



VIRGINIA PROSTATE CENTER Newsletter

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Prostate Testing Among Men Greater Than 75 Years

By: Paul F. Schellhammer, M.D.

A recent announcement from the American Task Force for Prevention of Disease which advised against PSA testing among men greater than 75 years of age was received with a significant amount of controversy and strong objections.

The position and sentiments of a large cohort of men aged 75 and older who rightfully consider themselves productive members of society and who are fit enough to anticipate many future golden years enjoying the fruits of their labor, their children and grandchildren is that they should avail themselves of PSA testing. In their lifetime they have witnessed medical advances which have extended life expectancy and they have been the grateful beneficiaries. To hear that a recommendation to avoid a simple blood test that could provide early identification of the most dreaded of diseases, cancer, seems totally illogical, counterproductive and at odds with the mantra "take good care of yourself by taking greater control of your health". When the concept of population and societal risks and benefits are brought to the table in a discussion about PSA testing in the aging male, patients listen with interest but the burning issue, nevertheless, distills to the concern "what about me?". For a 75 year old, who is vigorous and healthy, who is attentive to his health issues, who is blessed with familial longevity, and who desires to know his PSA status, strong advice against testing seems unreasonable and counter to the physician / patient relationship.

I am reminded of an experience I had several years ago in following a very healthy and well educated 80 year old gentleman with a PSA of 7. We had the discussion about the high likelihood of his prostate containing cancer cells because of his age and the likelihood that he was at very low risk for problems. He was satisfied with the explanation. The following year his PSA was 13, and he was quite alarmed and I no longer had the assurance that everything was in control. A biopsy was performed and both he and I were disheartened with the Gleason 4+5 readings from multiple cores. I could see his confidence evaporate and he sought opinion and received treatment. Several years later, when one of the Swedish trials was published that supported watchful waiting, he responded with a letter to the editor in our paper warning men against this strategy and citing his own case of aggressive cancer allowed to proliferate as he watched and waited. I have experienced similar encounters with other patients and I am sure every urologist has as well. (also see <http://www.evms.edu/vpc/docs/prostate-cancer-perspective.pdf>) Such anecdotes are not evidence-based medicine, but they cannot be

disregarded. However, when a PSA is done for a 75-year-old male, it cannot be the first of a number of reflex reactions. PSA testing need to be placed in context before a decision to obtain is made and before proceeding to any biopsy. Positive biopsy results need to be placed in context before processing to any recommendations for therapy. As urologists we wish to follow the admonition to first do no harm. To accomplish this for the 75 year old presenting for PSA test requires individual assessment, thoughtful discussion, and recognition of competing mortality as illustrated in the table – and we, as physicians must strive to reduce the numbers in each of the columns.

The challenge which thus far has not been solved by the PSA test or through multiple PSA derivatives (PSA velocity, PSA doubling time, % free PSA, pro-PSA, etc), rests in the discovery of a reproducible marker panel which both identifies prostate cancer when it is present (with very few false positive readings) and more critically distinguish cancers non-concern for disability and death, and this will be the majority, from those that threaten life and well being. ■

At age 75, men are much more likely to die of heart disease and other conditions than prostate cancer. How many of 1,000 men will die in the next decade from:

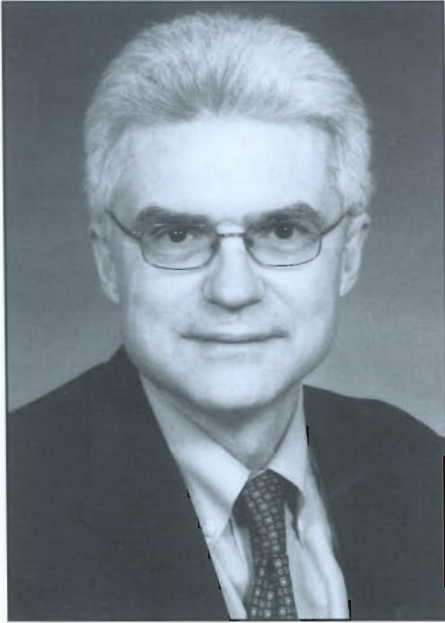
	Heart disease	Stroke	Lung cancer	Prostate cancer	Pneumonia
Never smoked	137	32	8	19	12
Smoker	140	39	109	15	16

Source: Journal of the National Cancer Institute

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Urologic Oncologist Dr. Troyer Joins the VPC

By: *O. John Semmes, Ph.D.*



Dr. Dean A. Troyer recently came to Norfolk and EVMS after 18 years as Professor of Pathology at the University of Texas Health Science Center. In addition to joining the team at the Virginia Prostate Center, he and his wife Peggy will be closer to their daughters, one living in Strasburg and the other in Sterling with their families. Peggy, an RN, works in the renal transplant clinic at Sentara Norfolk General Hospital.

He joined a pathology practice at Sentara Norfolk General Hospital where he leads the genitourinary pathology team interpreting bladder, prostate, and kidney biopsies. He believes there are tremendous opportunities for translational research here in Norfolk not least because there is a team of knowledgeable basic scientists, clinicians and pathologists attacking the problem.

EVMS has responsibilities for teaching and research, and utilizes the large extremely well-managed Sentara system for clinical teaching and training. Dr. Troyer believes that the successes of the interactions between the Virginia Prostate Center and Sentara will be a model for further collaborations of these fine institutions.

Dr. Troyer notes that very promising studies are ongoing to directly examine urine of men to look for signs of prostate cancer. In addition, there is a technique called imaging mass spectroscopy that may soon enable multiple measurements of key predictive factors in human biopsies to help doctors determine which cancers need aggressive treatment and which may be treated with watchful waiting. Dr. Troyer has teamed up with Dr. Aurora Kerscher to study certain types of RNA that are very promising because they are unique to cancers and can be measured in very small amounts in blood and tissue. These could be very helpful diagnostic and prognostic markers of disease. Finally, the Reader's Digest recently ran an article which spelled out the problems with early diagnosis of cancer. Basically, as odd as it sounds, early diagnosis doesn't necessarily translate into decreased deaths due to cancer. This is true of prostate and other cancers. There are a lot of cancers that wear grey hats and some that wear black hats and will be aggressive. It is these aggressive cancers that need treatment, and we need methods to tell them apart from their less aggressive counterparts. The Virginia Pro-

tate Center is well positioned to address this problem, particularly with cancers of the urinary tract. ■

NIH Awards Two Grants to VPC

By: *O. John Semmes, Ph.D.*

Researchers and clinicians at the Virginia Prostate Center were recently awarded two National Institutes of Health research grants to identify different diagnostic proteins in prostate fluids obtained in the Urology of Virginia clinics. Prostate-specific antigen (PSA) and prostatic acid phosphatase (PAP) are proteins secreted by prostate cells, and both have a long clinical history of use in blood tests for prostate cancers. These two proteins and many other proteins made by the prostate are present at much higher levels in the collected prostate fluids than in blood samples. New instrument technologies available in the associated laboratories of the George L. Wright, Jr. Center for Biomedical Proteomics will be used for the characterization of these proteins. The types of sugar residues that are present on proteins present in the prostate fluids will also be analyzed for comparison across different prostate diseases in order to develop new tests based on these differences. The collection of these prostate fluids is not disruptive to a standard urological exam, nor does it add excessive time to the visit. Defining all of the proteins present, and determining standards for collection and storage is also part of the awards. This type of research emphasis on proteins

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and sugars in the collected prostate fluids is unique nationally and internationally, and highlights the cutting edge research being performed by members of the Virginia Prostate Center. ■

Expressed Prostate Secretions Biomarker NIH Grant Awarded to the VPC Team

*By: Raymond S. Lance, M.D.
Richard R. Drake, Ph.D.*

Researchers at the VPC received two new grants from the NIH to further ongoing studies on prostate cancer. The VPC research team derives from members of Urology of Virginia, Pathology Services Medical Group and Eastern Virginia Medical School. Dr. Raymond Lance (Urology of Virginia), Dr. Dean Troyer (PSMG), Dr. Richard Drake (EVMS), Dr. O. John Semmes (EVMS) and Dr. Aurora Kersher (EVMS) form the leadership team for the planned studies, which are aimed at using expressed prostate secretions to identify individual prostate cancer proteins able to more precisely categorize these cancers by outcome. The problem for prostate cancer patients is the lack of precise molecular biomarkers that can guide how each man's cancer should be managed based upon the individual cancer's biology. To combat this problem we currently use multiple pieces of information such as PSA, clinical stage, Gleason grade of the biopsy, and the percent of biopsy cores involved with cancer to create an individual risk stratification. This approach represents our best guess about the true extent of the cancer and its ability to spread beyond the

prostate gland or even if it is confined to the prostate at diagnosis. The work funded by these grants takes us away from traditional PSA type blood samples and to the closest body fluid to the prostate we can obtain in the form of the so call expressed prostate secretions or EPS. EPS fluid is harvested from the urine following a digital rectal exam (DRE). The prostate is a spongy gland wrapped around the urethra with multiple tiny tubes that connect directly into the urethra so that when the doctor pushes on the prostate EPS leaks into the urethra which is then voided into a cup moments after the exam. In the case of PSA, blood spends very little time in the walnut sized prostate gland before circulating through much larger organs on its way to a needle stick in an arm vein and thus represents a more confusing biomarker arena to study prostate cancer. We believe that in the 21st century, the key to better prostate cancer treatment must begin with the most accurate initial understanding of each man's cancer. To illustrate this consider the vastly different cases of two of my recent patients. In the first case "Bill" was found to have a PSA of 5.7 and a normal DRE, but the biopsy showed 3 samples out of 12 with Gleason 3+4 prostate cancer. "Bill" underwent a robotic prostatectomy and the final pathology showed a completely confined cancer (all margins negative) with only 5% of his gland involved with cancer. This is what most men hope for when they receive the diagnosis. Contrast this with the case of "Roger" who had a PSA of 5.2, normal DRE, biopsy showed 4 of 12 biopsy cores with Gleason 3+4 prostate cancer. When his prostate was analyzed after radical prostatectomy it was found that 40% of the prostate was involved and that the cancer had already spread outside the gland and into a lymph node. The traditional risk stratification did not

help us understand that Roger was in trouble while Bill was in great shape. Our project seeks to clearly delineate from the EPS fluid just before biopsy what is truly going on with a given man's prostate cancer. Better information early will allow for better treatment choices to be made. Additionally, there are cases of prostate cancer that do not have the capability to take a man's life. This type of prostate cancer is called, "insignificant disease." You may be thinking, wait a minute how can cancer be "insignificant?" Insignificant prostate cancer does not have the capacity to spread and thus does not pose any risk of taking the man's life. It has been well demonstrated that many men who are diagnosed with prostate cancer in the PSA era harbor insignificant disease. Unfortunately the only precise way to know for sure who has insignificant disease is to take out the prostate gland with surgery and then it can be tested to see if it is significant or not. We must do better than that therapy could be designed to disrupt this switch, thereby controlling the progression of prostate cancer. ■

Foundation for Urological Research

By: Paul F. Schellhammer, M.D.

The expanding spectrum of new therapies directed towards the treatment of urological cancer has led us to broaden the scope of our research endeavors from the Virginia Prostate Center, and its focus on prostate cancer, to the Foundation for Urological Research. The Foundation will continue to escalate its research and current clinical trial activity with regards to prostate cancer, but will now also apply the same principles of investigation towards the treatment of kidney and bladder cancer. It will also address benign conditions that, while not life-threatening, significantly impact the quality of life.