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Questions and Answers Prostate Cancer Incidence and Mortality in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study

1. What is the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study?

The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study or ATBC Study was a chemoprevention trial conducted by the National Cancer Institute (NCI) and the National Public Health Institute of Finland. The purpose of the study was to see if certain vitamin supplements would prevent lung cancer and other cancers in a group of 29,133 male smokers in Finland. The 50- to 69-year-old participants took a pill containing either 50 milligrams (mg) alpha-tocopherol (a form of vitamin E), 20 mg beta-carotene (a precursor of vitamin A), both, or a placebo (inactive pill that looked like the vitamin) daily for five to eight years.

2. What is a chemoprevention trial?

A chemoprevention trial is a type of clinical trial, which is a research study conducted with people. In a cancer chemoprevention trial, natural or man-made substances are tested to see if they prevent cancer. The people who participate in such a study are healthy or are at risk of developing cancer, or in some studies, people who have been treated for cancer and are at a risk of developing a second cancer.

3. What were the results of the ATBC Study?

In 1994 and 1996, the ATBC researchers reported that 16 percent more lung cancers were diagnosed and 14 percent more lung cancer deaths occurred in study participants taking beta-carotene. Vitamin E had no effect on lung cancer.

In the new report, ATBC researchers have shown that the participants taking vitamin E had 32 percent fewer cases of prostate cancer and 41 percent fewer deaths from prostate cancer.

4. Why was the ATBC Study conducted in Finland?

The study was conducted in Finland because of the high lung cancer rates in men in that country, which are due primarily to cigarette smoking. Furthermore, Finland had a clinic system for the screening and treatment of lung diseases (mainly tuberculosis) through which the recruited population of smokers could participate in the study. Finland also has a national cancer registry, which keeps track of all the cancer cases identified in that country, a vital measurement for the large trial.

5. Why was the trial conducted only in men?

Finnish women were not included in the study because their rate of lung cancer was substantially lower than the rate for Finnish men. In 1985, the annual age-adjusted lung cancer rate for Finnish men was 67 cases per 100,000 men and for women was eight cases per 100,000 women.

6. Are the ATBC Study results applicable to Americans?

As a whole, the white men of Finland are similar to white men in the United States, and live similar Western lifestyles. However, in Finland the population is very uniform, with few ethnic and racial differences, so the relationship of these study results to specific minorities is less clear.

7. How do prostate cancer rates compare in U.S. men and Finnish men?

Using world standardized rates, the incidence rate of prostate cancer in the United States was 118.6 per 100,000 in 1994, including all races. The U.S. mortality rate was 17.3 per 100,000. In Finland, the 1995 incidence rate was 61.4 per 100,000 and the death rate was 17.9 per 100,000.

8. Why are prostate cancer incidence rates higher in the United States?

Although there are no clear answers, prostate cancer incidence rates in the United States may be higher in part because of the popularity of prostate-specific antigen (PSA) testing, which identifies cancers that cannot be found by clinical exam. PSA testing for early detection of prostate cancer is generally not done in Finland. Prostate cancer is also a disease of aging and affluence, and historically Finns had a lower life expectancy and standard of living than Americans. Currently, Finns and Americans share very similar lifestyles.

9. What causes prostate cancer?

The causes of prostate cancer are not yet understood. Age is a factor: most cases are diagnosed in men over age 55 years. Some families have higher incidence of prostate cancer, suggesting inherited genetic susceptibility may influence the development of the disease. Hormones, including testosterone, may play a role. Many other possible factors may be involved, but are not proven or not well understood — men who have had vasectomies, farmers, workers exposed to the metal cadmium, workers in the rubber industry, and smokers may have a greater chance of developing prostate cancer.

Diets high in fat have been suggested to increase risk while diets high in fruits and vegetables seem to decrease risk. A recent study suggested that supplements of selenium may reduce risk of prostate cancer.

10. How does the normal Finnish diet compare to the U.S. diet?

The average Finnish diet used to be very high in saturated fat and low in fruits and vegetables. At the time the ATBC Study began, the fat content of the Finnish diet was about 38 percent of total calories. However, the national average fat intake has decreased to about 34 percent of calories from fat, equal to the current U.S. average. The Finns also eat a lot of whole-grain products, like dark rye breads, which gives them a higher fiber intake and they eat more dairy products. Dietary vitamin E intake is somewhat lower in Finland than in the United States (10 mg versus 17 mg per day).

11. Why were vitamin E and beta-carotene chosen for this trial?

Vitamin E and beta-carotene were chosen because epidemiologic studies have linked high dietary intake and high serum levels of these micronutrients to a reduced risk of cancer, particularly lung cancer. Both are anti-oxidants, compounds that may prevent carcinogens from damaging DNA.

12. How might vitamin E protect against prostate cancer?

The mechanisms by which vitamin E may reduce prostate cancer risk are not clear. Vitamin E is an anti-oxidant. Anti-oxidants are compounds that may prevent carcinogens from damaging DNA. In addition to its anti-oxidant activity, there are a number of possible mechanisms by which vitamin E may be working: vitamin E affects cell membranes, may inhibit the proliferation of cells, may stimulate the immune system or alter sex hormones, and could play a role in inhibiting or increasing apoptosis (programmed cell death). It also plays a role in inducing differentiation (the maturing of cells) and protecting the metabolic pathways that rid the body of toxins.

13. What doses of these supplements were given in the ATBC Study?

The dose of vitamin E was 50 mg/day of synthetic dl-alpha-tocopheryl acetate, which is equal to 50 international units of vitamin E. Most multivitamins have about 30 i.u. of vitamin E and singular supplements most often have a minimum of 100 i.u. of vitamin E.

The dose of beta-carotene was 20 mg/day of synthetic beta-carotene. The men in the study took one pill each day, which contained either vitamin E, beta-carotene, both, or neither.

14. Did vitamin E have any effect on other causes of death?

Overall, the number of deaths in men taking vitamin E was similar to men not taking vitamin E.

The men taking vitamin E were found to have fewer deaths from ischemic heart disease and ischemic stroke (a deficit of blood to the brain due to a constriction of a blood vessel), but more deaths due to all cancers and hemorrhagic stroke (a deficit of blood to the brain due to the rupture of a blood vessel).

15. What foods are major sources of alpha-tocopherol (vitamin E)?

Vitamin E is found mainly in oils, such as vegetable oils, and in nuts and grains. The amount in the U.S. diet varies, but is estimated to be about 17 mg/day. The top sources of vitamin E in the U.S. diet are salad dressings and mayonnaise, margarine, ready-to-eat cereals, cakes/cookies/donuts, tomatoes, and eggs.

16. Should Americans avoid taking beta-carotene supplements?

NCI has never recommended that Americans take supplements. The results from the ATBC Study and the Beta-Carotene and Retinol Efficacy Trial (CARET) suggest that smokers should avoid taking beta-carotene supplements. The best advice for smokers who want to reduce their risk of lung cancer and many other cancers is still the most direct: Stop smoking.

The results of the only large-scale study of beta-carotene in primarily nonsmoking men, the Physicians' Health Study, showed no benefit or harm from taking beta carotene supplements every other day for 12 years. For all Americans who wish to reduce their risk of cancer, a low-fat diet with plenty of fruits, vegetables, and grains remains the choice to make.

17. How much did the study cost?

NCI allocated about \$20 million over 10 years for the trial, with a similar sum contributed by the government and research institutions in Finland. In addition, F. Hoffmann-LaRoche, Ltd, a pharmaceutical company based in Basel, Switzerland, supplied the 60 million pills the men took during the trial, without charge, at a cost to the company of about \$3 million.

18. What other large-scale chemoprevention studies are under way?

NCI has a number of different agents under study, including calcium, fiber, tamoxifen, finasteride, and others. The only ongoing large-scale study of vitamin E is the Women's Health Study, headed by researchers at Boston's Brigham and Women's Hospital.

In the Women's Health Study, which began in 1992, 40,000 healthy women age 50 and older were recruited to take combinations of 50 mg beta-carotene, 600 mg vitamin E, 100 mg aspirin, or placebos every other day. After disappointing results from other beta-carotene trials were announced in January 1996, the beta-carotene portion of the study was dropped. The women are being monitored for cancer and heart disease benefits.

For more information about cancer visit NCI's Website for patients, public and the mass media at <http://rex.nci.nih.gov> or NCI's main website at <http://www.nci.nih.gov>.