Interactions not clear-cut

Physiology Influences Diet's Link to Cancer

Washington—Researchers at a two-day conference here reported new links between cancer and diet, but they warned that nutrition's role in carcinogenesis is complicated by often-overlooked genetic and metabolic factors.

New data. Researchers refined or reworked the realm of assumptions about diet and cancer at a conference on calories and energy expenditure in carcinogenesis. Though the investigations are generally in early stages, many having not advanced beyond the animal study level, the researchers' data suggest:

- though some fibers protect against cancer, others may be carcinogenic.
- seafood may be more important than vegetables in supplying nutrients that can ward off cancer.
- total caloric intake and body fat may be more important than dietary fat in carcinogenesis.
- genetics and exercise may override dietary factors in some instances.
- body fat in obese postmenopausal women may act as a catalyst in producing additional estrogen and increasing the risk of cancer.

"The questions we need to explore are no longer simple ones dealing with single foods or nutrients but rather how foods interact and are influenced by other aspects of nutrition, such as exercise and caloric expenditure," said Dr. Saxon Graham, chairman of social and preventive medicine at the State University of New York at Buffalo. "The study of fats in cancer epidemiology is relatively new," he said, "and I suspect that in 10 years we will look back on this period as being one in which we had hardly begun to scratch the surface."

Several investigators reported findings on increased estrogen production in postmenopausal women who are more than 50 pounds overweight, which, combined with decreased progesterone, results in an endometrial cancer risk comparable to that linking smoking and lung cancer, as well as in a greater susceptibility to breast cancer.

A number of researchers cited studies showing that an increase in dietary fat is linked to an increased rate of tumor formation or tumor size or both in a range of animal models, and epidemiologic studies have also tied high fat consumption to a greater risk of cancer. But total caloric intake and body size can be mediating factors, one investigator pointed out at the conference, sponsored by the International Life Sciences Institute and the Nutrition Foundation, in cooperation with the AMA, the Department of Agriculture, the American Dietetic Association, and the American Chemical Society.

Implications. Dr. Michael W. Pariza, a professor of food microbiology and toxicology at the University of Wisconsin at Madison, said rats that attain a large body size on a high-fat and high-calorie diet have a greater incidence of chemically induced breast cancer than smaller rats on a high-fat but low-calorie intake. The findings could have public health implications, Dr. Pariza noted, because neither total calories nor body size is considered in the National Research Council's recommendation to lower fat in the diet from 40% to 30% to reduce cancer risk.

Genetic factors influencing body size and metabolism also play a role in the relationship of dietary fat to cancer. A strain of rats tending to become more obese as adults was found to be much more susceptible to the tumor-generating effects of a high-fat diet than was a slower-growing, leaner strain of rats. But the cancer-enhancing effects of dietary fats were less pronounced if animals were fed a natural diet as opposed to a purified diet, said Dr. Clement Ip, a cancer researcher at the Roswell Park Memorial Institute in Buffalo, N.Y. A natural diet may have certain unknown elements, such as ingredients other than protein in fish meal. But a purified diet, Dr. Ip told MWN, is one in which the composition of every ingredient is known exactly. He uses casein, for example, as a protein source in a purified diet.

Researchers from three major institutions cited evidence supporting the theory that fat plays a role in the development of endometrial and breast cancer by potentiating increased estrogen production. Adipose tissue functions as an endocrine organ, said Dr. Artemis P. Simopoulos, chairman of the National Institutes of Health nutrition coordinating committee, referring to fat tissue's ability to convert adrenal estrogen precursors into active, circulating estrogen through the action of the enzyme aromatase. Moreover, she said, obesity lowers the normally protective level of sex-hormone–binding globulins in the blood.

Efficient. Dr. Pentti K. Siiteri, a reproductive endocrinologist at the University of California, San Francisco, pointed out that postmenopausal women lack progesterone, which ordinarily counterbalances estrogen action. And clinical studies have shown, he said, that adipose tissue is among the most efficient in carrying out the estrogen conversion process.

Age also adds to increased estrogen production in fat tissue, said Dr. Evan R. Simpson, a professor of ob-gyn and biochemistry at the University of Texas Health Science Center at Dallas. His studies of cultured human fat cells show a decline in functioning growth factor receptors with aging, thus reducing the ability of epidermal growth factor and fibroblast growth factor to inhibit aromatase activity.

"Physicians may need to consider preventive estrogen therapy only for nonobese postmenopausal women," said Dr. Paul MacDonald, also a professor of ob-gyn and biochemistry at UTHSCD. He pointed to these findings in light of the 1984 NIH consensus development conference recommending that postmenopausal women be considered for supplemental estrogen to prevent osteoporosis.

'We need better human studies and fewer popular notions on fiber and cancer' without lumping fibers together.

Findings from other studies on the effects of fat and fiber on tumor growth were often conflicting. Dr. Rashida A. Karmali, an associate professor of nutrition at Rutgers University in New Brunswick, N.J., said studies with rats showed that dietary fish oil either inhibited the growth of transplanted breast or prostate tumors or reduced the number of chemically induced tumors.

An epidemiologic study of men with prostate cancer supports her findings, Dr. Karmali said. Of the dietary risk factors examined, a lack of seafood ranked the highest and was substantially higher than a lack of green vegetables, which are rich in both fiber and vitamins. She suggests that the omega-3 fatty acids in fish may inhibit certain tumors by blocking the production of prostaglandins.

Dr. Clifford W. Welsch, a professor of anatomy at Michigan State University in East Lansing, noted that some animal studies implicate polyunsaturated fats in the development of breast cancer and exonerate saturated fats. But other findings are contradictory. The researchers attribute the inconsistencies to the difficulty in quantifying dietary intake over long spans of time and a lack of consideration of factors such as exercise, total calorie intake, and the interaction of dietary components such as fat and fiber.

The National Cancer Institute may soon launch a multicenter clinical trial to determine whether diets with 20% or less of total calories from fat will reduce the incidence of breast cancer. "This study will permit more precise examination of the nature of dietary change and the potential influence of other factors that may interact, such as total calories, energy expenditure, and body weight," said Dr. Peter Greenwald, NCI director of cancer prevention and control. The study, if feasible, could enroll about 30,000 women at 30 centers, he said.

Fibers differ. Dr. Lucien Jacobs, an associate professor of medicine at the University of California, Davis, presented studies in animals implicating certain kinds of fiber in carcinogenesis. Rats fed diets high in pectin, oat or corn bran, carrageenan, or agar had a higher incidence of colon cancer than did controls. But rats fed diets high in cellulose, wheat bran, or lignin fibers had a lower incidence of colon cancer, he said.

His studies showed that the types of fiber linked to carcinogenesis were highly fermentable. Fermentation lowers the pH in the colon, prompting epithelial cell growth, and it "appears to enhance the initiation stage of carcinogenesis by stimulating cell proliferation following carcinogen-induced DNA alterations."

"We need better studies on humans and fewer popular notions on fiber and cancer," Dr. Jacobs said. "We can no longer lump fibers together when considering their effect on carcinogenesis." ■