



# VIRGINIA PROSTATE CENTER Newsletter

A PARTNERSHIP PROGRAM OF EASTERN VIRGINIA MEDICAL SCHOOL AND SENTARA CANCER INSTITUTE  
Spring 1998 Paul F. Schellhammer, M.D., Editor Volume 3 Number 1

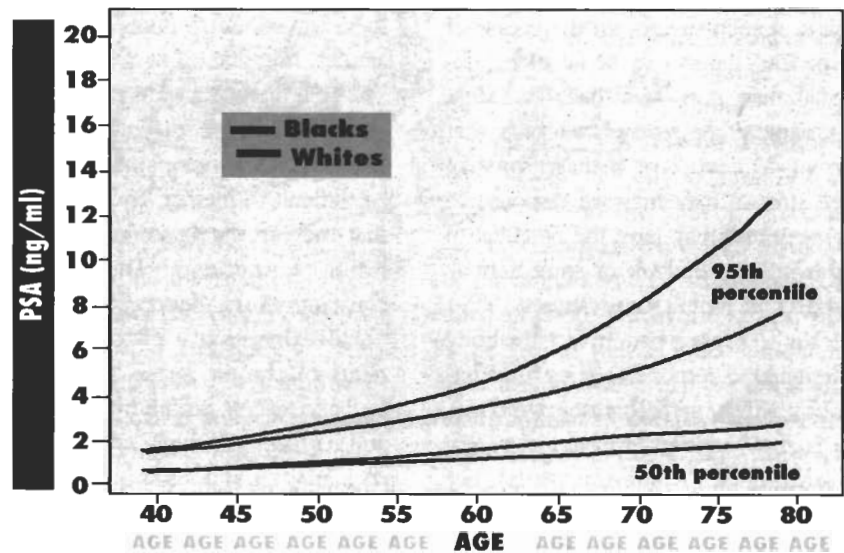
## Race and Increased Risk of Prostate Cancer

Prostate cancer exhibits considerable racial and ethnic variation. Men of Asian descent, for example, have a very low incidence and mortality from prostate cancer, while African-American men have the highest incidence and mortality from prostate cancer in the world.

Despite a recent surge in research in this clinical problem, the etiology of these striking racial differences remains unclear. While a number of studies have demonstrated that African-American men have lower survival than Caucasian, those studies originating from equal access health care systems do not confirm this finding. Data show that African-American men who participated in a screening program with the opportunity, therefore, of early diagnosis, were diagnosed at a similar state as their Caucasian counterparts.

Biological differences have been noted that may contribute to a higher risk of prostate cancer in African-American men. For example, African-American men have higher serum testosterone levels and 5 $\alpha$ -reductase activity than Caucasian and Japanese men. These hormones drive prostatic growth and activity. However, no direct relationship between circulating androgen levels and the development of prostate cancer has been thus far demonstrated.

Several studies have shown an inverse correlation between exposure to sunlight and prostate cancer incidence and mortality. It has been suggested that Vitamin D plays a role in prostate carcinogenesis. Variations in Vitamin D metabolism might contribute to racial differences in prostate cancer risk.



Other dietary factors, e.g. fat and micronutrient consumption, have been implicated in the racial disparity in incidence. The volume of tumor in African-American men tends to be larger and more poorly differentiated than Caucasian counterparts at the time of diagnosis. This may account for the higher PSA values measured in African-American men with prostate cancer. Investigation of disparity between serum PSA values among men of different races without cancer has resulted in a proposal for race-specific reference ranges. (RSRR)

The Virginia Prostate Center has studied this issue. Data from annual screening has yielded PSA levels for 1656 African-American and 2995 Caucasian men, all of whom had normal prostatic exams. A trend towards a higher PSA among African-Americans was seen in all age groups. This is visualized on the graph which plots the 50th and 95th percentile

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### VPC Researcher Receives Award

Antonia G. Vlahou, Ph.D., a research fellow in the VPC, has recently learned that she has been awarded a two-year fellowship from the American Foundation for Urological Disease (AFUD). Dr. Vlahou, a native of Athens, Greece, has joined the VPC for three years to receive advanced training in the cell and molecular biology of prostate cancer under the direction of Drs. Paul Schellhammer and George Wright. Specifically, Dr. Vlahou will be investigating the genetic regulation of a newly identified prostate cancer gene called prostate specific membrane antigen or PSMA. It is hoped that understanding the regulation of this novel gene will lead to new treatment strategies for prostate cancer. Congratulations to Dr. Vlahou for receiving this prestigious AFUD award to help support her research studies.

# Stress, Disease, and Cancer

Every disease, illness, or injury has physical or physiological as well as psychological or emotional components. Each disease state - whether it be a simple bladder or ear infection or a serious traumatic injury or complex malignant process - creates both physical and emotional stresses for the patient affected by it. While it has long been recognized that this is so, recent research suggests that the impact of such stresses on the course of the patient's illness may be far more substantial than previously believed. More important, other research suggests that learning to control or manage some of these stresses may improve response to treatment and may have the potential of improving the outlook of some serious disorders, including some cancers.

Not all stress is bad. In fact, the body is designed to respond to stressful situations by activating mechanisms which act like energy "boosters" to carry the individual through the stressful period. For example, if a person falls off a bridge into a river, his body automatically initiates increased secretion of the hormones adrenaline (epinephrine) and cortisone, which stimulate the body's physiology to better equip it to survive the plunge. Adrenaline causes dilation of the breathing tubes in the lungs to facilitate oxygenation of the blood. It stimulates the heart to beat both faster and stronger, to circulate the blood to the muscles, so that the individual can swim to shore or stay afloat until rescued. It causes the outer blood vessels to constrict, forcing more blood into the central circulation where it can be pumped to the muscles, an action which also preserves body heat. Both adrenaline and cortisone cause stored sugars to be released from the muscles and liver to provide energy for the muscles and other organs. Many other physiologic processes are also triggered by these two important hormones in the stress situation, all of which, in the short term, serve to assure the individual's survival - to prepare and equip him to swim to shore or stay afloat until rescued. This

process, called the "General Adaptation Syndrome," by the late Hans Selye, is intended to be a short-term mechanism to assure survival in acute stressful situations such as that described above.

It is when stress becomes chronic - when these physiologic processes designed to aid survival in the short term become switched on continuously - that stress becomes counterproductive. In these situations, patients' illnesses may actually be made worse by chronic stress.

Few illnesses create emotional stress as much as the diagnosis of cancer. Because the outlook of many cancers can be difficult to predict, patients often feel that they are living under the constant threat of recurrence. This can lead to constant worry, depression, and emotional exhaustion - all classic components of chronic stress. Chronic stress leads to excess secretion of adrenaline and cortisone, which can make such coexisting conditions as high blood pressure and diabetes much more difficult to control. Excess secretion of cortisone may reduce the body's capacity to fight off infection, making the individual more susceptible to viral illnesses and other infectious processes. Several studies by Kiecolt-Glaser and others have shown such compromise of the immune system to occur in medical students undergoing the stresses of final exams as well as among the caregivers of patients with Alzheimer's disease.

If stress has such an adverse impact on the immune system that it may predispose to infections, what is its impact for the patient whose immune system may be helping to defend his body against a recurrence of cancer? Evidence is building that learning successful stress management techniques may provide a patient with a means to counteract the adverse effects of stress and normalize the action of the immune system. Clearly, minimizing stress should allow the body's defenses to operate more productively. What is intriguing is the possibility of being able to teach patients to fur-

ther stimulate their body's immune system to make it an even more effective component in the defense against recurrent cancer. A fascinating study by David Spiegel showed that patients with metastatic breast cancer who both learned to manage their stress and create vivid visualizations of cancer-fighting images survived twice as long as a similar group of patients who did not pursue such techniques. This and other research in the relationship between stress and cancer management will be discussed further in a future article.

Managing stress does not have to be complicated or difficult. Basic stress management involves such things as mild regular exercise - such as walking or swimming. Involvement in a pleasurable activity or diversion - reading, crafts or a hobby - can do much to dissipate chronic stress. Of considerable importance is open communication with a spouse, friend, family member, or significant other, as well as good dialogue with the attending physician, to assure the disease and its prognosis are kept in realistic perspective. Other techniques for managing stress will be addressed in a future article. ■

## 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.

# Immunotherapy: A new and promising strategy

A new and promising strategy, called immunotherapy, is being intensely investigated as an alternative approach to treat a variety of cancers including cancer of the prostate. Immunotherapy represents a strategy to augment anti-tumor immune responses to either eliminate the tumor or inhibit tumor progression. Many changes occur when normal cells become transformed into cancer cells. Some of these changes result in new molecules being expressed on tumor cells which are not found or found in very limited quantities on normal cells. These molecules, which distinguish tumor cells from their normal counterparts, are called tumor associated antigens (TAA). The presence of TAA on the surface of a cancer cell elicits an immune response which potentially can result in elimination of the tumor. For many years, immunologists have been puzzled by the failure of the immune system to eliminate a progressively growing tumor despite the presence of TAA. However, this puzzle may have

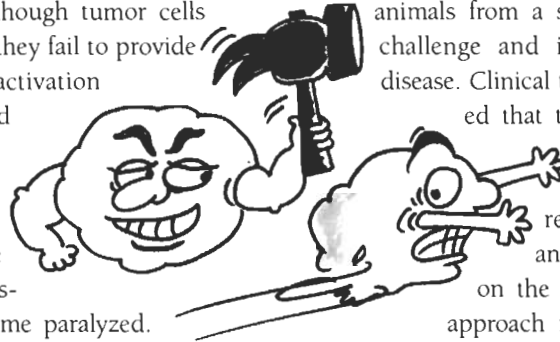
been recently solved with the demonstration that lymphocytes, effector cells of the immune system, require a second costimulatory signal in addition to antigen (eg., TAA), the first signal for activation. Although tumor cells express TAA, they fail to provide the second activation signal and indeed, in the absence of this second signal, the immune system can become paralyzed.

Armed with this information, investigators have developed several dendritic cell-based strategies to treat cancer. Dendritic cells (DC) represent specialized cells called antigen presenting cells (APC) which initiate anti-tumor immune responses because they display TAA and constitutively express costimulatory molecules. Thus, they deliver potent activation signals to anti-tumor lymphocytes. One DC-based approach

is to pulse DC with TAA (or TAA peptides) and then infuse these TAA "loaded" DC back into the cancer patient. Animal studies have demonstrated that this approach can protect animals from a subsequent tumor challenge and inhibit metastatic disease. Clinical trials have indicated that this treatment can enhance anti-tumor immune responses without any adverse effects on the patient. A second approach involves fusion of the tumor cells with DC producing a cell called a hybrid. The hybrid cell expresses the TAA as well as other stimulatory molecules typically expressed by DC. Again, animal studies have demonstrated the efficacy of this strategy to prevent cancer and to treat metastatic disease.

Although initial studies with TAA pulsed DC are encouraging, this approach

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## Increased Risk

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values by age for both races. Larger numbers of patients will be necessary to define accurate ranges. This study is ongoing.

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### Coming in the next issue

A story on ..

*New drugs for the Management of Erectile Dysfunction*

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

## Immunotherapy:

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requires identification and isolation of TAA for each individual tumor, a difficult and expensive procedure. Flt3 ligand, a recently described DC growth hormone, represents an alternative DC-based strategy. Flt3 ligand induces impressive increases in the number of DC in a variety of organs and this increase is associated with augmented anti-tumor immune responses. VPC scientists have demonstrated that flt3 ligand can suppress the growth of an established and progressively growing prostate cancer. In some animals treated with flt3 ligand, palpable tumors shrank to undetectable levels. The advantage of this approach is that it does not require isolation and characterization of prostatic TAA. Furthermore, increased DC numbers in organs such as liver and lung as a result of flt3 ligand immunotherapy raises the possibility that this treatment may have application in patients with disseminated disease. Studies at the VPC and other national cancer centers are currently evaluating the efficacy of flt3 ligand immunotherapy as a treatment for different stages of prostate cancer. ■

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