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Heavy Dosage No Argument Against Ban on Cyclamate



PROVING THE safety of food additives is one of the most difficult scientific challenges of advanced societies. We have enough problems assuring the adequacy of diets from basic farm sources that we might be tempted to dismiss new synthetic compositions altogether.

If this position is too extreme, we must at least place a great burden of responsibility on the promoters of dispensable additives to protect consumers against the side effects of hasty technology. That burden is multiplied for additives which are secondarily incorporated into processed foods to be eaten by vast numbers of people, often without their knowledge. These materials should surely be pretested at least as carefully as prescription drugs, which are used ideally only under the direction of professionals well informed about the balance of probable benefits and hurts.

THE DELANEY amendments of 1958 were the first U.S. law to require the pretesting of additives and to place the burden of proving their safety on industry rather than on the public. Rep. James J. Delaney's bill also contained the famous clause that specifically prohibited any additive "found to induce cancer in man or animal," apparently leaving no room for administrative judgment. The clause, however, has never been used (in my opinion) except to lend extra force to decisions that would have been prudently required for proof of safety.

Ironically, the "cancer clause" applies only to food additives and was never extended to pesticide residues, although Rep. Delaney said he was provoked into writing it by the Food and Drug Administration's vacillation about setting tolerances for a mite-killer, "aramite," when this was first found to cause liver tumors in rats.

The recent ban on cyclamate

has been applauded by most of my colleagues but was less popular with the editors of *Chemical & Engineering News*, who deplore "the unrealistic and unscientific constraints placed on food additives by the Delaney clause." They complain that no inference about safety for man should be drawn from tests on rats with 50 times the dosage likely to be used in men.

There is, unfortunately, some merit to this complaint—but it is a small one. There are undoubtedly cancer-causing compounds that would be unrevealed in less than ten years application, or for many other reasons would fail to be detected by animal tests like those that did indict cyclamates. There really is hardly any other way besides stressing animals with large doses that we can practically use to pick up potential hazards.

OBVIOUSLY, this principle could be used in a wooden-headed way, and sometimes is. When we know something of the chemical or biological actions of a compound like salt or a natural hormone or amino acid, we can cautiously attempt to relate the effects of lower doses to the natural environment of the body. There is no theoretical reason to believe, however, that the effect of cyclamate is proportionately much less at lower doses; with many carcino-

gens, the observed rule is that lower doses simply take a longer time to take effect.

Taking account of the failure to find any direct evidence so far of harmful effect in men, I would still have to judge that continued heavy exposure, especially starting with youngsters, might have caused a million cases of bladder cancer in the United States—even if humans are intrinsically no more sensitive than rats. This is only slightly better than a wild guess but it might err on either side.

Some cancer-inducers are more effective in malnourished subjects, which might enhance the effect of cyclamate taken in place of real food. Others interact with environmental injuries and other chemicals in ways never yet tested with cyclamates. There will be a great deal of variation among animal strains and among human individuals.

Finally, good scientific evidence of chromosome breakage by cyclohexylamine (a known derivative of cyclamate in the body) was reported a year before the ban. So we are not completely in the dark about how cyclamate works. The FDA's failure to ring the bell on cyclamate with this evidence alone may be the most important, realistic and scientific justification for the validity of the Delaney amendments.

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