The Effect of Diet and Supplements on Prostate Cancer

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H&O Does diet affect the risk of developing prostate cancer?

SF We think that it does, but we are not 100% clear about how, or about what specific dietary factors may influence the risk. Some of the most interesting studies that point to the importance of diet have looked at populations from Asia—where the risk of prostate cancer is extremely low—who move to the United States. Within just 1 or 2 generations, the prostate cancer risk in these populations approaches that found in Western society. Part of the increase is explained by the fact that we screen more in this country, but the difference in risk goes beyond that.

As far as specific lifestyle factors are concerned, the historical Asian lifestyle is so different from the modern US lifestyle that it is very challenging to pinpoint specific differences that would explain the disparity in cancer risk. Trying to identify foods that might increase or decrease the risk of prostate cancer is overly reductionist in my view, and clinical trials of specific dietary interventions are rarely able to detect an effect.

H&O What are some of the more important studies that have looked at dietary interventions or supplement use and prostate cancer risk?

SF There are a lot of negative data from clinical trials that were undertaken based on what we thought was good epidemiological evidence. For example, we had a wealth of epidemiological data pointing to an association between higher blood levels of vitamin E and selenium and reduced prostate cancer risk. When the National Cancer Institute studied this in the 30,000-person SELECT (Selenium and Vitamin E Cancer Prevention Trial) study, however, vitamin E and selenium supplements did not decrease prostate cancer risk, as reported in the *Journal of the American Medical Association* in 2009. Updated results published in the *Journal of the American Medical Association* in 2011 found that taking vitamin E actually increased the risk of developing prostate cancer. An analysis published in the *Journal of the National Cancer Institute* in early 2014 found that taking selenium increased the risk of developing high-grade prostate cancer in men who already had high selenium levels at the beginning of the study. We also have data from nonrandomized trials suggesting that multivitamins may increase the risk of developing prostate cancer.

We know that there is a relationship between low levels of sunlight and an increased risk of prostate cancer; the rate of prostate cancer is lower for men living in the southern part of the United States than in New England, and Scandinavian countries have some of the highest rates of prostate cancer in the world. Might vitamin D supplements reduce the risk of developing prostate cancer? Those studies have yet to be done, but it is an intriguing idea.

H&O Do dietary interventions or supplements have any effect on prostate cancer survival or recurrence?

SF Nothing has been proven. Soy intake was theorized to be helpful, but a 2013 paper in the *Journal of the American Medical Association* found that soy had no impact on prostate cancer recurrence.

One of the better-publicized studies, by Dr Dean Ornish, included 93 prostate cancer patients who were on active surveillance. The patients were randomly assigned either to continue their regular lifestyle or to embark on...
a global lifestyle change. The lifestyle change involved a low-fat, vegan diet; exercise; meditation; soy supplements; and vitamin E supplements. The patients who were randomized to the lifestyle change adhered quite well to the regimen. At the 1- and 2-year marks, these patients had lower prostate-specific antigen (PSA) levels than those in the control group, and were less likely to need treatment of their cancer. When prostate cancer cells were added in vitro to blood samples from these patients, the cancer cells actually grew more slowly than when blood samples from patients in the control group were used. With continued follow-up, we hope to see differences in mortality.

For me, the most interesting finding from this study is that the patients in the lifestyle intervention group lost weight. There are a lot of roads that lead to obesity, whether that means too much sugar, too much fat, or inactivity. We have compelling data that link obesity to more aggressive disease at diagnosis of prostate cancer, and increased prostate cancer mortality. The associations are not as large as what we see in some other cancers, but obese people are approximately 25% to 30% more likely to die of prostate cancer than normal-weight people. Although some of that increase might be explained by delays in diagnosis caused by excess weight, we saw this 25% to 30% increase even in the 1960s, before we routinely screened for prostate cancer.

Our clinical research increasingly has been focusing on weight loss. I think that losing the weight is probably more important than how you lose the weight, but that is just a theory.

Dr William Aronson from UCLA’s Jonsson Comprehensive Cancer Center has shown that having men follow a low-fat diet and take fish oil capsules before surgery for prostate cancer can lower the proliferative rate of the tumor cells. Of course, we do not know if this leads to better survival. Dr Wendy Demark-Wahnefried of the University of Alabama at Birmingham reported similar effects with flaxseed supplements before prostate cancer surgery.

SF We have 2 clinical trials that are up and running. The first trial is designed to see whether weight loss using a low-carbohydrate diet can reduce the side effects of hormone therapy in men with advanced prostate cancer (NCT00932672). The second trial, called CAPS2 (Carbohydrate Restriction and Prostate Cancer Growth; NCT01763944), includes men whose prostate cancer has failed to respond to initial therapy, but who are not ready for hormone treatment. We are looking at whether weight loss can slow the rate of PSA rise in these men.

The approach to weight loss in both of these studies is a diet that is extremely low in carbohydrates. When we tested a low-carbohydrate diet in multiple animal models, we found that it slowed tumor growth—even when the animals did not lose weight. Studies in humans have shown that this type of diet can lead to profound weight loss, and that is what we are seeing in our studies. In the first study, the median weight loss at 3 months was nearly 15 pounds.

Forty years ago, before the US Dietary Guidelines started recommending a low-fat diet, the obesity rates in this country were less than half what they are today. I think the recommendation to avoid fat has been one of the key drivers of the obesity epidemic. If you look at countries in Europe, there is a direct relationship between higher fat intake and lower body weight. Fortunately, I think that researchers are slowly coming around to realizing that sugar is probably a greater enemy than fat.

H&O What is the mechanism by which diet appears to affect prostate cancer?

SF There are probably multiple mechanisms at work. We know that improved diet and weight loss can lower levels of insulin, insulin-like growth factor 1, and cholesterol, all of which promote the growth of tumors. Weight loss also reduces markers of inflammation in the body, and inflammation has been tied with tumor growth. These are just a few of the potential mechanisms at work.

Cholesterol plays a role in another interesting mechanism that may be at work. We think that cholesterol may promote tumor metastasis by affecting blood vessel formation—and we do have some intriguing data from a recent meta-analysis published in PLoS One suggesting that statins may reduce the risk of developing prostate cancer, and also prostate cancer progression.

H&O What other important studies of diet and prostate cancer have been done?

SF We have some very good animal data showing that weight loss slows the progression and reduces the risk of developing prostate cancer. Epidemiological data in humans support that finding, but we have yet to conduct clinical trials looking at weight loss and prostate cancer in humans.

Regarding diet and other types of cancer, one study whose results appeared in several articles in the Journal of the American Medical Association in 2006 involved putting healthy women on a low-fat diet for 7 years, and seeing whether the risk of cancer was affected. The women in this study did not lose weight, and there was no effect on the incidence of breast cancer, colon cancer, or heart disease. In another study, which was published in the Journal of the American Medical Association in 2007, women who were randomly assigned to increase their intake of fruits and vegetables had no decrease in cancer risk.
The problem is that when doctors tell their patients to eat more fruits and vegetables, the patient may do so but continue to go overboard on unhealthy foods.

**H&O Do omega-3 fatty acids have an effect on prostate cancer?**

**SF** This question has become relatively controversial. There are semi-strong epidemiological data suggesting that eating fish may be protective for both prostate cancer risk and progression, but a couple of studies have come out in the past year or 2 that have questioned that notion. Two studies by Brasky and colleagues showed that people who had the highest levels of omega-3s in their blood had slightly more high-grade prostate cancers than those with the lowest levels, although we do not know whether the omega-3s were from supplements or from diet. Most people think of fish and nuts as the main dietary sources of omega-3s, but red meat also contains omega-3s. So, we really do not know whether omega-3s can help. The patients in the intervention group in the Aronson study ate a low-fat diet, took fish oil, and lost weight, so we do not know which component was beneficial.

**H&O What are the risks of dietary supplements for prostate cancer?**

**SF** The major risk is that you actually may make things worse, which is what we saw in SELECT. We have seen in multiple studies that when men take more than one multivitamin a day—or a multivitamin plus another supplement—the rate of prostate cancer increases. This supports the idea that the body is designed to work within a certain range of each micronutrient, neither too much nor too little. Overloading on micronutrients can turn them from antioxidants into pro-oxidants, so taking more than a single multivitamin a day is risky. This is definitely a case of more not being better.

**H&O Could there be an argument for taking a daily multivitamin plus additional vitamin D?**

**SF** Perhaps, because the amount of vitamin D in most multivitamins does not begin to approach what would have been present in the blood of our early human ancestors. Another issue with vitamin D is that it is fat-soluble, so people who do not get enough fat in their diet cannot absorb the vitamin D and thus miss out on the potential benefits. I have seen patients who start taking regular vitamin D supplements but are on an ultra–low-fat, vegan diet, and their vitamin D levels do not go up at all. We see the same issue of absorption with tomato paste, which has been linked to less prostate cancer. People are unable to absorb the lycopene or whatever other compounds in the tomato paste may be beneficial unless there is fat in the diet.

**H&O Is there anything else you would like to add?**

**SF** I would say that the key to affecting prostate cancer through diet is to focus on reversing and eliminating obesity. Even though obesity has less of a link to prostate cancer than to other types of cancer, we know that obesity increases the risk of prostate cancer mortality. That is the one fact about diet and lifestyle that we know for sure.

**Suggested Readings**