances." The existing tolerance (20 parts per million) is anything but "conservative." It predates test results the EPA says suggest that a breakdown product of Alar, UDMH, is a carcinogen. The EPA recently estimated the cancer risk of current dietary exposure to UDMH at 45 in a million, or 45 times greater than their own definition of a "socially acceptable" risk level of 1 per million (*2*). On the basis of the residues associated with that estimate, the level of Alar in processed apple products consistent with a risk of 1 per million is roughly 0.01 ppm, 1/2000 of the current tolerance. The EPA plans to ban Alar and intends to leave the current tolerance in place only for as long as it takes to complete the cancellation process. Koshland's implication that Alar residues are safe by a wide margin is both scientifically untenable and in direct opposition to the EPA's own current policy posture on the risks of the chemical.

Koshland correctly stresses that *socially* unacceptable risks—big enough that the EPA should worry about them—are still small enough that an individual is unlikely to be harmed, and there is no reason for public panic. But, like most scientists pontificating on risk, he shows that he has severe tunnel vision. The scientific facts (estimates of how big the risk is, with all their inherent uncertainties) are just *part* of what the public knows about Alar. The policy choices—both the personal and the public kind—depend on far more than facts. However big a risk may be, whether it is acceptable or not is a value judgment and is heavily influenced by *moral* dimensions of the risk.

For instance, most people probably do not know whether Alar poses a real cancer threat or not, but they know some experts think it *may*. And they prefer not to gamble with their own or their children's health. The fact that Alar is present in apple products without their consent or knowledge and that consumers can do nothing on their own to detect or remove it makes this sort of risk inherently *outrageous*, whether it's a tiny risk or not. As Slovic (*3*), Sandman (*4*), and others have pointed out, public response to risk depends far more heavily on such value and ethical dimensions of the risk than it does on the quantitative magnitude of the hazard.

Risk management must balance values and ethical choices and is unavoidably a political, not a scientific, process. Koshland nevertheless attacks the NRDC for acting politically, accusing them of being unscientific in the process. As the EPA risk data above indicate, the NRDC and EPA are not grossly far apart in their scientific assessments of the Alar problem. Where they do differ is in their sense of urgency. NRDC says the EPA is not acting vigorously enough to protect public health from Alar and from pesticide residues in general. They seek publicity because publicity translates into pressure for political action, not to recruit members, as Koshland asserts. Interestingly, Koshland has no harsh words for the FDA Commissioner or for the Secretary of Agriculture, whose reassuring statements that apples are safe to eat were just as aggressively publicized and just as politically motivated. Nor does he question the "facts" offered on that side, which are at least as debatable as NRDC's.

Koshland's suggestion that NRDC's right to speak out should be constrained to protect "victims of irresponsible information" amounts to a plea to suppress opinions he finds unpalatable. Redress for willfully or recklessly false publicity is already available, under libel and product-disparagement laws. But the statements Koshland decries do not come close to exceeding the bounds of protected expression of views. Koshland's reaction is much more dangerous than the statements that triggered it.

The nub of the issue, for *Science* and for scientists, is how we should respond to public outcries over problems like Alar. Yes, we must teach people to see risks in perspective. At the same time, we must *listen* to what people say about risks. It is not the size of the risk but its moral offensiveness that makes the public respond so strongly. People are not just frightened, they are angry—in large part, because they believe industries, the government, and now even the editor of *Science*, have not told the truth about Alar. When spokesmen for the scientific community give in to the reflex that spawned Koshland's editorial, the posture they strike makes scientists seem arrogant, insensitive, and unconcerned about things that matter a lot to average people. If such reactions predominate, both the quality of the public debate and the perception that science has helpful solutions will suffer grave damage.

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REFERENCES AND NOTES

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3. P. Slovic, *Science* **236**, 280 (1987).
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## Pesticides, Risk, and Applesauce

The tremendous attention in the media to the growth-regulator Alar raises important issues about the nation's efforts to prevent human cancer by regulating chemicals that are carcinogenic in animal studies. Leslie Roberts, in her Research News articles "Pesticides and kids" (10 Mar., p. 1280) and "Is risk assessment conservative?" (24 Mar., p. 1553), did not address several points that we think are important for putting possible risks in perspective.

1) *Pesticides, 99.99% all natural.* Although regulatory efforts are focused on identifying and controlling synthetic chemicals that are estimated to pose a possible carcinogenic risk to society greater than one in a million

(such as Alar), we are ingesting about 10,000 times more natural than synthetic pesticides (*1*). All plants produce toxins to protect themselves against fungi, insects, and predators such as man (*2, 3*). Tens of thousands of these natural pesticides have been discovered, and every species of plant contains its own set of different toxins, usually a few dozen. When plants are stressed or damaged, such as during a pest attack, they increase their natural pesticide levels manyfold, occasionally to levels that are acutely toxic to humans (*4*). Very few of these plant toxins have been tested in animal cancer bioassays, but among those tested, about half (20/42) are carcinogenic (*4, 5*).

It is probable that almost every plant product in the supermarket contains natural carcinogens. The following foods contain natural pesticides that cause cancer in rats or mice and are present at levels ranging from a few parts per billion to 4 million parts per billion (ppb) (*3, 4*): anise, apples, bananas, basil, broccoli, Brussels sprouts, cabbage, cantaloupe, carrots, cauliflower, celery, cinnamon, cloves, cocoa, comfrey tea, fennel, grapefruit juice, honeydew melon, horseradish, kale, mushrooms, mustard, nutmeg, orange juice, parsley, parsnips, peaches, black pepper, pineapples, radishes, raspberries, tarragon, and turnips. Of the pesticides we eat, 99.99% are all natural, and, like man-made pesticides, most are relatively new to the modern diet because of the exchange of plant foods among the Americas, Europe, Asia, and Africa within the last 1000 years. It is reassuring, however, that the many layers of general defenses in humans and other animals (*1, 6, 7*) protect against toxins, without distinguishing whether they are synthetic or natural.

2) *Trade-offs*. In response to fears about residues of man-made pesticides, plant breeders are active in developing varieties that are naturally pest-resistant. Such varieties contain increased amounts of natural pesticides. It should be no surprise, then, that a newly introduced variety of insect-resistant potato had to be withdrawn from the market, due to acute toxicity to humans caused by much higher levels of the teratogens solanine and chaconine than are normally present in potatoes (*8*). Similarly, a new variety of insect-resistant celery recently introduced widely in the United States is causing outbreaks of dermatitis in produce workers due to a concentration of the carcinogen 8-methoxypsoralen (and related psoralens) of 9000 ppb, rather than the usual 900 ppb (*9*). Many more such cases are likely to crop up. Thus, there is a fundamental trade-off between nature's pesticides and man-made pesticides. The Environmental Protection Agency (EPA) has strict regulatory requirements for new synthetic pesticides and is steadily weeding out old substances such as Alar that are thought to pose a significant hazard; however, natural pesticides are almost completely neglected. Natural pesticides that are possibly hazardous to humans could easily be decreased by plant breeding.

Given the background of human exposures to natural carcinogens (*1–7*), the finding that about half the chemicals tested in rodents (whether synthetic or natural) are carcinogenic (*1, 5*), and the difficulties in risk assessment (discussed below), we have ranked possible hazards on a HERP index (daily *H*uman *E*xposure dose/*R*odent *P*otency dose, as a percent) in order to achieve some perspective on human exposure to the plethora of carcinogens (*1*). Our ranking suggests that carcinogenic hazards from current levels of pesticide residues or water pollution are likely to be minimal relative to the background levels of natural substances.

To put Alar in perspective, we estimate that the possible hazard from UDMH (the carcinogenic breakdown product of Alar) in a daily lifetime glass (6 ounces) of apple juice is HERP = 0.0017% (*10*). This possible hazard is less than that from the natural carcinogenic hydrazines consumed in one daily mushroom (HERP = 0.1%) (*1*) or that from aflatoxin in a daily peanut butter sandwich (HERP = 0.03%) (*1*). It is also less than other possible hazards from natural carcinogens in food, although few have been tested. These include 8-methoxypsoralen in a daily portion (100 grams) of celery (*3, 11*), allyl isothiocyanate in a daily portion of cabbage or Brussels sprouts (*3, 12*), and alcohol in a daily glass of orange juice (*13*). The possible hazard of UDMH in a daily apple is 1/10 that of a daily glass of apple juice. Other HERP comparisons are shown in (*1*). Apple juice has been reported to contain 137 natural volatile chemicals (*14*), of which only five have been tested for carcinogenicity (*5*); three of these—benzyl acetate, alcohol, and acetaldehyde—have been found to be carcinogenic.

The EPA has proposed cancellation hearings on Alar, and the Natural Resources Defense Council (NRDC) is trying to speed this process up by a year or two. The trade-offs must be considered in efforts to prevent hypothetical carcinogenic risks of $10^{-6}$ or $10^{-5}$, because the results could be counterproductive if the risks of the alternatives are worse. What risks might we incur by banning Alar? Alar is a growth regulator that delays ripening of apples so that they do not drop prematurely, and it also delays overripening in storage. Alar plays a role in reducing pesticide use for some types of apples, particularly in the Northeast (*15*). For example, without Alar, the danger of fruit fall from leafminers is greater, and more pesticides are required to control them. Also, when apples fall prematurely, pests on the apples remain in the orchard to attack the crop the next summer, and more pesticides must be used. Since Alar produces firmer apples, and results in fewer falling to the ground, treated fruit may be less susceptible to molds. Therefore, it is possible that the amounts and variety of mold toxins present in apple juice, for example, patulin (*16*), will be higher in juice made from untreated apples. The carcinogenicity of patulin has not been adequately examined (*17*). The EPA should, as NRDC emphasizes, also take into consideration that children consume large amounts of apple juice. Another trade-off is that fewer domestically grown, fresh apples would be available throughout the year, and the price would be higher; thus, consumers might substitute less healthy foods.

3) *Risk assessment*. Currently, neither theory nor experimental evidence is adequate to guide scientists in extrapolating from rodent cancer tests at the maximum tolerated dose (MTD) to human exposures that are thousands or millions of times lower. Therefore, for prudence's sake, federal regulatory agencies routinely make worst-case assumptions to estimate the upper limit on risk for low doses; however, the real risks at low doses may well be zero. Conventional risk assessments at the low levels of human exposure thus are really quite speculative (*1*) and should not be viewed as if they were real risks. Accumulating scientific evidence (*1, 6, 7, 18*) suggests that chemicals administered in animal cancer tests at the MTD are causing cancer in quiescent tissues primarily by increasing cell proliferation, an essential aspect of carcinogenesis for both mutagens and nonmutagens. Because endogenous rates of DNA damage are enormous (*6*), cell proliferation alone is likely to be tumorigenic. Cell proliferation converts DNA adducts (either spontaneous or exogenous) to mutations or to epimutations (such as loss of 5-methylC) and exposes single-stranded DNA, a much more sensitive target for mutagens. It also allows mutant cells to escape from growth inhibition signals coming from surrounding cells (*1, 6, 7*).

If animal cancer tests are primarily measuring cell proliferation, then the dose-response curve should fall off sharply with dose, even for mutagens [as with diethylnitrosamine (*18*)] and should have a threshold for nonmutagens. Thus, the hazards at low doses could be minimal. Furthermore, humans have numerous inducible defense systems against mutagenic carcinogens, such as DNA repair, antioxidant defenses, glutathi-

one transferases, and so forth, which may make low doses of mutagens protective in some circumstances. Even radiation—the classical DNA-damaging agent and carcinogen—may be protective in small doses against DNA damage at higher doses, as shown by recent work in human cells (*19*). Also, recent radiation experiments in mice show a dose threshold for the latency of tumor appearance (*20*). Thus, low doses of carcinogens appear to be both much more common and less hazardous than is generally thought. These scientific questions about mechanisms of carcinogenesis and the preventable causes of human cancer, in any case, are being resolved by the scientific community as quickly as resources allow.

Regulation of low-dose exposures to chemicals based on animal cancer tests may not result in significant reduction of human cancer, because we are exposed to millions of different chemicals—almost all natural—and it is not feasible to test all of them. Most exposures, with the exception of some occupational, medical, or natural pesticide exposures, are at low doses. The selection of chemicals to test, a critical issue, should reflect human exposures that are at high doses relative to their toxic doses and the numbers of people exposed. Epidemiology has been reasonably successful in identifying risk factors for human cancer, such as smoking, hormonal and dietary imbalances, asbestos, and several occupational chemicals; the data suggest that pesticide residues are unlikely to be a significant risk factor (*6, 21*). Epidemiology, with molecular approaches, is becoming more sophisticated and will continue to be our main tool in analyzing causes of cancer. In order to minimize cancer and the other degenerative diseases of aging [which are associated with our constantly increasing life expectancy (*6, 7*)], we need to obtain the knowledge that will come from further basic scientific research.

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*Erratum*: Table 3 of the report "Seroprevalence and epidemiological correlates of HTLV-I infection in U.S. blood donors" by Alan E. Williams *et al.* (29 Apr. 1988, p. 643) contained errors. The correct table is printed below.

| Variable | Cases | Controls | Odds ratio | 95% Confidence interval |
|---|---|---|---|---|
| History of IV drug use or sex with IV drug user | 4/7† | 0/35 | 20.0 | NA§ |
| Black race | 6/7 | 4/35 | 14.0 | (3.2–62.0) |
| History of more than two STDs | 1/7‡ | 0/35 | 14.0 | NA |
| HAV seropositive | 5/7 | 3/35 | 8.9 | (3.5–17.1) |
| Unmarried | 6/7 | 17/35 | 7.5 | (1.2–47.6) |
| No education past grade 12 | 4/7 | 5/35 | 6.0 | (1.4–25.9) |
| History of transfusion | 2/7 | 2/35 | 5.0 | (0.9–29.2) |
| History of skin rash | 2/7 | 3/35 | 4.5 | (0.6–33.9) |
| One or more STDs | 2/7 | 3/35 | 4.5 | (0.6–33.9) |
| Sexual contact in Orient | 1/7‡ | 2/35 | NA | NA |
| HSV seropositive | 6/7 | 26/35 | 2.3 | (0.2–32.2) |
| Travel to HTLV-1 endemic areas | 1/7 | 14/35 | 1.5 | (0.1–48.0) |
| Family history of cancer | 2/7 | 9/35 | 1.2 | (0.2–8.5) |
| Exposure to swine | 1/7‡ | 5/35 | 1.0 | NA |
| Breastfed as infant* | 4/5 | 13/17 | 0.3 | (0.2–3.2) |
| CMV seropositive | 3/7 | 18/35 | 0.7 | (0.1–3.9) |
| Birth outside of the United States | 0/7 | 0/35 | 0.0 | 0.0 |
| Gay, lesbian, or bisexual | 0/7 | 0/35 | 0.0 | 0.0 |
| Exposure to cattle | 0/7 | 2/35 | 0.0 | 0.0 |
| Numbness or weakness, difficulty walking, or poor health | 0/7 | 0/35 | 0.0 | 0.0 |
| Neurologic disease in family | 0/7 | 0/35 | 0.0 | 0.0 |

*Two seropositive cases and eight controls did not know whether they were breastfed as infants. Only controls for whom case data were available were used. †Significantly different from controls: $\chi^2 = 14.5$, $P < 0.001$. ‡Not significantly different from controls. §Not applicable.