Letters

Cyclamate Ban

We are greatly alarmed over the summary ban on cyclamate, based on evidence that is at best inconclusive, and in the face of overwhelming evidence that cyclamate causes no deleterious effects on humans. The decision, as reported to the press, was based primarily on the results of experiments wherein 6 to 12 rats given 50 times the maximum recommended human daily consumption for their lifetime developed an "unusual" form of bladder cancer. We understand that the decision was also based on two other preliminary experiments which demonstrated that cyclamate and cholesterol pellets implanted into mouse bladders caused tumors, as did cyclamate injected into the bladder. Malformations have been reported in 15 percent of chick embryos injected with cyclamate, and cyclamate has been implicated in chromosomal breaks. According to the news media, the decision was made to ban cyclamate after a HEW official called a "hurried meeting of a scientific panel." In view of the many products, both foods and drugs, which have been proven to be carcinogenic, teratogenic, or mutagenic, that are still available to the American public, we believe that this action was premature and of too great import to be made by one or a few government officials at a "hurried meeting" without thorough investigation and review by the scientific community.

Before the results of such scientific experiments can be accepted as conclusive, several criteria are required. First, the experiments should be reproducible in the laboratories of the original author and by independent investigators. Next, the agent in question should be tested in other animal species and other biologic systems to determine whether the results are species specific or have broader biologic significance. To test the specificity of the agent, controls should be injected or implanted with other materials in a parallel manner to the agent being investigated. Furthermore, the results must be analyzed in statistical terms, which generally means large-scale experimentation. If positive results are obtained, basic research should be conducted into the mechanisms of action of the substance. Finally, human epidemiologic data should be collected in prospective or retrospective studies to determine whether any undesirable effects have been produced. Epidemiologic information is especially pertinent to the cyclamate question since millions of Americans, including pregnant women, have consumed vast quantities of this compound.

Since the production of bladder cancer was the recent discovery that led to this precipitous decision, let us review briefly some well-established data on the etiology of carcinoma of the urinary bladder. For over 50 years, carcinoma of the bladder has been recognized as an occupational disease in persons working in the coal-tar aniline dye industry (*1*). While many measures are taken to protect the health of these workers and of the consumers of their products, nonetheless this industry has not been eliminated. Crayons and hair-coloring are readily available. Tryptophan, an amino acid found in proteins, has been shown to be carcinogenic for the urinary bladder (*2*). Would the Food and Drug Administration have us all become vegetarians? Both laboratory and epidemiologic studies conclusively demonstrate that cigarette smoking causes many diseases, one of which is bladder cancer. Yet in the 20-year period during which cyclamate has been so widely used, there has been no increase in the mortality from bladder carcinoma (*3*).

Regarding teratogenicity and chromosome damage resulting from cyclamate, although 15 percent of chick embryos showed deformities, studies in other animals, such as rats, were negative (*4*). Furthermore, a variety of foods and drugs have been found to be teratogenic in one or more species. Excess vitamin D in the rabbit, hypervitaminosis A in the rat (*5*), cortisone in some strains of mice (*6*), and aspirin in the rat (*7*) are prime examples. Chromosome breakage in vivo has been produced by cyclohexylamine, a metabolite produced in the intestinal tract by a small percentage of animals. With the usual rate of conversion, a huge amount of cyclamate would be required to show this effect. Work in our laboratory and elsewhere (*4*) has shown no mutagenic effect when very high concentrations of cyclamate were put into cultures of normal human cells.

Restricting the availability of cyclamate will have serious consequences for the health and well-being of the American public. In recent years, millions of diabetics have finally been able to obtain a palatable and varied diet because of the incorporation of cyclamate into so many food products. Persons who are prediabetic or have a genetic predisposition to diabetes may prevent the development of the clinical disease by a prudent diet, wherein artificial sweeteners play an important role. The dental profession has acclaimed the role of cyclamate in the prevention of tooth decay. Children now happily take baby aspirin and oral penicillin because they have been sweetened. Certainly the major nutritional problem in America today is obesity. Individuals who are attempting to limit their caloric intake will be greatly handicapped by the cyclamate ban. Can we afford to lose the positive benefits of this chemical? According to news releases, a new sweetening agent will be available by 1 January 1970. How can this product be adequately tested in a short period of time, compared to the 10-year developmental period of careful testing of cyclamate prior to 1950? How can the FDA guarantee that this new product will not eventually be found to produce carcinoma of the left adrenal in Chinese hamsters?

In conclusion, we find it inconceivable that when there is so much human data available, that cyclamate be discarded on the basis of experiments employing only 12 rats. We can see no other explanation for this hasty action on the part of the FDA and Secretary of Health, Education, and Welfare except that political or economic pressure caused them to bypass the established scientific evaluation procedures.

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References and Notes

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Reactors and the Public Good

It is dismaying to find that *The Careless Atom,* by Sheldon Novick, was assigned to a book reviewer (1 Aug., p. 483) who admits to "not being an expert in these matters." I find *The Careless Atom* a thinly disguised antireactor tract which seems more intended to alarm than to inform. It contains statements taken out of context, misrepresentations and partial presentations of fact, and depictions of conjectures and events of low probability as seeming imminent disasters.

Novick uses several excerpts from hypothetical studies of reactor accidents to support his allegation that the potential consequences of a reactor malfunction are unacceptably great. . . . One finds in the book no accompanying indication of the assumed succession of human, mechanical, and structural failures on which these postulated incidents are based, and hence of their extremely small probability. He states that the dozen atomic power plants which were to be built by the utilities alone or in cooperation with the Atomic Energy Commission "ran into trouble from the outset. . . ." The Fermi and the Hallam plants, both novel types (which have presented economic problems to their backers but no radiation hazard to the public), are cited. From reading *The Careless Atom* one would not know of Yankee, Indian Point I, or Shippingport, not to mention the total of about 100 other reactors in the United States, that operate routinely and dependably.

Besides offering a one-sided picture of the safety and reliability of nuclear reactors, Novick has made a sensational rather than a factual presentation to suggest that the current radiation protection standards for the routine discharge of low-level radioactivity from nuclear facilities are inadequate to protect man and the environment from present serious risk and future calamity. He describes radiation effects quite graphically, but without relating them to dose or dose-rate. Thus he gives his lay readers no quantitative basis for assessing the degree of the risk involved. Although the releases of radioactivity during past years to White Oak Lake and to the Columbia River, which Novick uses as examples, were considerably in excess of the amounts from modern reactor power and fuel reprocessing facilities, neither has constituted a demonstrated radiation safety hazard to even the immediate populations. With regard to current releases Novick asserts that "reactors will continue to function just within AEC limits." This is contradicted by Bloemke and Harrington (AEC Report ORNL-4070), from which I conclude that most reactors function at less than 1 percent of these release limits.

Novick attacks the basis of public radiation protection standards which are set in comparison to background and at which no measurable damage is anticipated. He says, "It is past time that we realized that in radiation 'no measurable damage' eventually means 'not quite fatal' for everyone." This is a large assertion which indicates either Novick's bias or his ignorance of the painstaking search of the considerable available data on radiation effects made by such bodies as the International Commission on Radiation Protection, of the careful interpretation made by them in recommending radiation protection standards, and of the conservative practices of health physicists in their application.

In my view, to live in the health and well-being made generally possible by a technologically developed society is also to live at risk from a host of potentially deleterious agents. Before getting upset about the possible risk from the operation of nuclear reactors and associated activities, a reasonable person, it seems to me, would want to arrive at the best possible quantitative judgment of how this compares with other accepted risks. I believe that anyone who does not have an a priori conviction otherwise will find it small.

This is not to suggest that there are no disagreements about safety within