



VIRGINIA PROSTATE CENTER Newsletter

A PARTNERSHIP PROGRAM OF EASTERN VIRGINIA MEDICAL SCHOOL AND SENTARA CANCER INSTITUTE
Fall 1997 Paul F. Schellhammer, M.D., Editor Volume 2 Number 2

Cancer prevention may be linked to diet

The ability to make correlations between diet and cancer incidence is very difficult. There is no doubt that we have become an "over-nourished society." However, the risk of cancer can be associated with undernutrition as well as over-nutrition. For instance, gastric cancer and cancers of the head and neck are common in underdeveloped and nutrition-deficient countries. However, breast cancer, colon cancer, ovarian cancer, endometrial cancer and prostate cancer are more common in populations where food is plentiful,

specifically food high in fat content.

The difficulty with identifying dietary intake as causal, both with regard to specific substances and/or overall consumption evaluations, is as follows: Prospective studies that detail diet in real time, and therefore the most accurate, require long, expensive, tedious evaluations over a period of 20 or more years. This is the case because of the long-term cumulative effects of dietary intake over a lifetime and the appearance of cancer late in life. Retrospective studies, which look back at

dietary habits of the past, depend upon recall, and we are all aware how difficult it is to remember what our dietary habits may have been in the prior year and certainly in the prior decade. Population studies (for instance, comparing the dietary habits in Japan to the dietary habits in California as causal) suffer from the fact that issues other than diet, e.g. environmental or genetic, may offer explanations for differences between populations. Finally, single substances or compounds might behave quite differently

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Virginia Prostate Center investigates novel drugs to treat advanced prostate cancer

Traditional antitumor drugs act as cell poisons and are designed to kill cancer cells. Many of these drugs, unfortunately, also affect normal tissues and cause deleterious side effects in cancer patients. To improve upon the limitations of current cytotoxic cancer drugs, researchers are now developing a variety of alternative antitumor drugs with novel modes of action. Through collaborations with cancer scientists at the NCI and in the biopharmaceutical industry, VPC investigators have begun to examine the potential clinical usefulness of several of these novel antitumor drugs for the treatment of human prostate cancer.

The drugs being studied are referred to as cytostatic agents because of their ability to stop the replication of growing tumor cells. One drug, called CAI, blocks cellular calcium, an important intracellular molecule that VPC scientists have discovered is important to the ability of prostate tumor cells to respond to growth-promoting hormones and pre-

sent in the tissue environment of the tumor. Another class of drugs are tyro-phostins, which inhibit important tyrosine kinases that control biochemical reactions necessary for the relay of growth signals throughout tumor cells.

Through support from the nationally recognized prostate cancer organization CaP CURE, the Norfolk-based VPC investigators have determined that both of these cytostatic drugs not only block the growth of several different types of prostate tumor cells in the laboratory, but also inhibit the ability of malignant cells to invade artificial tissue components. Thus, cytostatic therapies may help to delay the appearance of androgen-independent prostate tumors and suppress the growth of prostate tumor cells once they have spread to the bone and other sites in the patient. Because the reactions targeted by the cytostatic agents are more active in tumor cells than normal cells, the researchers anticipate these novel drugs will be less toxic when adminis-

tered to cancer patients. In laboratories at the VPC and other national cancer centers, tumor biologists are now hard at work developing cytostatic drug therapies for future clinical applications in the treatment of prostate cancer. ■

VOLUNTEERS NEEDED

The Heitzer family has graciously donated their time to organize and manage a bingo parlor (**Bingo Palace**) every Saturday from 1:00 to 5:00 p.m. with all proceeds going to the Foundation for Specialized Surgery to support the research programs of the **Virginia Prostate Center**. They need 3-5 volunteers each Saturday to help with this important fundraising effort. Won't you please consider serving as a volunteer (or come and play bingo) to help in this important support of prostate cancer research? Please call (757) 622-5900 for more information on how you can help.

Nutrition

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when tested as a solitary ingredient evaluated in the test tube or as a dietary supplement in an animal model as compared to its effect in companion with other substances in the human. An example of this was seen in the betacarotene study conducted by the National Cancer Institute, which randomized over 20,000 men with a smoking history to beta carotene and vitamin E (alpha tocopherol) supplements or placebos.¹ The study was initiated because of the numerous retrospective investigations that suggested foods containing beta carotene, an antioxidant, had a powerful protective effect in the development of lung cancer. However, when the study was analyzed the incidence of lung cancer was actually higher in the group receiving the beta carotene supplement. The potential explanations are several, but one seems most logical: foods containing beta carotene contain other substances as well

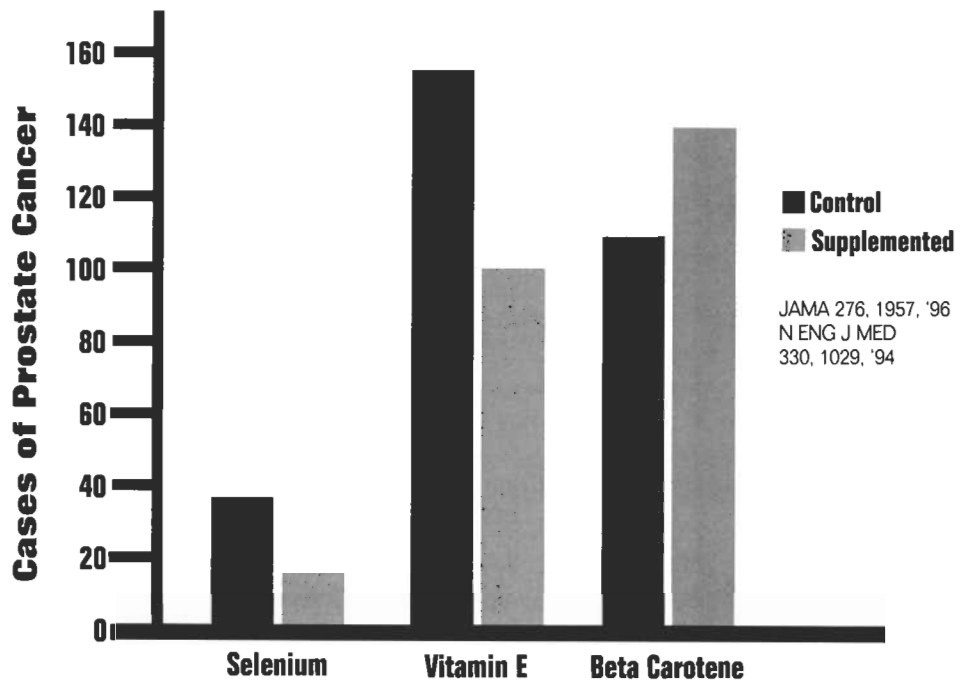


Figure 1

A Changing Diet and Lifestyle for Prostate Cancer Prevention/Treatment

Is there ultimate proof that changes in diet and lifestyle can prevent prostate cancer? Not yet. CaP CURE is planning three studies to address nutrition in prostate cancer patients. These studies will take many years to complete, but the good news is that there is something you can do now. Some facts to consider for the case for good nutrition:

- Improved nutrition is not harmful (unless you take toxic amounts of vitamins).
- It is something you can do now without waiting for additional research. Advice to stop smoking was provided long before we could prove the connection of smoking and lung cancer.
- Improved nutrition usually has effects that improve quality of life. You may look younger, wear your clothes better and have an extra bounce in your step if you achieve a healthier weight by eating a healthier diet.
- It may help to prevent prostate cancer progression. We do not know this yet, but we are working hard to develop the evidence that nutrition makes a difference.

which may be indeed more important than beta carotene or may be required together with beta carotene to produce a protective effect. However, beta carotene as a stand-alone substance was obviously not the answer. For patients with prostate cancer, a very interesting sidebar to this study was the fact that the incidence of prostate cancer was lower in patients receiving vitamin E than in the control group. This serendipitous finding brings back the study dealing with selenium that I discussed in the last newsletter; namely that selenium supplementation was not effective in decreasing the incidence of skin cancer in a large study, but on further review of the data its use was found to be associated with a lower risk of prostate cancer.² (See Figure 1)

Another food product that is widely consumed in Eastern and underdeveloped countries, but much less so in the U.S., is soy protein. In fact, the consumption of soy protein in Japan and Okinawa is 10-30 times that of the U.S. Soy protein contains a group of compounds called isoflavonoids.³ Genestin, an isoflavonoid, has been found in experimental studies to be a modulator of cellular growth and proliferation. Therefore, investigational efforts in the evaluation of this product as a potential preventive dietary supplement in a number of cancers, prostate cancer included, are presently in process.

In general terms, a healthy diet initiative should be directed at reducing total fat intake. The relationship of prostate cancer, breast and ovarian cancer to fat intake may relate to the increased hormone levels, androgens and estrogens, associated with increased fat intake. Reduction in dietary fat is not only a useful measure with regard to malignancy prevention, but obviously tremendously useful in preventing cardiac and vascular disease as well. The average

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Interstitial Brachytherapy:

Radioactive seed implant for localized prostate cancer

Radiation has long been an accepted option in the treatment of prostate cancer. There are two methods by which to treat the prostate gland: external beam therapy and radioactive seed implant. With the former, x-rays are delivered from outside-in by a large machine called a linear accelerator. With the latter method, small seeds which continuously emit radiation are inserted into the prostate and left in place.

A new technique to more accurately and less traumatically place the seeds within the prostate gland was developed in the mid-1980s. Using transrectal ultrasound to visualize the prostate gland in three dimensions, needles were inserted

through the skin beneath the scrotum. Seeds, the size of rice grains, were then injected into the prostate gland through the needles.

Prior to the availability of ultrasound and the development of this procedure, seed implants were done using a major open surgical procedure through an anterior pelvic incision, exposing the prostate gland. Follow-up analysis showed this old method to be relatively inaccurate with regard to seed and needle placement within the gland, leading to the areas of over-treatment (higher doses) and under-treatment (lower doses). Oftentimes, this meant that the tumor recurred. In addition, studies have suggested that the dose rate of the isotope used previously,

Iodine-125, was too low to eradicate more rapidly dividing cells.

A newer isotope with a higher dose rate, Palladium-103, is now available. At the Virginia Prostate Center, a Palladium-103 seed implant program was initiated in 1994. The transperineal ultrasound-guided technique is currently used to insert 20 to 25 needles and 80 to 100 seeds. As of July 31, 1997, 50 patients have been so treated. This is usually done under spinal anesthesia as an outpatient procedure. Most patients resume normal activity in less than a week. Complications have been minimal. Outcome analyses from multiple centers across the country show results at five

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Nutrition

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American diet consists of a caloric proportion from fat reaching 35 to 40%. Reducing the total calories from fat to less than 30% and optimally less than 20% (very difficult) is recommended. The significant source of fat is from meat products, specifically beef, veal, pork and lamb, which are marbled meats high in fat.

It goes without saying that reduction of most consumption will lower fat intake. A number of correlations of fat to increasing prostate cancer risk have been suggested. (See Figure 2) ■

REFERENCES

1. The Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group: The Effect of Vitamin E and Beta Carotene on the Incidence of Lung Cancer and Other Cancers in Male Smokers. *N Engl J Med* 330:1029-1035, 1994.
2. Clark LC, Combs GF, Tumbull BW, et al: Effects of Selenium Supplementation for Cancer Prevention in Patients with Carcinoma of the Skin. *JAMA* 276:1957-1963, 1996.
3. Wei H, Wei L, Frenkel K, et al: Inhibition of Tumor Promoter-induced Hydrogen Peroxide Formation in vitro and in vivo by Genistein. *Nutr-Cancer* 20(1):1-12, 1993.

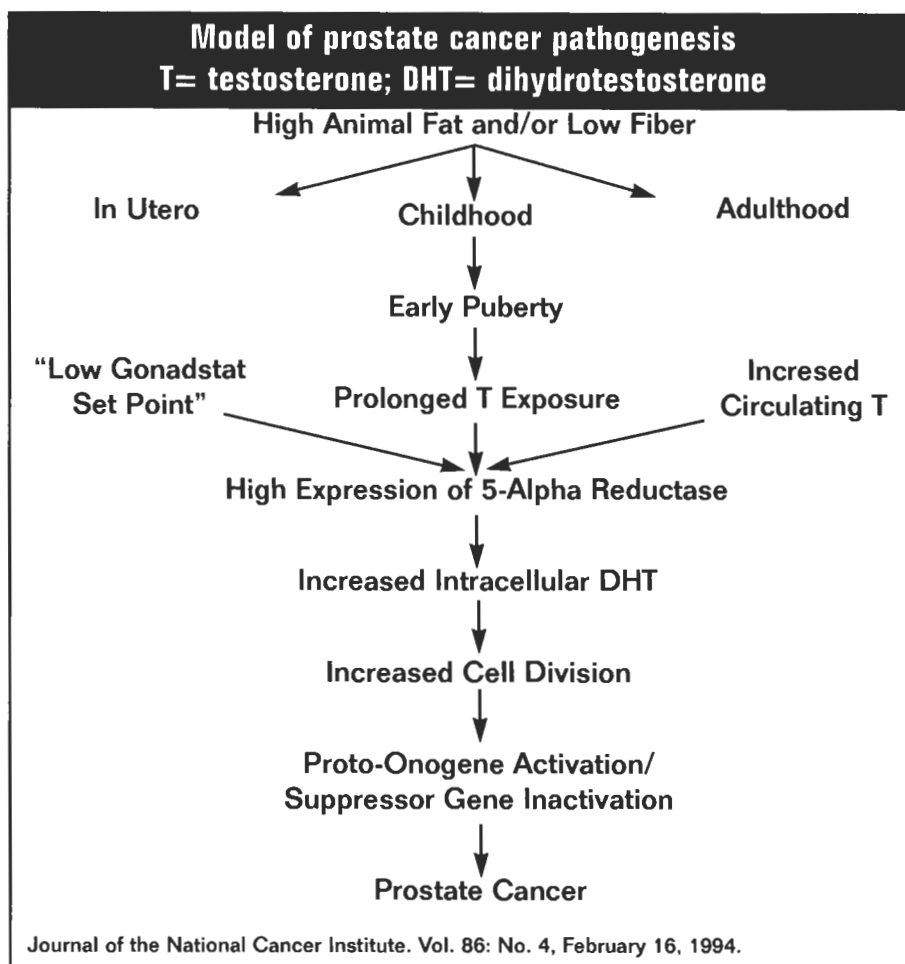


Figure 2

Yes! I want to help support the Virginia Prostate Center

I want to help support the Virginia Prostate Center and its efforts to find more effective treatments and hopefully a cure for prostate and other urologic cancers. (Please also consider a \$5.00 donation to support publication cost and postage for circulation of this newsletter.)

- Enclosed is my contribution
- Please contact me about gift opportunities to the VPC

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Radioactive seed implant

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years post-treatment, which appear similar to external beam therapy and surgery.

Candidates must be chosen carefully, however. Implant is best suited to patients with small, localized tumors with low Gleason scores. For later stage, prostate cancers with higher Gleason scores, a combination of external beam therapy and implant can be used, often together with androgen deprivation (hormone therapy). For this type tumor, there is usually a fairly high risk of disease extension to the areas surrounding the prostate or to the pelvic lymph nodes. Therefore, the entire region must be treated. Seed implant treats only the prostate gland.

The Virginia Prostate Center will monitor the outcomes of patients treated by interstitial therapy and continue to expand its investigation of adjuvants that may improve the rate of success, and continue to update the technologic advances that are aimed at improving implant symmetry and dosimetry. ■

Please clip and mail to: Virginia Prostate Center, Office of Development, Eastern Virginia Medical School P.O. Box 5, Norfolk Virginia 23501-0005.



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