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Cancer Phobia

For more than 10 years, the public has been subjected to a media barrage leading to widespread, misinformed fear of chemicals. Through the use of questionable evidence, many major substances have been labeled carcinogens. If data are adjusted to eliminate effects of cigarette smoking, there has been no overall increase in cancer due to other factors. The highly publicized cancer epidemic that was predicted earlier has not materialized.

With increasing use of synthetic chemicals, it was desirable to screen them for possible carcinogenicity by tests on shorter lived animals such as mice and rats. The general procedure is to subject the mice or rats to massive doses of the chemical to be tested, usually by feeding, gavage, or inhalation. Preliminary experiments determine a maximum tolerated dose. This amount, repeated over a 2-week period, usually leads to a noticeable but tolerated reduction in weight. A chronic dose regimen is then employed in experiments that last for the animal's lifetime. The levels used vastly exceed those to which humans are likely to be exposed.

Many of the experiments that have been cited as proving a potential carcinogenicity of a chemical for humans have been performed on inbred strains of mice that have a natural incidence of liver tumors. In humans, there are taboos against inbreeding, which often leads to genetic impairments. Thus the use of inbred mice, though convenient experimentally, is suspect. More important is the fact of high natural incidence of liver tumors in the test mice. The usual response of these animals to massive doses of a chemical is to develop an even higher incidence of liver tumors. When this happens, the chemical is labeled a potential carcinogen in humans. It so happens that in humans primary liver cancer is rare with the exception of alcoholics and those who have suffered from hepatitis. With these exceptions, incidence of liver cancer in the United States decreased substantially during the times when use of industrial chemicals expanded greatly. Thus extra liver tumors in a naturally tumorigenic mouse is of dubious relevance to humans.

Results from the massive doses are extrapolated linearly to low doses, and the assumption is made that humans are as sensitive as the most cancer prone of the species of animals tested. Use of a linear extrapolation to low doses implies that humans do not have repair mechanisms against injury.

Countless millions of animals have been sacrificed in testing chemicals. Comparatively little effort has been devoted to studying the mechanisms of chemical carcinogenesis. An important exception is work conducted at the Chemical Industry Institute of Toxicology (CIIT). The CIIT, which has achieved an excellent reputation among toxicologists for its careful work, has examined the detailed mechanism of the interaction of formaldehyde with nasal passages of rats and has shown that the linear model is not correct in predicting nasal cancer in the rats. Rather, a more relevant measure is the extent of interaction of formaldehyde with the nasal DNA. The amount of binding of formaldehyde to DNA decreases much faster than the concentration of formaldehyde in the nasal passages and is a better predictor of carcinogenesis.

Another important study of CIIT has been an investigation of the mechanism of the carcinogenesis of branched-chain hydrocarbons in male rats. These hydrocarbons are key components of unleaded gasoline. The studies showed that the hydrocarbons interfere with the mechanism for excreting a low-molecular-weight protein by the male rat. Research at CIIT indicates that this may be the cause of kidney cancer in male rats exposed to gasoline. A similar mechanism with related cancer does not exist in female rats, in male or female mice, or in humans. This type of result calls into question the practice of the regulatory agencies in selecting for extrapolation to humans data from the most sensitive animal.

Animals differ by more than a factor of 1000 in the levels required for lethal response to dioxin. Rodents and humans are known not to be identical in their biochemistry. To attain a realistic estimate of the hazard—if any—presented by a chemical, specific information about its metabolism and physiological effects is needed. The two examples involving formaldehyde and hydrocarbons illustrate the power of an approach in which detailed mechanisms of chemical carcinogenicity are examined.—PHILIP H. ABELSON