SCIENCE

10 JANUARY 1992
VOLUME 255
NUMBER 5041

Diet and Cancer in Humans and Rodents

The impact of diet on incidence of cancers in humans and rodents is well known to some scientists and physicians. It is slowly being comprehended by the public. The knowledge has been ignored by Congress and the Environmental Protection Agency.

We now know that cigarette smoking, alcohol, and ordinary foods together are associated with almost all of excess cancer.* The contribution from foods is about as great as that from smoking. Two examples of causative agents in foods are excessive amounts of fats and salt. Western populations that derive 40 to 45 percent of their food calories from fats experience comparatively high mortality from cancers of the postmenopausal breast, distal colon, ovary, endometrium, pancreas, and prostate.† Those Japanese who obtain only about 15 percent of their calories from fat have a dramatically lower incidence of these forms of cancer. In contrast, Japanese who consume heavily salted food have an elevated incidence of stomach cancer.

In rodents, substantial effects of diet on longevity and occurrence of cancer have long been known. Inbred strains of animals fed ad libitum (ad lib), that is, food always available, were found to be not nearly as long-lived nor free of cancer as animals having a calorie-restricted (CR) diet. The longevity of CR rodents is variable depending on strain but usually is of the order of 120 to 150 percent that of ad lib animals. The rats and mice fed a restricted diet are smaller, healthier, and sleeker than the obese, sluggish counterparts fed ad lib. Occurrence of tumors is variable with species, strain, and site. However, many studies have shown that incidence of tumors in ad lib animals usually exceeds that of CR rodents by factors of 3 and more. In effect, excessive fat or calories in the food intake are promoters of cancers. According to usual practice, in which ad lib–fed inbred rodents are provided food that includes the maximum tolerated amounts of test substances, ordinary foods should be categorized as carcinogens. Furthermore, when other potential carcinogens are tested using ad lib–fed animals, the results of experiments are clouded by the fact that two kinds of carcinogens have been administered. A more scientifically sound procedure would be to use CR feeding.

Benefits from a restricted diet are not confined to longevity and relative freedom from spontaneous tumors. Rodents on a CR diet experience fewer tumors when exposed to substances that promote cancer in the ad lib animals.≠ Examples include substantially reduced effects of methylazoxymethanol, diethylnitrosamine, benzo[*a*]pyrene, methylcholanthrene, and dimethylbenz[*a*]anthracene.

It has been conventional practice to test potential carcinogens using highly inbred strains of rodents. The rationale was the supposed superior reproducibility of results compared with those obtained from wild-type animals. However, that assumption can be questioned. At least three examples of genetic drift of inbred strains can be cited. Rao◊ has recently said that male Sprague-Dawley rats that once typically weighed 700 grams now weigh 1000 grams and that typical male Fischer 344 rats have had a 25% increase in weight. The higher body weights are associated with increased incidence of tumors and a substantial decrease in survival at 24 months. Earlier, Roe‖ reported on genetic drift in an inbred strain of mice. In the course of 10 years, mean body weight had increased. Many of the animals were obese. Lifetime expectation of developing one or another form of neoplasm had risen from 10 to 80 percent.

The use of inbred strains as test animals can further be questioned on the basis that they often develop spontaneous tumors in organs where cancers are not frequent in humans. For example, incidences of mouse liver tumors in 2-year-old B6C3F1 males has ranged from 17.8 to 46.9 percent. In contrast, death rate from liver cancer in the United States is about 0.005 percent.

Results of the animal studies raise questions about the validity of federal regulations that are based on ad lib–fed inbred strains of rodents. Are humans to be regarded as behaving biochemically like huge, obese, inbred cancer-prone rodents? Sooner or later Congress must recognize a new flood of scientific information that renders suspect the Delaney clause and procedures for determining carcinogenicity of substances.—PHILIP H. ABELSON

* B. E. Henderson, R. K. Ross, M. C. Pike, *Science* **254**, 1131 (1991). † G. M. Williams and J. H. Weisburger, in *Casarett and Doull's Toxicology: The Basic Science of Poisons*, M. O. Amdur, J. Doull, C. D. Klaassen, Eds. (Pergamon, New York, 1991), p. 127. ≠ W. T. Allaben *et al.*, *Korean J. Toxicol.* **6**, 167 (1990). ◊ G. N. Rao, in *Biological Effects of Dietary Restriction*, L. Fishbein, Ed. (Springer-Verlag, New York, 1991), p. 321. ‖ F. J. C. Roe, *Proc. Nutr. Sci.* **40**, 57 (1981).