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### POWELL URGES MEN TO DETECT PROSTATE CANCER EARLY

Looking fit after traveling some 2,900 miles on diplomatic business in four countries over eight days, Secretary of State Colin Powell still looks back on his successful prostate cancer surgery as carrying an important message for all men.



"Detect prostate cancer early," Powell says. Otherwise, if you don't, "it will kill you."

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PROSTATE CANCER  
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# HOT SHEET

**AUGUST 2004**

### FAST-RISING PSA LEVELS SIGNAL AGGRESSIVE PROSTATE CANCER

Men with prostate cancer whose PSA levels increased significantly the year before diagnosis and surgery had more aggressive forms of the disease and were more likely to die within seven years. This suggests that delaying treatment and just monitoring the situation may be dangerous for such men.

That's the finding of a new study that concludes that PSA (prostate-specific antigen) testing results should be tailored to the health profile of each man. The study was led by Dr. William Catalona, director of prostate cancer screening at Northwestern University, and was done when he held a similar job at Barnes-Jewish Hospital in St. Louis.

It also may give a way to identify men who aren't likely to be cured by having their prostates removed. Hormones or other treatments instead of or in addition to surgery may be better options for them. In the study, up to 28% of men with rapidly rising PSA scores died of prostate cancer despite having their prostates taken out.

"This study shows fairly conclusively that it is not the absolute number but how it changes over time," said Dr. Anthony D'Amico, lead author of the study appearing in the July 8 issue of the New England Journal of Medicine.

"Just like with mammograms, you don't look at a single snapshot in time, you look at the continuous spectrum. The PSA velocity [how it changes over time] is the most important predictor," he said.

D'Amico is radiation oncologist at Brigham and Women's Hospital, Harvard Medical School and Dana Farber Cancer Institute, all in Boston.

Interestingly, half of the men who had the greater PSA velocity in this study were classified, by conventional means, as low-risk patients.

The findings may help solve one of the biggest dilemmas facing men with prostate cancer: whether to have it treated or to wait to see if it starts to cause problems, researchers said.

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## US TOO PUBLICATIONS

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## PROSTATE CANCER ADVOCACY GROUPS WORK TO CHANGE THERAPY APPROVAL PROCESS

For the first time, the four major prostate cancer advocacy groups are combining forces with the common goal of working with the U.S. Food and Drug Administration (FDA) to streamline the approval process for critical prostate cancer treatments by changing the traditional measures of a research study's success or failure, known as clinical trial endpoints, without compromising safety.

The four prostate cancer advocacy groups are the Prostate Cancer Education Council, National Prostate Cancer Coalition, Prostate Cancer Foundation, and Us TOO International Prostate Cancer Education and Support Network.

"Prostate cancer is the most common non-skin cancer in America, striking one in six men. As the baby boom men reach the target zone for prostate cancer, beginning at age 50, the annual incidence rate will increase from 230,000 to 300,000 men," stated Prostate Cancer Foundation Vice Chairman and Chief Executive Officer Leslie D. Michelson.

"These four organizations are united in our desire to accelerate the development of better treatments for these men. Determining clinical trial endpoints that everyone can support is an important step in that process."

Traditional clinical trial endpoints, such as survival time, have proven difficult in trials of drugs for men with advanced prostate cancer because prostate cancer typically grows slowly, many prostate cancer patients typically have other diseases and prostate cancer attacks different men in different ways.

There is a growing body of evidence that surrogate endpoints, such as doubling time of Prostate Specific Antigen (PSA), changes in PSA, and time to disease progression may be useful in predicting which patients will gain true clinical benefits, such as longer survival time.

At the recently convened American Society of Clinical Oncology 2004 Meeting, E. David Crawford, MD, council member of PCEC and professor of surgery and radiation oncology with the Division of Urologic Oncology at the University of Colorado Health Sciences Center, presented a paper showing a correlation between PSA measurements and survival benefit in advanced prostate cancer patients being treated with a Taxotere regimen.

According to Crawford, "Prostate cancer has significantly lagged other cancers in the development of therapeutic options that provide patient benefit.

"Using straightforward measures, like PSA in conjunction with other accepted measures of anti-tumor activity and patient benefit, has the potential to simplify the clinical trial process, making trials more feasible and more attractive for sponsoring organizations.

"If we are going to significantly improve treatment options for men with advanced prostate cancer, we need to introduce into clinical trial design surrogate endpoints that can enable shorter, smaller trials and, thus, facilitate more rapid evaluation of new therapies for this devastating disease.

"We now have data from a large pivotal trial that suggest that such a marker has been identified."

The Prostate Cancer Education Council is dedicated to providing free prostate cancer screenings as well as increasing the awareness and education of the disease to men and their families.

The National Prostate Cancer Coalition's goals are to increase awareness by educating the public about the disease through dynamic programs with corporate sponsors, to reach out at-risk communities by conducting free screenings for prostate cancer onboard the Drive Against Prostate Cancer mobile medical unit, and to engage citizens and associations to build an advocacy network that encourage increases in federal funding of prostate cancer

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research.

The Prostate Cancer Foundation is dedicated to finding better treatments and a cure for recurrent prostate cancer. The Foundation has raised more than \$210 million and funded more than 1,100 critical research projects in 100 research centers around the world.

Us TOO International Prostate Cancer Education and Support Network is a non-profit, prostate cancer education and support network, established in 1990 by five men who had each been diagnosed with and treated for prostate cancer. Since then, Us TOO has grown to more than 330 chapters throughout the United States and internationally.

## PROSTATE SPECIFIC ANTIGEN RATIOS OFFER A BETTER WAY TO DETECT PROSTATE CANCER

Medical investigators in Scotland performed a study "to compare the performance of various ratios using total prostate specific antigen (PSA), complexed PSA (cPSA) and free PSA (fPSA) in the early detection of prostate cancer. The study included 535 consecutive patients evaluated at a prostate cancer detection clinic between January 1998 and October 1999. Patients had blood samples drawn before transrectal ultrasonography and prostate biopsy to measure PSA, cPSA and fPSA."

"Receiver operating characteristic (ROC) curves (sensitivity vs. 1 - specificity) were used to evaluate the performance of PSA, cPSA, f/tPSA, cPSA/tPSA, fPSA/cPSA, tPSA/prostate volume (PV), fPSA/PV, and cPSA/PV. The areas under the curve (AUC) were calculated for each ratio. The performance of each ratio over all patients or in those with a tPSA of 4-6 or 4-10 ng/mL were evaluated," wrote O.L. Ozdal and colleagues, Hairmyres Hospital.

"Of the 535 patients, 204 (38%) had biopsy-confirmed prostate cancer. The AUC obtained with tPSA alone was 0.64; when measured for all

patients the cPSA/PV (0.78), PSA/PV (0.77), f/tPSA (0.76) and fPSA/cPSA (0.75) performed better than tPSA alone. Furthermore, in patients with a tPSA of 4-10 ng/mL, tPSA/PV (0.72), cPSA/PV (0.71), f/tPSA (0.69), fPSA/cPSA (0.69) and cPSA/tPSA (0.62) performed better than tPSA alone (0.52).

"Finally, in patients with a tPSA of 4-6 ng/mL, PSA/PV and cPSA/PV performed better than the other ratios. The use of PSA ratios gives a higher sensitivity and specificity for detecting prostate cancer than the use of tPSA alone," investigators concluded.

Ozdal and colleagues published their study in *BJU International* (Comparative evaluation of various prostate specific antigen ratios for the early detection of prostate cancer. *BJU Int*, 2004;93(7):970-974).

For additional information, contact S. Tanguay, Hairmyres Hospital, E Kilbride, Lanark, Scotland.

## WATCHFUL WAITING FOR PROSTATE CANCER NOT APPROPRIATE FOR YOUNGER MEN

Researchers report that watchful waiting could be an appropriate approach to certain older men with prostate cancer.

"Expectant management has evolved to include cure as its ultimate goal," scientists writing in the journal *Current Opinion in Urology* report.

"Early data regarding such a strategy indicate that it may be a reasonable alternative for a select group of older men," wrote M.E. Allaf and colleagues, Johns Hopkins Medical Institute, Brady Urology Institute.

The researchers concluded: "For men with a long life expectancy, disease is likely to progress and such a strategy is not currently recommended. The long-term efficacy of this approach will be determined with further follow-up."

Allaf and colleagues published their study in *Current Opinion in Urology*

(Update on watchful waiting for prostate cancer. *Curr Opin Urol*, 2004;14(3):171-175).

Additional information can be obtained by contacting H.B. Carter, Johns Hopkins Medical Institute, Brady Urology Institute, 600 N. Wolfe St., Marburg 403, Baltimore, MD 21287 USA.

## HOUSE RESOLUTION ENCOURAGES ACCESSIBILITY TO PROSTATE CANCER TREATMENT OPTIONS

The U.S. House of Representatives has adopted a resolution encouraging doctors to inform their prostate cancer patients of all of the proven treatment options available.

According to the resolution (H. Res. 669), "the Federal Government and the States should ensure that health care providers supply prostate cancer patients with appropriate information and any other tools necessary for prostate cancer patients to receive readily understandable descriptions of the advantages, disadvantages, benefits, and risks of all medically efficacious treatments for prostate cancer, including brachytherapy, hormonal treatments, external beam radiation, chemotherapy, surgery, and watchful waiting."

The non-binding resolution was introduced and sponsored by Congressman Nathan Deal (R-GA) through the Subcommittee on Health of the House Committee on Energy and Commerce.

"Prostate cancer is the second leading cause of cancer death of men in the United States, and the effort to raise public understanding about treatment options is, therefore, crucial," said Deal.

"Patients deserve accessible and comprehensive information about treatment options. They must be empowered to select the most appropriate therapy. Essential in making that decision is an understanding of both the cure rate

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## HOUSE RESOLUTION SEEKS ACCESS TO PCA TREATMENT OPTIONS

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and the quality of life implications of  
all approaches.

“Congressman Deal and his colleagues are to be commended for their foresight and involvement in such a worthwhile resolution.”

## PROSTATE CANCER PATIENTS DESIRE MORE INFORMATION ABOUT THE AFTERMATH OF THERAPY

Researchers in Canada completed a study “to identify the preferences for sexual information resources of patients before and after definitive treatment for early-stage prostate cancer with either radical prostatectomy (RP) or brachytherapy.”

Two hundred patients (mean age 64 years) treated with either RP or brachytherapy were recruited from radiation oncology (100) and urology (100) outpatient clinics. Patients completed a survey questionnaire to identify the types of information used, preferred sources of information, knowledge of treatments for erectile dysfunction (ED), effect of sexual function on the treatment decision, and the International Index of Erectile Function (IIEF) to assess their current level of sexual function,” said B.J. Davison and colleagues, Vancouver General Hospital.

“Urologists were identified as the main source of sexual information. Written information, Internet access and videos were identified as preferred sources of information before and after treatment. The effects of treatment on sexual function had no apparent significant influence on the men’s definitive treatment choice.

“Compared with patients in the brachytherapy group, patients in the RP group reported having significantly higher levels of sexual desire ( $p < 0.001$ ) after treatment, but otherwise the erectile domains of the

groups were remarkably similar. Two-thirds of patients wanted more information on the effects of treatment on sexual function, and on available treatments for ED,” investigators noted.

“These results support the need for physicians to offer patients access to information on the effect of treatment for early-stage prostate cancer on erectile function before and after treatment.”

Davison and colleagues published their findings in *BJU International* (Preferences for sexual information resources in patients treated for early-stage prostate cancer with either radical prostatectomy or brachytherapy. *BJU Int*, 2004;93(7):965-969).

Additional information can be obtained by contacting B.J. Davison, C328-2733 Heather St., Vancouver, BC V5Z 3J5, Canada.

## QUALITY OF LIFE ISSUES SHOULD BE CONSIDERED BEFORE ANDROGEN SUPPRESSION THERAPY

According to recent research published in the journal *BJU International*, a study was conducted “to investigate the effects of different management strategies for non-localized prostate cancer on men’s quality of life and cognitive functioning.”

“Men with prostate cancer were randomly assigned to one of four treatment arms: leuprorelin, goserelin, cyproterone acetate (CPA), or close clinical monitoring. In a repeated-measures design, men were assessed before treatment (baseline) and after 6 and 12 months of treatment,” wrote H.J. Green and colleagues, Inner North Brisbane Mental Health Service.

“A community comparison group of men of the same age with no prostate cancer participated for the same length of time. The men were recruited from public and private urology departments from university teaching hospitals. All those with

prostate cancer who were eligible for hormonal therapy had no symptoms requiring immediate therapy.

“In all, 82 patients were randomized and 62 completed the 1-year study, and of the 20 community participants, 15 completed the study. The main outcome measures were obtained from questionnaires on emotional distress, existential satisfaction, physical function and symptoms, social and role function, subjective cognitive function, and sexual function, combined with standard neuropsychological tests of memory, attention, and executive functions.

“Sexual dysfunction increased for patients on androgen-suppressing therapies, and emotional distress increased in those assigned to CPA or close clinical monitoring. Compared with before treatment there was evidence of an adverse effect of leuprorelin, goserelin, and CPA on cognitive function.

In deciding the timing of androgen suppression therapy for prostate cancer, consideration should be given to potential adverse effects on quality of life and cognitive function,” investigators recommended.

Green and colleagues published their study in *BJU International* (Quality of life compared during pharmacological treatments and clinical monitoring for non-localized prostate cancer: a randomized controlled trial. *BJU Int*, 2004;93(7):975-979).

For additional information, contact H.J. Green, INBMHS, 162 Alfred St., Fortitude Valley, Qld 4006, Australia.

## INTERLEUKIN 6 MEDIATES CROSS-TALK BETWEEN PROSTATE CANCER CELLS

“The interaction between stromal and epithelial cells is critical for the initiation and progression of prostate cancer, but the molecular determinants responsible for the cross-talk between these two cell types remain largely unknown. Here, we used a coculture cell assay to

identify messengers involved in the cross-talk between human prostate stromal PS30 and epithelial LNCaP cells. Stimulation with lysophosphatidic acid (LPA) activates the mitogenic extracellular signal-regulated kinase (ERK) signaling pathway in PS30, but not LNCaP cells," scientists in the United States report.

"The coculture of PS30 and LNCaP cells results in the activation of ERK in LNCaP cells and that is further increased in response to stimulation with LPA. Physiologic relevance of the interaction between PS30 and LNCaP cells is demonstrated using LNCaP xenograft tumor assays. Animals implanted with a mixture of both cell types develop larger tumors with higher frequency compared with those injected with LNCaP cells alone," according to P. Sivashanmugam and colleagues, Duke University, Medical Center.

"Conditioned medium transfer experiments reveal the PS30-derived inducing factor is soluble and promotes mitogenic ERK and STAT3 signaling pathways in LNCaP cells. Protein analysis demonstrates that treatment of the PS30 cells with LPA induces synthesis of interleukin 6 (IL-6). Antibody neutralization experiments reveal that IL-6 is responsible for the LPA-induced mitogenic signaling and growth of the LNCaP cells.

"Our findings reveal that the LPA-regulated secretion of IL-6 is an important messenger linking stromal and epithelial prostate cells, which may be exploited for the effective treatment of patients with advanced prostate cancer," scientists concluded.

Sivashanmugam and colleagues published their study in *Journal of Biological Chemistry* (Interleukin 6 mediates the lysophosphatidic acid-regulated cross-talk between stromal and epithelial prostate cancer cells. *J Biol Chem*, 2004;279(20):21154-21159).

For more information, contact Y. Daaka, Duke University, Med Center, Department Surgery, 2607, Durham, NC 27710 USA.

## DIETARY ELEMENTS ALTER THE RISK FOR PROSTATE CANCER

According to scientists in the Netherlands, "we reviewed 37 prospective cohort and four intervention studies on potential dietary risk factors for prostate cancer, published between 1966 and September 2003. Some studies were limited by small size, crude measurement of dietary exposure and limited control for confounders. Intervention and prospective cohort studies support a protective role against prostate cancer for selenium, and possibly for vitamin E, pulses and tomatoes/lycopene."

"Overall consumption of meat, eggs, vegetables, fruit, coffee, tea, carotenoids and vitamins A, C and D was not consistently related to prostate cancer risk. Intervention studies also indicate that supplementation with beta-carotene does not lower prostate cancer risk, except possibly in men with low beta-carotene status at baseline," reported P.C. Dagnelie and colleagues, Maastricht University, Department of Epidemiology.

"For specific types of meat, alcoholic drinks, dairy products, fat and anthropometric measures, most cohort studies suggest either an increased risk or no relation with prostate cancer. For calcium, two cohort studies suggest an increased risk at very high calcium intakes (>2000 mg/day).

"In conclusion, prospective studies are consistent with a protective role for selenium, and possibly vitamin E, pulses and tomatoes/lycopene, in the etiology of prostate cancer. Studies are inconclusive on the role of meat, dairy products, fat, vegetables, fruits, alcohol and anthropometric measures, whereas a very high calcium intake appears to be positively associated with prostate cancer risk," researchers concluded.

Dagnelie and colleagues published their study in *BJU International* (Diet, anthropometric measures and prostate cancer risk: a review of prospective cohort and intervention

studies. *BJU Int*, 2004;93(8):1139-1150).

For more information, contact P.C. Dagnelie, Maastricht University, Department of Epidemiology, POB 616, NL-6200 MD Maastricht, Netherlands.

## COMMON 'SIGNATURE' FOUND FOR DIFFERENT CANCERS; DISCOVERY YIELDS HOPE FOR UNIVERSAL TREATMENT

Researchers at the University of Michigan, Johns Hopkins and the Institute of Bioinformatics in India have discovered a gene-expression "signature" common to distinct types of cancer, renewing hope that a universal treatment for the nation's second leading killer might be found.

Scientists essentially abandoned the search for a common approach to cancer therapy after research launched by the 1970s "War on Cancer" revealed the many varieties of cancer and the differences among even the same type of cancer in different people. As a result of these discoveries, the focus largely has been on tailoring treatments to specific forms of cancers and even to the precise biology of cancer in a particular person.

"Perhaps we'd learned so much about the differences among cancers that we stopped looking for the similarities. Not having the right tools to look for similarities on a global level didn't help, either," says Akhilesh Pandey, assistant professor of biological chemistry in the McKusick-Nathans Institute of Genetic Medicine at Johns Hopkins and chief scientific advisor and founder of the Institute of Bioinformatics, a nonprofit institute located in Bangalore, India.

In the team's hunt for an overall genetic signature of cancer, which could be useful for diagnosis as well as for developing therapies, the scientists mined a mind-boggling amount of raw information by first creating an online searchable database

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## COMMON CANCER SIGNATURE FOUND

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of 40 published data sets that had collectively analyzed the gene expression “fingerprints” of more than 3,700 cancer tissue samples.

Searching the collected data for common patterns of altered gene expression, the researchers uncovered a “signature” common to all cancers and another that distinguished some kinds of aggressive tumors from their less aggressive counterparts. Their report appears in the June 22 issue of the Proceedings of the National Academy of Sciences.

The signature consisted of 67 genes that were abnormally expressed in all cancers. These genes largely are involved in the cell’s preparation for division — called the cell cycle — and cell proliferation, the researchers report. Since cancers are characterized by uncontrolled cell division, the discovery is logical, even though it wasn’t easy, says Pandey.

“A lot of the available data on gene expression in cancers was just ‘warehoused’ — it was there, but not connected to anything,” he says. “We took that data, analyzed it and connected it to relevant information. Now it’s both available and useful.”

Pandey and staff at the Institute of Bioinformatics last year reported creation of the Human Protein Reference Database [<http://www.hprd.org>], an online, searchable, information-rich database of known human proteins and their interactions.

The new project, initiated by Arul Chinnaiyan, M.D., Ph.D., at Michigan, took a similar approach to the cancer problem by developing a way to statistically analyze microarray data and applying the new approach to data from microarray experiments on tumor samples.

Microarray experiments let researchers determine the expression of tens of thousands of genes all at once, providing a molecular “fingerprint” of the tissue sample. Scientists then compare the fingerprint of one sample to that of

another — a prostate tumor to normal prostate, or aggressive breast cancer to non-aggressive breast cancer — to identify genes whose expression is higher or lower than “normal.” The idea is that those genes may contribute to the two tissues’ differences.

The mounds of data these experiments create — each identifying hundreds of gene candidates — can be difficult to sift through. But for Chinnaiyan and the research team, the ease with which the data is created meant that a wealth of information about cancers’ genetic profiles already existed, although not in a single form or place.

Answering some critics who claim that experimental differences make microarray data virtually impossible to compare, Pandey says that the difficulty actually supports their results. “If some people consider these sets to be so different as to be incomparable, then anything that does turn out to be common to all of them seems pretty likely to be real,” he suggests.

The researchers also validated their proposed cancer signature by examining data sets published after creation of the database, dubbed ONCOMINE. The same signature discriminated between cancer and normal tissue in seven of nine new data sets, including properly discriminating three types of cancer not used to create the database, the scientists report.

ONCOMINE connects the cancer microarray database to several sources of additional information, including the scientific literature, the Human Protein Reference Database and Online Inheritance in Man, the online catalog of all proven disease-gene connections. ONCOMINE is owned by the University of Michigan, and is available online to academic researchers free-of-charge following registration.

Authors on the report are Daniel Rhodes, Jianjun Yu, Radhika Varambally, Debashis Ghosh, Terrence Barrette and Chinnaiyan of the University of Michigan Medical School; Kalyan Shanker and Nandan Deshpande of the Institute of

Bioinformatics; and Pandey of Johns Hopkins. Pandey does not receive compensation for his role as scientific adviser to the Institute of Bioinformatics.

On the Web:

<http://www.pnas.org>

## WATERMELON, PACKS MORE THAN WE THINK!

By June Lay

Watermelon is a fruit that packs more than we may think, more in the way of nutritional value that is. It’s post July 4th, and summertime, and watermelon is a popular American summer fruit. Many of us (this included me once upon a time), think that watermelon is high in calories containing only our enemy sugar, and water, but, this sweet red fruit does pack more than we think!

Before we discuss the full value of watermelon, let’s look at just how much sugar and water it contains. One cup of diced watermelon is about 90% water, and contains 50 calories (doesn’t sound too bad to me). 44 of these calories do come from sugar, but let me say that this is a natural, healthy fruit sugar. If we remember our “Sugar, Not an Enemy” tip, we will remember that sugar is vital for our energy, and it is the sole source of fuel for our brain. Along with water and sugar, watermelon contains vitamin C while our cup has less than 1 g of fat, with no cholesterol.

Now, what else does watermelon have? Watermelon contains the phytochemical lycopene, one of our colorful disease preventing carotenoids! This time if we remember our “Tomato, a Superstar” tip, tomato was the leading source of lycopene when cooked (so much for the raw diet all the time?). Lycopene appears to be released from the plant cell wall and used by our body (defined as bioavailable) when sources such as the tomato are cooked. Unfortunately, we don’t always eat tomato sauce, or heat processed tomato juice, do we? Now, we have a study which has shown that raw watermelon unlike the raw tomato, contains a source of bioavailable lycopene! More about

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## FAST RISING PSA SIGNALS AGGRESSIVE DISEASE

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"This is something that is really urgently needed -- we need a way of judging the danger of a prostate cancer," said William J. Catalona, a prostate cancer specialist at Northwestern University who led the study. "This is the most powerful predictor we have."

The study authors suggest men get a baseline PSA test at age 35, then additional PSA tests once a year thereafter.

"While I recommend a biopsy with a PSA level of 2.5 (ng per milliliters) or higher, this study shows us that no single value of PSA is as important as the trend," Catalona said. "And the only way you can recognize a trend is if the testing is done early and every year."

Prostate cancer is the second most common cancer in American men. Despite substantial advances in recent years, some 82 men in the United States still die of the disease every day, according to an accompanying editorial in the journal. In the editorial, Mario Eisenberger and Alan Partin, prostate cancer experts from Johns Hopkins University, write that measures of PSA dynamics "may eventually be the key factor" in determining which men can safely try watchful waiting.

PSA is a protein produced by the cells of the prostate gland. The prostate-specific antigen test measures the level of PSA in the blood. When the prostate enlarges, PSA levels typically rise. The levels can rise due to cancer or benign conditions, according to the National Cancer Institute.

While PSA testing has become commonplace, physicians have been unclear how to interpret the results. In particular, they have been wrestling with what absolute number might predict the presence of cancer, D'Amico said.

The new study analyzed PSA data from 1,095 men, all approximately 65 years old, who had undergone a radical prostatectomy within about a month of their diagnoses. PSA levels were measured every six to 12 months both before and after surgery.

Men whose PSA levels increased by more than 2 nanograms per milliliter of blood during the year before being diagnosed had a higher risk of dying from prostate cancer within seven years, even if they underwent a radical prostatectomy. "There was a tenfold increased risk of death from prostate cancer if you went up by two points in a year" prior to diagnosis, D'Amico said.

Men with rapidly rising PSAs also were more likely to have tumors that were at more advanced stages. Five percent of them had cancer that had spread to their lymph nodes vs. only 0.7% of the others.

"For these men, who are otherwise in good health, watchful waiting may not be the best option," the researchers conclude.

"While some physicians counsel watchful waiting, the men I see in my office have the same attitude as women facing the possibility of breast cancer: they want it treated, they want it taken care of and they want it to be over," Dr. Catalona said. The lifetime risk of being diagnosed with prostate cancer -- 1 in 6 -- is higher than the 1-in-8 risk of breast cancer in women. "It's still a big problem and it kills a lot of men."

Robert Donnell, associate professor at the Medical College of Wisconsin and co-director of the prostate center at Froedtert Memorial Lutheran Hospital in Wauwatosa, agreed.

"PSA is a better indicator of what has happened than what will happen," Donnell said. "We can't predict whose PSA will rise

2 nanograms per milliliter per year, so watchful waiting becomes a gamble."

Other studies have found value in analyzing change in a man's PSA rather than establishing a cutoff point such as 2.5 or 4 as cause for concern, they write.

Such research is forming a growing body of evidence that may help fine-tune interpretation of the PSA test and make it a more useful tool for detecting prostate cancer and evaluating its seriousness, experts say.

"This study shows us that no single value of PSA is as important as the trend," Catalona said in a statement.

Surgery or local radiation may not be enough for men whose PSA levels are in the fast-rising group, D'Amico added. "They could have surgery but then expect to follow that with radiation and hormonal treatments," he added. Certainly "watchful waiting" would not be a good option.

What the study doesn't reveal is how to treat a man whose PSA levels rose less than two points in a year.

"Significant rises of more than two are ominous. Rises of less than that are still amenable to cure with local therapy [but] we don't know the lower threshold," D'Amico said.

Still, said Dr. Mark H. Kawachi, director of the Prostate Cancer Center at City of Hope Cancer Center in Duarte, Calif., the study does "help us refine the way we look at prostate cancer patients."

"Individualized treatment becomes the issue here," Kawachi said. "The exciting thing about this study is it comes at a time when chemotherapy for advanced prostate cancer is demonstrating bona fide benefit. So we do have options now, whereas two to three years ago we wouldn't have had very many options to even consider."

## COLIN POWELL URGES MEN TO DETECT PROSTATE CANCER EARLY

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And the younger you are, the more aggressively the cancer will grow, Powell said during a July interview on PBS' Tavis Smiley show.

African-Americans have to be more careful, and have more examinations on a regular basis to detect the disease as early as possible, Powell said. "That's just a fact of life."

"We are at a higher risk to prostate cancer than our white brothers," Powell said. "It's well-known. It's documented."

But, he said, all men are at risk.

Powell's experience bears out how elusive prostate cancer can be.

Referring to a test given routinely to men at about 50 and usually to African-Americans a few years earlier, Powell said that a test about six years ago showed that his PSA (Prostate Specific Antigen) level was high.

He had two biopsies in the late 1990s that did not detect cancer, he said. Last August, with the PSA level still elevated, he had a "very intrusive biopsy" at Walter Reed Army Medical Center and the tumor was found.

Out of 13 samples, only one had shown the cancer.

Powell elected surgery over radiation and other options.

"Nobody likes to have surgery," he said. "And, believe it or not, even though I am 67 years old, until that operation last December I had never spent one day or night in a hospital. I've been in remarkably good health."

Suddenly, to hear you have cancer and it's got to be removed "is a little unnerving," Powell said. "But you have got to face it."

## WATERMELON

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this Press Release from the USDA research agency titled "Watermelon Shows its Lycopene Stripes" appears in the June 2002 Agricultural Research Magazine. Here's just a small quote about how much lycopene watermelon contains from the USDA research team :

"Watermelon is fat free and is a source of vitamins A, B6, C, and thiamin. Studies have shown that a cup and a half of watermelon contains about 9 to 13 milligrams of lycopene. On average, watermelon has about 40 percent more lycopene than raw tomatoes. Red, ripe flesh is the best indicator of the sweetest and most nutritious watermelon, though it's hard to choose the ripest melon when it's uncut".

Do we need a quick refresher on the disease fighting merits of lycopene? Well, studies indicate that lycopene protects against cardiovascular disease, and certain types of cancer most notably prostate with some studies showing protective properties against breast, endometrium and lung cancers as well.

So, Watermelon definitely packs more than sugar and water. It packs a lot of Lycopene even when it's raw!

A cup of watermelon anyone?

## RETINOID-RELATED MOLECULE POTENTLY INDUCES APOPTOSIS IN PROSTATE CANCER CELLS

"Synthetic retinoid-related molecules, such as N-(4-hydroxyphenyl)retinamide (fenretinide) and 6-[3-(1-adamantyl)-4-hydroxyphenyl]-2-naphthalene carboxylic acid (CD437) induce apoptosis in a variety of malignant cells. The mechanism(s) of action of these compounds does not appear to

involve retinoic acid receptors (RARs) and retinoid X receptors (RXRs), although some investigators disagree with this view," scientists in England report.

"To clarify whether some retinoid-related molecules can induce apoptosis without involving RARs and/or RXRs," said R.G. Keedwell and coworkers, "we used 4-[3-(1-heptyl-4,4-dimethyl-2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-3-oxo-E-propenyl] benzoic acid (AGN193198) that neither binds effectively to RARs and RXRs nor transactivates in RAR- and RXR-mediated reporter assays."

"AGN193198 potently induced apoptosis in prostate, breast, and gastrointestinal carcinoma cells and in leukemia cells. AGN193198 also abolished growth (by 50% at 130-332 nM) and induced apoptosis in primary cultures established from prostatic carcinoma (13 patients) and gastrointestinal carcinoma (1 patient)," Keedwell reported.

"Apoptosis was induced rapidly, as indicated by mitochondrial depolarization and DNA fragmentation." The authors continued, "Molecular events provoked by AGN193198 included activation of caspase-3, -8, -9, and -10 (by 4 - 6 hours) and the production of BID/p15 (by 6 hours)."

Investigators concluded, "These findings show that caspase-mediated induction of apoptosis by AGN193198 is RAR/RXR-independent and suggest that this compound may be useful in the treatment of prostate cancer."

Keedwell and colleagues published their study in Cancer Research (A retinoid-related molecule that does not bind to classical retinoid receptors potently induces apoptosis in human prostate cancer cells through rapid caspase activation. Cancer Res, 2004;64(9):3302-3312).

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