Women with raised CRP levels are not at increased risk of colorectal cancer

A reduced risk for development of some cancers has been associated with use of anti-inflammatory agents, and an increased risk has been associated with inflammatory bowel diseases. It has therefore been suggested that C-reactive protein (CRP, a marker of inflammation) might play a role in development of colorectal cancer. The mechanisms underlying this association are still unclear, and it is uncertain whether the inflammation is the cause or an effect of cancer. This 10-year, prospective, randomized, placebo-controlled study of the risks and benefits of vitamin E supplementation and low-dose aspirin, evaluated the prognostic value of CRP levels in determining risk of colorectal cancer in women.

Baseline plasma levels of CRP were analyzed for 27,913 women aged at least 45 years. Subjects were asked to complete a questionnaire (twice in the first year and annually thereafter) reporting development of colorectal cancer. Medical records were used to confirm reports. Subjects were categorized according to baseline CRP level and postmenopausal use of hormones, and smoking status, among other factors. Various statistical analyses were performed to assess the roles played by the demographic characteristics of the women.

The rate of colorectal cancer incidence (63.1 cases per 100,000 person-years) was similar to the rate for the entire Women's Health Study, of which this group formed a part. Although, when assessed in the multivariate analysis, there was an apparent 56% reduction in risk of proximal colon cancer in women whose baseline CRP was >3 mg/ml, there was no clear indication that baseline CRP level correlated with risk of colorectal cancer.

Original article Zhang SM *et al.* (2005) C-reactive protein levels are not associated with increased risk for colorectal cancer in women. *Ann Intern Med* **142:** 425–432

HOPE-TOO results: vitamin E supplements do not protect against cancer or cardiovascular disease

Epidemiological and experimental studies have pointed to a role for vitamin E in cancer and cardiovascular disease prevention. A daily dose of this antioxidant produced no benefit, however, in the Heart Outcomes Prevention Evaluation (HOPE) trial, which randomized patients with diabetes mellitus or vascular disease to vitamin E supplementation or placebo over a median period of 4.5 years. To determine whether a benefit might be observed over the longer term, the study was extended; results from the HOPE—The Ongoing Outcomes (HOPE-TOO) trial extension have recently been published.

The trial extension included approximately half of the 9,541 patients who participated in the original study. A total of 3,994 participants continued to take the study intervention, whereas 738 were followed up passively. After a median follow-up of 7.0 years for the whole study population, and 7.2 years for those included in the HOPE-TOO extension, there were no significant differences between the placebo and vitamin E groups in the incidence of cancer or cancer-related deaths, or in the incidence of major cardiovascular events. As shown in the initial HOPE study, however, there was an unexpected increase in the rate of heart failure, and hospitalization for heart failure, among patients receiving vitamin E supplementation.

In summary, the study indicated that long-term vitamin E supplementation does not protect against major cardiovascular events or cancer. The observed increased risk of heart failure warrants further study, say the investigators, and in the meantime they recommend that vitamin E supplements "should not be used in patients with vascular disease or diabetes mellitus".

Original article The HOPE and HOPE-TOO Trial Investigators (2005) Effects of long-term vitamin E supplementation on cardiovascular events and cancer: a randomized controlled trial. *JAMA* **293:** 1338–1347