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Response: Davis takes issue with our documentation that carcinogenic hazards from current levels of pesticide residues or water pollution are likely to be of minimal concern relative to the background levels of natural substances. She indicates that humans, as opposed to rats or mice, may have developed *specific* resistance to these natural chemicals, since we have been selected by evolution to deal with plant toxins or cooked food. This is unlikely, because, as we discussed in our article, both rodents and humans have developed many types of *general* defenses against the large amounts and enormous variety of toxic chemicals in plants (nature's pesticides). These defenses include the constant shedding of the surface layer of cells of the digestive system, the glutathione transferases for detoxifying alkylating agents, the active excretion of hydrophobic toxins out of liver or intestinal cells (*1*), numerous defenses against oxygen radicals (*2*), and DNA excision repair. The fact that defenses appear to be mainly general, rather than specific for each chemical, makes good evolutionary sense and is supported by various studies. Experimental evidence indicates that these general defenses will work against both natural and synthetic compounds, since basic mechanisms of carcinogenesis are not unique to either.

We also pointed out that humans ingest about 10,000 times more of nature's pesticides than man-made pesticides. Relatively

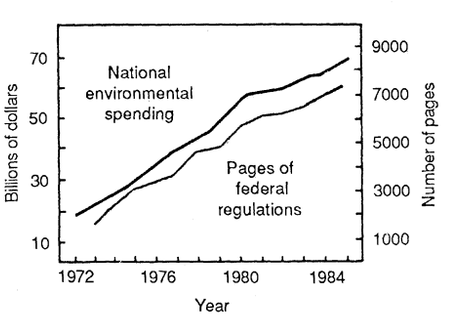

Fig. 1. Expenditures for environmental protection (*8*).

few of nature's pesticides that we are eating have been tested for carcinogenicity, but about half of the naturally occurring substances that have been tested in rats and mice are carcinogens. We also pointed out that the modern diet is vastly different from that of a few thousand years ago or of primitive man (*3*). Davis dismisses dietary and other life-style factors too readily as potential causes of cancer that do not change; they do change all of the time. For example, as part of the back-to-nature movement we are eating canavanine in alfalfa sprouts, carcinogenic hydrazines in raw mushrooms, and carcinogens in herb teas. Cooking food does destroy some carcinogens but also makes others, such as the variety of nitrosamines and nitropyrenes formed when food is cooked in gas ovens, a relatively recent invention. Davis' argument that natural selection eliminated all hazards from carcinogens acting late in life because they are reproductive toxins is not supported by good evidence and appears unlikely.

We have discussed why "risk assessment" based on worst-case scenarios may not have much to do with biological reality for either synthetic or natural chemicals. Linear extrapolations from results at the maximum tolerated dose may enormously exaggerate risks at low dose if, as appears to be true, an important aspect of carcinogenesis is cell proliferation, which may frequently result from the high (maximally tolerated) doses of test chemicals administered in rodent bioassays (*4*). Concern with very low doses is even more likely to be misplaced for agents suspected of causing birth defects, because of a threshold effect. In this respect it would be useful to compare rodent data for particular synthetic chemical pollutants with those for a representative set of natural chemicals, analogous to our HERP index comparisons. One important comparison to be made would be that between alcohol and other rodent teratogens. Alcohol is a leading cause of mental retardation in humans (fetal alcohol syndrome), and such a comparison would put possible teratogenic hazards into perspective.

The key issue is not that production of synthetic chemicals has gone up markedly in recent years, but whether the tiny amounts of pesticide residues or water pollutants we are ingesting are likely to be important in human cancer. In our ranking, such exposures are very low compared with the background of natural carcinogens, but we also pointed out that workplace exposures often rank high (*5*).

Davis contends that the incidence of brain tumors and multiple myelomas in the elderly has clearly increased. However, Doll and Peto, in a detailed analysis of the causes of human cancers, convincingly point out why such apparent increases may be due to recent improvements in diagnosis (*6*). Peto concluded, in commenting on this matter (*7*, p. 283), that "Future trends may differ substantially from recent trends, of course, but at present the U.S. data contain no clear evidence for any generalized increase in cancer over and above that due to the delayed effects of tobacco. Opposite conclusions by other commentators appear to derive chiefly from methodological oversights."

From a policy perspective, we discussed in our article that it is prudent to consider the benefits of modern technology and also the alternative substances that might replace regulated compounds. Modern chemicals commonly replaced more hazardous substances, for example, chlorinated solvents replaced flammable solvents. Modern technology, which concomitantly causes the increase in production of synthetic chemicals, has contributed in important ways to our steadily increasing life-span. Currently, as a society our expenditures on pollution abatement and control are more than $80 billion annually (Fig. 1), despite the uncertainty of whether environmental pollutants at parts-per-billion levels have public health significance. We believe that the potential carcinogenic hazards of pollutants should be evaluated in the context of background level exposures to natural substances until science makes the further understanding of mechanisms clearer, as we emphasized in our article.

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Definition Required

Concerning "Science and mutual self-interest" by David Dickson and Colin Nor-