

BIOMEDICINE

From Seattle at the National Conference on Nutrition in Cancer

Bacterial enzyme seen as anti-cancer tool

An enzyme isolated from a common soil bacterium has extended the lifespan of tumor-bearing rats by 300 percent, according to Joseph R. Bertino of the Yale University School of Medicine in New Haven. Discovered in mud dredged up from Long Island Sound, the enzyme, called carboxypeptidase G, inhibits the formation of folic acid, a vitamin required for the division of cancer cells. It does so by converting the folic acid to pteric acid, a chemically similar, but inactive substance, Bertino said. The enzyme, which is now in early clinical trials, was active against Walker 256 sarcoma, an animal tumor that will not grow well if its folic acid supply is cut off by dietary restriction. On the other hand, the tumor is not sensitive to methotrexate, a folic acid antagonist that is used to treat various forms of cancer, including childhood leukemia, but that becomes less effective as the malignant cells build up resistance to the drug. For that reason, Bertino believes that carboxypeptidase G may be especially useful in treating tumors after they have grown resistant to methotrexate. Clinical trials are proceeding more slowly than they might because of the expense involved in preparing the enzyme, Bertino told the conference sponsored by the National Cancer Institute and the American Chemical Society.

Vitamin C versus cancer—again

Vitamin C in the American diet may explain why there is a lower incidence of stomach cancer in the United States than there is in Japan, according to John H. Weisburger of the American Health Foundation. He said that vitamin C in lettuce and other vegetables may protect against the conversion of nitrites into mutagenic nitrosoureas by biological action in the stomach. Weisburger reported that laboratory studies showed that doses of vitamin C equivalent to the concentration of nitrites found in mackerel and other fish eaten in large amounts by the Japanese suppress nitrosourea formation under conditions approximating conditions found in the stomach. The decline in stomach cancer in the United States during the last 40 years is probably due to the increasing consumption of foods that contain vitamin C, he said, noting that when Japanese migrate here and begin eating an American-style diet, their risk of stomach cancer becomes equivalent to our own. Weisburger recommended that if the correlation holds up, it would be worthwhile for the Japanese to initiate a large-scale dietary intervention study to determine if increased vitamin C intake will decrease the stomach cancer rate there.

Cancer from mushrooms?

Discovery of a potent carcinogen in a wild mushroom known as the "false morel" suggests that other mushrooms should be investigated for the presence of similar materials, according to Phillippe Shubik, director of the Eppley Institute for Research in Cancer in Omaha. He reported that the false morel (*Gyrometra esculenta*) contains small amounts (microgram quantities) of N-methyl-N-Formyl hydrazine, which causes liver tumors in hamsters. As such, the hydrazine derivative is as potent a carcinogen as dimethylnitrosamine, one of the most active cancer-causers known. About 100,000 people in the United States eat the false morel, he estimated, although it is eaten on a much wider scale in Europe. Shubik added that the mushroom used most commonly in the United States (*Agaricus bisporus*) contains a hydrazine derivative called agaritine. Although it is not known to cause cancer, it is chemically related to other hydrazine derivatives that do, he said. Based on his findings, Shubik said there is no need for Americans to cut back on their mushroom consumption. However, he suggested that the hydrazine-mushroom-cancer link be studied more extensively than it has been until now.

Colon cancer in Finland

Even though the Finns take in as much dietary fat as Americans do, the incidence of colon cancer in Finland is much lower than it is in the United States. The observation seems to contradict epidemiological studies and animal experiments which indicate that colon cancer may arise when dietary fats are converted by the liver into bile acids, which in turn act on other dietary components to produce carcinogens. Ernst H. Wynder, president of the American Health Foundation in Valhalla, N.Y., explained that the Finns may have a lower than expected colon cancer rate because their greater intake of dietary fiber and the increased stool bulk that results may act to dilute the levels of fat metabolites associated with carcinogen formation. Wynder says the Finns get much of their dietary bulk from the large amounts of rye bread they consume with their meals.

Research on cancer-nutrition link

If there isn't enough research being done on the connection between cancer and nutrition, it may be due to the fact that clinical researchers aren't very interested in the supposed connection. Following recent congressional criticism of National Cancer Institute expenditures on the cancer-diet connection, NCI Director Arthur C. Upton pointed out that only one percent of the grant applications currently received by the agency are in the nutrition area. He said that the lack of interest may be due to the difficulty and very long time involved in producing useful results. For example, he said, a definitive study tracing the link between nutrition and breast cancer might mean placing a large number of baby girls on a carefully controlled diet and then following them for 60 years to determine the effect of the diet.

Alcohol, cigarettes and cancer

Alcohol and cigarettes, when used at the same time, may act synergistically to induce several forms of cancer, according to David Schottenfeld, chief of epidemiology and preventive medicine at the Memorial Sloan-Kettering Cancer Center in New York. He estimated that three-quarters of all cancer deaths resulting from cancers of the mouth, pharynx, larynx and esophagus are associated with the cigarette-alcohol combination. In addition, smoking alone is responsible for 85 percent of deaths from lung cancer and for 39 percent of bladder cancer deaths. Schottenfeld said that most heavy drinkers smoke heavily and that the combination is especially prevalent among men at the lower socioeconomic level, especially among blacks. This, he suggested, may help explain the greater incidence of cancer of the mouth, esophagus, larynx, etc., found in those groups, compared with their prevalence in higher socioeconomic groups.

Total parenteral nutrition for cancer

Total parenteral nutrition (TPN) should be beneficial to the 10 percent of cancer patients who die from malnutrition, rather than from the disease itself. Stanley Dudrick, developer of TPN, a technique that involves intravenous administration of amino acids, carbohydrates, minerals and other nutrients to malnourished cancer patients, said that the technique helps build up the patient's immune defenses after they begin to run down following cancer therapy with drugs and radiation. He said that recent work at the M.D. Anderson Hospital and Tumor Institute in Houston indicates that 66 percent of 240 patients with decreased immunocompetence regained their immune defenses after being given total parenteral nutrition for 12 days. Not only do the patients feel better following TPN, they show a better response to continued chemotherapy than do cancer patients whose immune defenses remain low, Dudrick said.