

## Preventing Prostate Cancer

Prostate cancer is one of the most common cancers affecting men in Western Societies. Nearly 200,000 men in the United States are diagnosed with prostate cancer each year, of whom nearly 40,000 die from the disease. While the cause of prostate cancer is not known, a growing body of evidence indicates that various dietary and lifestyle factors are involved. Following are several strategies that men might employ to help reduce their risk of developing prostate cancer.

### Lifestyle and dietary factors

Some studies have suggested that engaging in regular exercise and avoiding obesity may help reduce the risk of developing prostate cancer. Although these associations have not been firmly established, there are so many other benefits associated with exercising and maintaining a proper body weight that any prevention program should include these factors.

Eating large amounts of red meat, high-fat dairy products, or other sources of saturated fat is associated with an increased risk of prostate cancer, whereas consuming more fruits, vegetables, legumes, garlic, and soy milk may reduce the risk. Tomato products appear to be particularly important. In a prospective study of 47,894 men participating in the Health Professionals Follow-up Study, combined intake of tomatoes, tomato sauce, tomato juice, and pizza, was inversely associated with the risk of prostate cancer. Compared with men consuming less than 1.5 servings of these foods per week, those eating more than 10 servings per week had a 35% reduction in prostate cancer risk and a 53% reduction in the chance of having an advanced case of the disease.<sup>1</sup> In a randomized, phase II clinical trial, supplementation with a tomato extract (Lyc-O-Mato®) at a dose that provided 15 mg/day of lycopene significantly decreased the growth rate of prostate cancer in men awaiting radical prostatectomy.<sup>2</sup>

The protective effect of tomato products appears to be due in part to lycopene, a carotenoid that is present in high concentrations in tomatoes. Lycopene has demonstrated anti-cancer

activity in animal and test-tube studies, but the effects have not been as pronounced as those of tomato extracts. Tomatoes also contain phytoene, phytofluene, beta-carotene, tocopherols and other compounds that might account for some of their beneficial effect. Consequently, tomato products are preferable to synthetic lycopene as a source of this carotenoid. Studies have shown that the absorption of lycopene from tomato paste or puree is greater than from whole tomatoes, but plasma lycopene concentrations increased after ingestion of any of these tomato products.

### Selenium

Thirteen hundred-twelve patients with a history of basal cell or squamous cell carcinoma of the skin were randomly assigned to receive, in double-blind fashion, 200 mcg/day of selenium from high-selenium yeast or placebo. Patients were treated for a mean of 4.5 years, and the mean total follow-up period was 6.4 years. Although selenium did not reduce the recurrence rate of skin cancers, the incidence of prostate cancer was 63% lower in the selenium group than in the placebo group (relative risk = 0.37; 95% confidence interval, 0.18-0.71).

While numerous studies have demonstrated anti-cancer effects of selenium, it is not clear whether all selenium compounds have the same activity. A variety of selenium compounds are present in high-selenium yeast, including selenomethionine, selenocystine, Se-methylselenocysteine, selenoethionine, and unidentified selenopeptides. Until the relative importance of each of these different compounds is determined, it would seem logical to supplement with the preparation that was used in the human study (e.g., Selenomax®).

### Vitamin E

In the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study, 29,133 male smokers (aged 50-69 years) from southwestern Finland were randomly assigned to receive vitamin E (alpha-tocopherol, 50 IU), beta-carotene (20 mg), both compounds, or placebo during a median of period of 6.1 years.

During the follow-up period, there was a 32% decrease (95% CI, -47% to -12%) in the incidence of prostate cancer among individuals receiving vitamin E, compared with those not receiving it. Mortality from prostate cancer was 41% lower (95% CI, -65% to -1%) among men receiving vitamin E.<sup>3</sup>

This study demonstrates that even a small amount of supplemental alpha-tocopherol may reduce the risk of prostate cancer, at least in smokers. The other major form of vitamin E in food (gamma-tocopherol) also appears to be important for prostate cancer prevention, possibly more important than alpha-tocopherol. In a prospective study of 10,456 male residents of Washington County, MD, serum vitamin E levels were measured at baseline, and the incidence of prostate cancer was determined over the ensuing seven years.<sup>4</sup> The relative risk of prostate cancer comparing the highest vs. the lowest quintiles of serum gamma-tocopherol was 0.19 (95% CI, 0.07-0.56), indicating an 81% reduction in risk among individuals with high concentrations of gamma-tocopherol. In contrast, the risk reduction associated with high serum concentrations of alpha-tocopherol was only 35%. Moreover, high levels of alpha-tocopherol were protective only when gamma-tocopherol concentrations were also high. In another study, gamma-tocopherol was more effective than alpha-tocopherol in inhibiting the growth of human prostate cancer cells *in vitro*.<sup>5</sup>

Most vitamin E supplements on the market contain only alpha-tocopherol, even though the predominant form of vitamin E in food is gamma-tocopherol. Studies have shown that supplementing with alpha-tocopherol decreases serum concentrations of gamma-tocopherol. Consequently, any beneficial effect of alpha-tocopherol on prostate cancer risk might be partly negated by a depletion of gamma-tocopherol. For this and other reasons, "mixed tocopherol" preparations (which contain all four naturally occurring vitamin E isomers: alpha-, beta-, gamma- and delta-tocopherol) are preferable to pure alpha-tocopherol for vitamin E supplementation. Two of the most potent

▶ dietary sources of gamma-tocopherol are soybean oil and walnuts.

## Does alpha-linolenic acid cause prostate cancer?

Several epidemiological studies have found that high dietary intake of the essential fatty acid alpha-linolenic acid (ALA) is associated with increased risk of prostate cancer. The results of these studies have raised concern that flaxseed oil, a popular nutritional supplement and one of the richest known dietary sources of ALA, might be unsafe. After reviewing the available evidence, however, this writer is not convinced that men should throw away their bottles of flaxseed oil.

Despite the fairly consistent findings in epidemiological studies, associations do not prove causation. It is possible that ALA intake is just a marker for some other dietary or behavioral factor that promotes the development of prostate cancer. For at least two reasons, the idea that ALA causes prostate cancer lacks biological plausibility. First, the content of ALA in a typical Western diet has declined considerably over the years, as a result of partial hydrogenation of edible oils and less grazing by farm animals on ALA-rich grasses. If anything, the modern diet is marginally deficient in ALA.<sup>6</sup> It is difficult to believe that the lower end of the

historical range for an essential nutrient is still too much. Second, ALA at a concentration less than 10 microM inhibits the enzyme 5alpha-reductase activity *in vitro*.<sup>7</sup> This enzyme catalyzes the conversion of testosterone to its more biologically active metabolite, dihydrotestosterone, which is believed to play a role in the development of both benign prostatic hyperplasia and prostate cancer. A substance that inhibits 5alpha-reductase might, therefore, help prevent, rather than promote, prostate cancer.

While it seems unlikely that ALA itself is a carcinogen, it is possible certain foods that contain ALA have cancer-causing effects that are unrelated to their ALA content. One such food might be rapeseed oil (canola oil). In one study, male rats were fed one of three different types of fat: canola oil, palm oil, or fish oil. The mean plasma androgen concentration was significantly higher ( $p < 0.05$ ) in rats fed canola oil than in those fed the other two oils.<sup>8</sup> If canola oil also increases androgen concentrations in humans, it could increase the risk of prostate cancer. In another study, mice fed canola oil had a decreased capacity to metabolize hexobarbital in the liver.<sup>9</sup> If that finding reflects a general inhibitory effect on drug-metabolizing enzymes, canola oil might also inhibit the breakdown of various carcinogenic xenobiotic compounds. Thus, it may be in eating that canola oil causes problems, even though the ALA it contains is innocuous.

Another factor that relates to the biological effects of ALA is its unstable nature. ALA is more highly unsaturated than its omega-6 counterpart linoleic acid and is, therefore, more prone to become oxidized, either spontaneously or in the presence of heat. Cooking with soybean oil or canola oil (the two main plant sources of ALA in most human diets) might lead to the formation of carcinogenic byproducts, more so than cooking with oils that contain primarily linoleic acid, monounsaturated

fatty acids, or saturated fats. Heating of canola oil or soybean oil creates volatile mutagenic compounds that are released into air; these compounds could account for the reported association between exposure to rapeseed cooking-oil emissions and lung-cancer risk among Chinese women.<sup>10</sup> To the extent that similar compounds remain in the food, high-temperature cooking with either soybean or canola oil might increase the risk of other forms of cancer, as well.

While many questions remain unanswered, the available evidence does not lead to the conclusion that men should minimize their intake of ALA. On the contrary, research suggests that restricting ALA intake might increase the risk of developing heart disease and some other chronic diseases, as well. However, oils rich in ALA probably should not be used for high-temperature cooking, and care should be taken to prevent these oils from becoming rancid. In addition, studies cited previously, when combined with evidence that canola oil causes cardiac damage in animals, leads one to question the safety of this oil for human consumption.

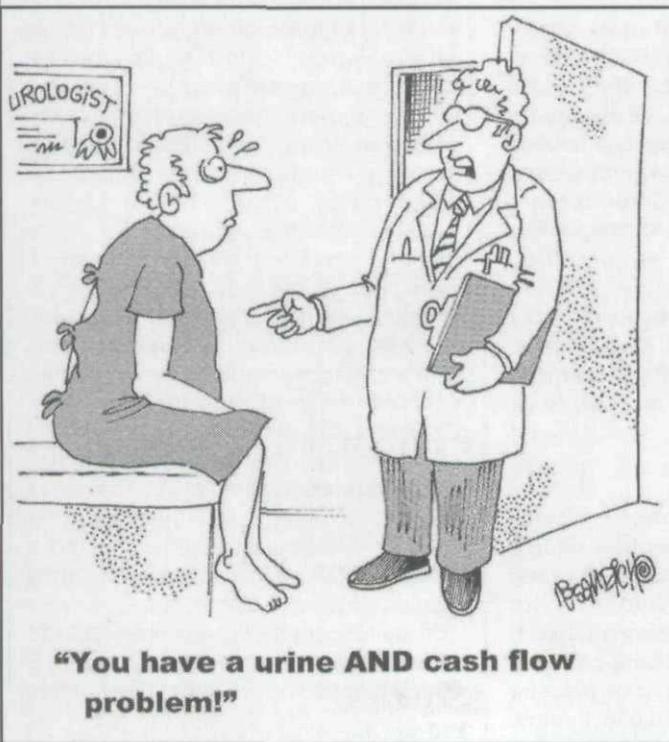
## Conclusion

We still have a great deal to learn about prostate cancer. However, based on what we already know, it should be possible for men to take some fairly easy, inexpensive and safe actions to reduce the likelihood that they will develop this disease.

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