The cancer prevention supplement of choice is probably not beta carotene after all, according to two large-scale studies released last month prior to publication.

The Physicians' Health Study failed to show a benefit from beta carotene supplements given for more than 12 years to 22,071 male doctors. "Beta carotene can neither substitute for a good diet nor compensate for a bad one," summed up Charles H. Hennekens, M.D., of Brigham and Women's Hospital and Harvard Medical School in Boston, who led the trial.

In 1988, Hennekens and his colleagues were able to show, through the same study, that aspirin could reduce risk of first heart attack by 44%. The beta carotene supplement, however, did not decrease the number of cancers, heart attacks, or any type of death in men taking a 50 mg dose every other day.

And contrary to intuition, epidemiology, and animal studies, another study showed that smokers may be harmed by beta carotene and vitamin A.

The investigators heading the Beta Carotene and Retinol Efficacy Trial, known as CARET, stopped the intervention 21 months early because 28% more of the participants taking a combination of 30 mg of beta carotene and 25,000 international units of vitamin A got lung cancer than those on a placebo. The vitamin-takers also had 17% higher total mortality and 26% higher cardiovascular mortality after an average of 4 years in the study. The participants will be followed for at least 5 more years to determine the long-term effects of the intervention.

No Explanation

"We have no explanation for the possible adverse effects we observed to date," said Gilbert Omenn, M.D., Ph.D., of the Fred Hutchinson Cancer Research Center and University of Washington School of Public Health in Seattle. "There can be little enthusiasm about the efficacy or safety of supplemental beta carotene or vitamin A in attempting to reduce the population burdens of cancer or heart disease."

The participants in CARET were 14,254 current and former smokers with a long history of smoking and 4,060 asbestos-exposed individuals, most of whom also smoked. Omenn noted that the former smokers (about 34% of the population at the beginning of the trial) who took beta carotene and vitamin A seemed to respond more favorably, but that the data were too limited to draw any conclusions or to exclude them from the decision to stop the intervention.

The CARET study is the second to show a possible adverse effect from beta carotene supplements. In April 1994, results of the Alpha-Tocopherol, Beta-Carotene Lung Cancer Prevention Trial were published in the *New England Journal of Medicine* and showed an 18% increase in lung cancers and an 8% increase in deaths in the portion of the 29,133 male smokers who took 20 mg of beta carotene daily for 5 to 8 years. At the same time, even the researchers involved thought the finding might be due to chance.

At the press conference where Hennekens and Omenn released their findings, National Cancer Institute Director Richard Klausner, M.D., emphasized that the laboratory data and epidemiologic studies that have linked dietary intake of beta carotene and high blood levels of the nutrient to reduced risk of cancer gave a strong hypothesis that the ATBC and CARET interventions might help stave off lung cancer in these high-risk populations.

"But such hypotheses cannot be presumed to be true because of hope or belief, no matter how fervently they are held," said Klausner. "These studies demonstrate how hard it is to isolate a single component of a healthful diet as the beneficial element. . . We do not know how to replace a healthful diet and a healthful lifestyle with simple pills."

— Kara Smigel