See corresponding article on page 990.

Colorful cancer prevention: α-carotene, lycopene, and lung cancer[1,2]

David Heber

Diets that provide 400–600 g fruit and vegetables daily are associated with a reduced risk of lung and other aerodigestive epithelial cancers (1). Fruit and vegetables contain a variety of carotenoids that have been shown to have antioxidant and antitumor effects. Although smoking is the cause of >90% of all lung cancers, an increased intake of fruit and vegetables has been associated with a decreased risk of lung cancer in smokers and nonsmokers (2). HPLC has enabled the development of the National Cancer Institute–US Department of Agriculture nutrient database, which specifies the carotenoid contents of commonly eaten foods (3). Before the development of this new database, most epidemiologic studies relied on estimates of total dietary vitamin A or β-carotene intake, which served as a surrogate for fruit and vegetable intake. This led to the erroneous assumption that β-carotene was responsible for all of the cancer preventive effects of diets rich in fruit and vegetables.

Michaud et al (4) report in this issue of the Journal that increased α-carotene intakes were related to a 63% lower risk of lung cancer in nonsmokers. In addition, inverse risk associations were noted for β-carotene, lutein, and β-cryptoxanthin, but these were not statistically significant. Smoking attenuated all of the risk reduction associations noted except those for lycopene. A significant reduction in cancer risk was noted in association with an increased intake of lycopene, even in smokers. Interestingly, smoking alters the concentrations of most carotenoids, including α-carotene and β-carotene, but not lycopene (5). Therefore, lycopene may have a special role in lung cancer prevention.

Studies of the carotenoid contents of frequently consumed foods have shed light on where α-carotene and lycopene are found in the typical American diet (2). Carrots consumed in a cooked or raw form provide ≈51% of dietary α-carotene. Tomatoes and multicomponent foods containing tomatoes are also an important source of α-carotene. Tomatoes and tomato products, including juices, pastas, soups, and ketchup, are the single most important source of lycopene in the diet, providing >85% of dietary lycopene. Heat processing increases the bioavailability of lycopene by breaking cell walls and allowing extraction of the lycopene from the chromoplasts, where it is found in raw tomatoes (6).

The study by Michaud et al (4) suggests that several different carotenoids may be involved in reducing lung cancer risk; therefore, increased fruit and vegetable intakes should be recommended for the prevention of lung cancer rather than an increased intake of a single "drug-like" chemopreventive carotenoid. Smoking cessation efforts should nonetheless continue at the same time that dietary changes are advocated because only 10% of lung cancer is unrelated to smoking.

Although the evidence is building for the association of increased fruit and vegetable intake with reduced cancer risk, inadequate attention is still paid to changing dietary patterns. In 1997, my colleagues and I at the University of California Los Angeles Center for Human Nutrition developed the California Cuisine Pyramid, which recommends reversing the order of the 2 lowest levels of the US Department of Agriculture pyramid so that fruit and vegetables form the base of the pyramid rather than refined and whole breads, cereals, and grains (7). Whole grains and cereals play an important role on the second level of the California Cuisine Pyramid by providing fiber additional to that found in fruit and vegetables to reach a total goal of 25–35 g/d. However, the USDA pyramid does not specify a difference between whole and refined grains. Although a significant source of energy, refined yeast breads do not provide phytochemicals thought to be involved in cancer prevention. The primary rationale for having fruit and vegetables at the base of the California Cuisine Pyramid is to increase the number of phytochemicals consumed for chronic disease prevention.

Fruit and vegetables are functional foods. The study by Michaud et al (4) adds further support for the concept that the phytochemicals in fruit and vegetables are important in cancer prevention. A recent study by Broekmans et al (8) showed both the feasibility of increasing fruit and vegetable intakes and the effect of fruit and vegetable intake on important biomarkers. These investigators compared the effects of the daily intake of 100 g fruit and vegetables and 500 g fruit and vegetables in 47 healthy volunteers over a 4-wk period. Concentrations of lutein were higher by 46%, lycopene by 22%, β-carotene by 45%, and vitamin C by 64%. The group with the high fruit and vegetable intake also had a 15% higher serum folate concentration and an 11% lower homocysteine concentration than did the group with the lower intake. This evidence from a nutritional intervention trial complements the data from epidemiologic investigations and strengthens the scientific basis for dietary recommendations that will significantly increase fruit and vegetable intake to increase serum carotenoids and other phytochemicals that may prevent common forms of cancer.

[1] From the Center for Human Nutrition, University of California, Los Angeles.

[2] Address reprint requests to D Heber, UCLA Center for Human Nutrition, 900 Veteran Avenue, Room 1-2-213, Los Angeles, CA 90095-1742. E-mail: dheber@mednet.ucla.edu.

Received June 20, 2000.

Accepted for publication June 26, 2000.

The recent US Dietary Guidelines provide more encouragement for fruit and vegetable intake than did previous versions but did not provide consumers with enough information to allow them to meaningfully increase their intakes of specific fruit and vegetables. For example, consumers have become aware of the benefits of lycopene and lutein through information about dietary supplements, but inadequate attention has been paid to enhancing the intake of plant-based foods, such as tomato products and green or yellow vegetables, which provide these phytochemicals. Changes in dietary patterns to emphasize the intake of specific fruit and vegetables, together with dietary supplementation with combinations of key antioxidants and phytochemicals, could provide a powerful strategy for the reduction of the risk of lung cancer and other common epithelial cancers (9). More research is needed on the effects of combinations of individual carotenoids obtained from foods and dietary supplements using specific and relevant biomarkers to strengthen the scientific base for more aggressive and specific dietary recommendations aimed at reducing the incidence of common forms of cancer, including lung cancers not related to smoking, gastric cancer, prostate cancer, and other common forms of cancer in which carotenoids appear to play an important role.

REFERENCES

1. World Cancer Research Fund/American Institute for Cancer Research. Food, nutrition and the prevention of cancer: a global perspective. Washington, DC: American Institute for Cancer Research, 1997.
2. Ziegler RG, Mayne ST, Swanson CA. Nutrition and lung cancer. Cancer Causes Control 1996;7:157–77.
3. Chug-Ahuja JK, Holden JM, Forman MR, Mangels AR, Beecher GR, Lanza E. The development and application of a carotenoid database for fruits, vegetables, and selected multicomponent foods. J Am Diet Assoc 1993;93:318–23.
4. Michaud DS, Feskanich D, Rimm EB, et al. Intake of specific carotenoids and risk of lung cancer in 2 prospective US cohorts. Am J Clin Nutr 2000;72:990–7.
5. Rao AV, Agarwal S. Effect of diet and smoking on serum lycopene and lipid peroxidation. Nutr Res 1998;18:713–21.
6. Stahl W, Sies H. Uptake of lycopene and its geometrical isomers is greater from heat-processed than from unprocessed tomato juice. J Nutr 1992;122:2161–6.
7. Heber D. The resolution diet. New York: Avery Publishing Group, 1999.
8. Broekmans WMR, Klopping-Ketelaars IAA, Schuuman CRWC, Verhagen H, van den Berg H, Kok FJ, van Poppel G. Fruits and vegetables increase plasma carotenoids and vitamins and decrease homocysteine in humans. J Nutr 2000;130:1578–83.
9. Heber D, Go VLW, Blackburn GL, eds. Nutritional oncology. San Diego: Academic Press, 1999.