CANADIAN PROSTATE CANCER SUPPORT GROUP

Newmarket, Ontario **Volume 12, Issue 5, January 15th, 2008**

**A support group that provides understanding,
hope and information to prostate cancer patients and their families**

Doctor Anthony Joshua, of Princess Margaret Hospital will be the guest speaker at our January 17th meeting. His talk will be quite different from the majority of previous speakers because he will be focussing on the clinical/research side of the battle to defeat prostate cancer. Dr. Joshua recently won an award for his groundbreaking study of telomeres and their role as indicators of the likelihood of an individual developing prostate cancer. A telomere is a segment of DNA that occurs at the ends of a chromosome and gives each one a fixed lifespan. According to Dr. Joshua, "the changes we see in telomeres seem to be one of the many new and emerging markers that may help us work out which men are at high risk of getting and dying from prostate cancer." Come out to the meeting, I'm sure you'll be glad that you did.

Meeting Date: **January 17th, 2008**

Place: **Newmarket Seniors Meeting Place**
474 Davis Drive, Newmarket

Time: **7:00 to 9:00 pm**

Speaker: **Dr. Anthony Joshua, PMH. Clinical Research**

Subject: **"Advances in the understanding and treatment of prostate cancer"**

Canadian Prostate Cancer Support Group,
Newmarket, Ontario. 905-830-0447
a member of the

Canadian Prostate Cancer Network

Assisted by the Canadian Cancer Society
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The Newmarket Prostate Cancer Support Group does not recommend products, treatment modalities, medications, or physicians. All information is, however, freely shared.

While we didn't have a speaker, plenty of other voices made our December meeting/party another great success. Executive member Bill Tuplin and the Upper Canada Cordsmen Choir entertained us with their annual Christmas concert and then led us in a rousing singalong. They continue to make our December meeting one of the biggest attended nights each year.
Because we don't have speakers notes for this edition of the newsletter, it gives us an opportunity to present information on some of the studies and research going on right now in the ongoing battle to defeat prostate cancer.

Aspirin could hinder prostate cancer therapy

By Liz Szabo, USA TODAY

Doctors are investigating whether low-dose aspirin could interfere with some prostate cancer treatments. Many older people take a daily baby aspirin to reduce their risk of a heart attack. In a letter published in the *New England Journal of Medicine*, doctors from Boston's Dana-Farber Cancer Institute and the University of Connecticut describe a study of men taking hormone therapy for prostate cancer.

Hormonal treatments suppress the testosterone that feeds prostate tumors, says Anthony D'Amico, a co-author of the letter and Dana-Farber's chief of genitourinary radiation oncology. But testosterone appears to play an important role in the way the body processes aspirin, D'Amico says. Without testosterone, even a small dose of aspirin can be too much for the body to handle. In this study, 37% of men on aspirin had to stop taking one of their hormone treatments — a drug called flutamide — because of abnormal liver test results, compared with 13% of men who weren't using aspirin.

Stopping hormones early is risky, D'Amico says, because it gives tumors a chance to grow. After following men for nearly eight years, he found that men who prematurely discontinued flutamide were 3.5 times as likely to die as those who completed all six months of treatment.

D'Amico suggests that men talk to their doctors about whether it's safe to stop taking aspirin for six months while being treated with hormones. But Otis Brawley, the American Cancer Society's chief medical officer, says it's too soon to change the way doctors treat prostate cancer patients, many of whom are older and at risk for heart disease. The issue is complex, because hormone therapy has been shown to increase the risk of heart disease. He says doctors need to study the drugs' relationship further in order to give the best advice.

Low Testosterone Might Shorten Men's Lives

TUESDAY, Nov. 27 (HealthDay News) — Men aged 40 or over with low levels of testosterone may be at increased risk of fatal heart attacks or death from any cause, a British study suggests. In fact, "The magnitude of the effect was very similar to that of [high] cholesterol or blood pressure," said lead researcher Dr. Kay-Tee Khaw, professor of clinical gerontology at the University of Cambridge School of Clinical Medicine. However, more work is needed to see whether testosterone supplements should be recommended for men with naturally low levels of the hormone, she said.

"We need to replicate these findings," Khaw said. "We hope we can entice other investigators to look at testosterone levels and see if these findings are confirmed."

Her team published the findings in the Nov. 27 issue of Circulation. The study included more than 11,600 men ages 40 to 79 who were free of known cardiovascular disease and cancer at the start of the trial. It was done because "there have been lots of studies suggesting that low testosterone may not be good for health," Khaw said. "So, we wanted to see if this could be demonstrated in a large population.

The men were divided into four groups based on their blood testosterone levels. Those men in the highest quarter of testosterone readings — with at least 19.6 nanomoles of the hormone per liter of blood — had a 41 percent lower risk of dying over 10 years than those in the lowest quarter of testosterone readings — less than 12.5 nanomoles of testosterone per liter of blood.

One major question is whether low testosterone is a risk factor itself or just a marker for other risk factors, said Dr. Victor Montori, associate professor of medicine at the Mayo Clinic in Rochester, Minn. He has done his own studies on testosterone replacement therapy. "It does not mean that replacing or normalizing levels of testosterone would reverse the outcome," he said. "There are other hormones in the blood that are related to other risk factors, such as diabetes and hypertension." In any case, a testosterone replacement regimen "would not be a walk in the park," Montori said. "It would be a major intervention."

According to Dr. Jorge Plutzky, director of the Vascular Disease Prevention Program at Brigham and Women's Hospital in Boston, the experience of women taking hormone replacement therapy (HRT) shows that hormonal regimens can have their dangers. Beginning in the 1990s, millions of older American women took HRT, which replaced two female hormones, estrogen and progestin. Early trials had indicated that the therapy might reduce the risk of cardiovascular diseases such as heart attack and stroke in older women. Instead, the Women's Health Initiative, a major study released in 2002, found that women taking HRT were at increased incidence of stroke, blood clots and breast cancer, noted Plutzky, who is also a spokesman for the American Cancer Society. HRT prescriptions dropped off precipitously after the study's release.

So, much more research is needed on the link between testosterone levels and mortality before doctors can recommend the regimen to men, Khaw said. Such studies might provide "insights and better understanding of disease mechanisms, such as how and why testosterone might be related to poorer health through, for example, insulin metabolism, lipid metabolism or inflammation," she said.

Potential Drug Target For Treatment-resistant Prostate Cancer Discovered

ScienceDaily (Jan. 1, 2008)

Scientists at Jefferson's Kimmel Cancer Center in Philadelphia have found that a signaling protein that is key to prostate cancer cell growth is turned on in nearly all recurrent prostate cancers that are resistant to hormone therapy. If the findings hold up, the protein, called Stat5, may be a specific drug target against an extremely difficult-to-treat cancer.

In addition, the researchers, led by Marja Nevalainen, M.D., Ph.D., associate professor of Cancer Biology at Jefferson Medical College of Thomas Jefferson University, also showed that the convergence of two biological pathways could be responsible for making such hormone-resistant prostate cancers especially dangerous. They have found that a synergy between Stat5 and hormone receptors in recurrent prostate cancer cells helps each maintain its activity. Dr. Nevalainen and her co-workers report their findings January 1, 2008 in the journal Cancer Research.

"These findings validate Stat5 as a potential drug target in prostate cancer, and in particular, in a form of prostate cancer for which there are no effective therapies," Dr. Nevalainen says.

Men with primary prostate cancer usually have either surgery or radiation, whereas subsequent disease is frequently treated by hormone therapy. But if the cancer recurs again, years later, it can be more aggressive and typically fails to respond to hormone treatment. In previous work, the researchers showed that when Stat5 is turned on in primary prostate cancer, men are more likely to have recurrent disease.

In the current study, the team examined human prostate cancer cells of 198 patients with prostate cancer recurrence. They found that Stat5 was active in 74 percent of all recurrent prostate cancers. Of these patients, 127 had been treated with androgen deprivation therapy. The researchers found Stat5 was active in 95 percent of these hormone resistant tumors, meaning it was more likely to be active if the patient had been treated with hormone deprivation therapy.

Dr. Nevalainen shows that Stat5 interacts with the androgen receptors and keeps them "transcriptionally active." Next, the scientists would like to conduct tests in animal models to see if this synergy promotes androgen-independent prostate tumor growth, and whether or not Stat5 synergizes with androgen receptors activated by adrenal androgens, which are present in the absence of testicular androgens during the hormone therapy of prostate cancer in patients. *Adapted from materials provided by Thomas Jefferson University.*

Hormone Therapy for Prostate Cancer Linked to Heart Risks

But researchers say more study is needed, and the therapy is valuable

TUESDAY, Oct. 9 (HealthDay News) — Prostate cancer patients receiving androgen-deprivation therapy, a common form of hormone treatment proven to slow tumor growth and prolong life, may face a nearly threefold higher risk of dying from heart disease, a new study suggests. The apparent danger results from a drop in testosterone levels that is central to androgen-deprivation therapy's (ADT) effectiveness at curbing prostate cancer, the study authors said. This drop in testosterone can provoke insulin resistance, leading to type 2 diabetes, as well as a gain in body mass, body fat and so-called bad cholesterol. Collectively, this group of problems is called the "metabolic syndrome," a condition long-associated with cardiac complications. "However, I think overall ADT does help people with prostate cancer, and until it's studied further this can't be considered proof that there's a connection between the cardiac effects and hormone therapy," said study author Dr. Henry K. Tsai, who throughout the study period served as a resident in training in the Harvard Radiation Oncology Program in Boston. "But patients need to think about being evaluated carefully by their doctor to see whether they're appropriate candidates for hormone therapy and be informed about the potential risks," Tsai added.

This new finding, published in the Oct. 17 issue of the Journal of the National Cancer Institute, follows research released in 2005 that highlighted ADT's link to an increased risk for bone fractures and osteoporosis. The new findings are based on an analysis of medical records and questionnaires completed by nearly 4,900 patients between the ages of 39 and 86 who had been diagnosed with localized prostate cancer between 1995 and 2004. All the patients had participated in a larger nationwide prostate cancer research project involving more than 13,000 men, during which all had indicated whether they had any preexisting medical complications in addition to cancer. Of the 4,900 patients, nearly 3,300 had undergone prostate removal surgery following diagnosis. The remainder underwent nonsurgical treatments, such as external beam radiation therapy; brachytherapy (involving the insertion of small radioactive pellets directly into the prostate); and/or cryotherapy (involving the freezing of tumor cells). In addition, 266 of those patients who underwent surgery and 749 of those receiving an alternate treatment also received androgen-deprivation therapy.

The patients were tracked for an average of about four years following the start of all treatments; the patients receiving ADT did so for an average of about four months.

Tsai and his colleagues found that patients over the age of 65 who had undergone both prostate removal surgery and ADT had a 5.5 percent increased risk of dying from a cardiac event within five years of starting the hormone treatment. This compared to a 2 percent greater risk among patients older than 65 who had surgery alone.

The "relative risk" jump was similar among younger patients. Those under 65 who had surgery and hormone therapy had a 3.6 percent greater risk of death from heart disease within five years, compared with a 1.2 percent risk among those undergoing surgery alone. ADT was not associated with any increased cardiac risk among patients undergoing any of the nonsurgical treatments.

An editorial accompanying the study calls for more research into the topic.

Jerome Seidenfeld and his colleagues at the University of Connecticut Health Center suggest that while Tsai's analysis of previously collected data raises an "interesting hypothesis," no definitive link to cancer risk can be proved until a clinical trial of prostate cancer patients currently undergoing hormone treatment is launched.

Tsai agreed. "I pretty much feel similarly," Tsai said. "The editorial emphasizes that this is a preliminary study, and clinical trials are the gold standard. And we need one to confirm our findings." Tsai, currently working as a radiation oncologist with Radiation Oncology Consultants in Princeton, N.J., said he doesn't want prostate cancer patients to view androgen-deprivation therapy with alarm. "I don't think patients should be afraid," he said. "This is just what I'd call emerging data, and while the relative increase in risk for heart disease is large, in absolute terms the risk is still very small." Dr. Nelson Neal Stone, a clinical professor of urology and radiation oncology at Mount Sinai School of Medicine in New York City, said the exact mechanism by which ADT might boost the risk for cardiac complications remains undefined, despite a widespread appreciation for the array of problems that accompany the metabolic syndrome.

In that light, he suggested that physicians should target the onset of the life-threatening syndrome as well as the life-prolonging treatment. The message is that we need to start paying attention to our patients' general health when we put them on hormonal therapy," he said. "And perhaps we should be putting them on a diet to control for the potential side effects of the therapy, and the serious impact it can have on their health." "We can't take away the hormones altogether because there's a major benefit to that treatment," Stone added. "But we need to develop a good strategy for dealing with the negative consequences that occur."

PSA Is Poor Predictor Of Lethal Prostate Cancer

ScienceDaily (Apr. 9, 2007)

The amount of prostate-specific antigen (PSA) in a man's bloodstream at the time of his prostate cancer diagnosis or its rate of change over the course of the disease does not adequately predict lethal prostate cancer, according to a study in the April 4 Journal of the National Cancer Institute.

Although men with untreated localized prostate cancer have high long-term survival rates, many patients undergo treatment anyway. In order to avoid unnecessary treatment, researchers want to identify methods to determine which patients will develop lethal prostate cancer. The rate of increase of PSA—a protein produced by the prostate—before prostate cancer treatment has been associated with the patient's prognosis, which suggests that early measurements of PSA may predict the behavior of the tumor.

To assess the accuracy of using PSA to predict prostate cancer outcome, Katja Fall, M.D., Ph.D., of the Karolinska Institute in Stockholm, and colleagues analyzed the rate of change of PSA levels in 267 men from Sweden, Finland, and Iceland who were diagnosed with early localized prostate cancer between 1989 and 1999. The researchers recorded the PSA levels for the first two years after diagnosis to capture the patients' early PSA patterns. The men in the study received no curative treatment for the first two years but were closely watched for signs of progression, which is called watchful waiting.

At the end of the follow-up in December 2003, 34 patients had died from prostate cancer, and 18 had developed metastatic prostate cancer but were still alive. Although initial PSA values and the rate of change were associated with later development of lethal prostate cancer, they were not accurate enough to predict lethal cancer.

"We conclude that PSA measurement is associated with prostate cancer prognosis and continues to be an important monitoring tool," the authors write. "However, early PSA characteristics perform poorly in distinguishing those who develop a lethal prostate cancer from those at low or no risk of disease progression. Therefore, better decision tools are needed for active monitoring of patients with early disease."

In an accompanying editorial, Dipen Parekh, M.D., of the University of Texas Health Science Center at San Antonio, and colleagues compared the results of this new study with their own work and found consistent results regarding PSA, as well as other measures that were related to prostate cancer risk. "These data demand that clinical trials commence now to examine surveillance strategies to help patients and their physicians identify and treat tumors that will otherwise be life threatening and to carefully follow those that will not. Our limited health care resources and the quality of life of an enormous number of men will benefit from this for decades to come," the authors write.

Article: Fall K, Garmo H, Andrén O, Axelson AB, Adolfsson J, Adami HO, Johansson JE, Holmberg L. Prostate-Specific Antigen Levels as a Predictor of Lethal Prostate Cancer. J Natl Cancer Inst 2007; 99: 526-532

Adapted from materials provided by Journal of the National Cancer Institute.

Don't forget to send in your questionaire

We need your response to the questionnaire we sent you with last months newsletter. It helps us to make decisions on speakers for each meeting and content for our newsletter. And most important whether you would like to continue getting the newsletter.
If you have misplaced it, or don't recall receiving it, give us a call and we'll send you another one.

Speakers for our 2008 meetings. Mark these dates on your calendar

- **January 17th, Dr. Anthony Joshua, PMH. Clinical Research**
- **February 21st Dr. Casey, Urologist,**
- **March 20th Dr. Juanita Crook, Princess Margaret Hospital**
- **April 17th Durhane Wong-Reiger, Pres. and CEO. Optimizing Health Org.**
- **May 15th Dr. Andrew Mather, PMH. on Depression**
- **June 19th Jerome Green, Urologist, Southlake Cancer Centre**

Pomegranate Juice Helps Keep PSA Levels Stable In Men With Prostate Cancer

ScienceDaily (Jul. 2, 2006

Drinking an eight ounce glass of pomegranate juice daily increased by nearly four times the period during which PSA levels in men treated for prostate cancer remained stable, a three-year UCLA study has found.

The study involved 50 men who had undergone surgery or radiation but quickly experienced increases in prostate-specific antigen or PSA, a biomarker that indicates the presence of cancer. UCLA researchers measured "doubling time," how long it takes for PSA levels to double, a signal that the cancer is progressing, said Dr. Allan Pantuck, an associate professor of urology, a Jonsson Cancer Center researcher and lead author of the study.

Doubling time is crucial in prostate cancer, Pantuck said, because patients who have short doubling times are more likely to die from their cancer. The average doubling time is about 15 months. In the UCLA study, Pantuck and his team observed increases in doubling times from 15 months to 54 months, an almost four-fold increase.

"That's a big increase. I was surprised when I saw such an improvement in PSA numbers," Pantuck said. "In older men 65 to 70 who have been treated for prostate cancer, we can give them pomegranate juice and it may be possible for them to outlive their risk of dying from their cancer. We're hoping we may be able to prevent or delay the need for other therapies usually used in this population such as hormone treatment or chemotherapy, both of which bring with them harmful side effects."

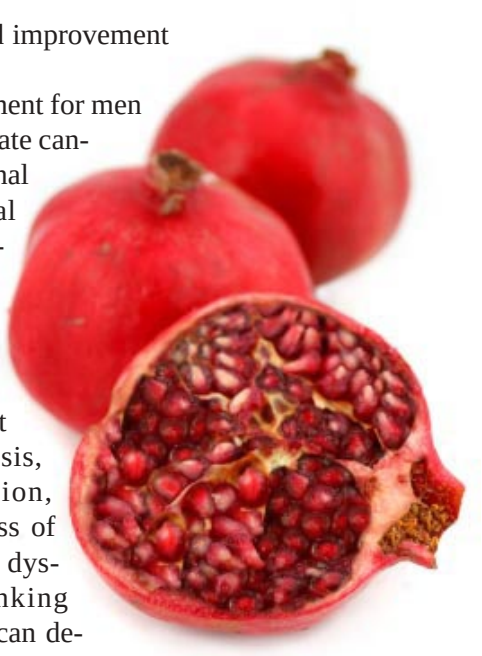
The study appears in the July 1 issue of Clinical Cancer Research, the peer-reviewed journal of the American Association of Cancer Research.

"This is not a cure, but we may be able to change the way prostate cancer grows," Pantuck said. "We don't know yet the specific factors behind this response - that's our next step in this research. We want to find out what cell signaling pathways might be affected, what is happening to keep PSA levels stable."

Pomegranate juice is known to have anti-inflammatory effects and high levels of anti-oxidants, which are believed to protect the body from free-radical damage. It also contains poly-phenols, natural antioxidant compounds found in green tea, as well as isoflavones commonly found in soy, and ellagic acid, which is believed to play a role in cancer cell death.

"There are many substances in pomegranate juice that may be prompting this response," Pantuck said. "We don't know if it's one magic bullet or the combination of everything we know is in this juice. My guess is that it's probably a combination of elements, rather than a single component."

The levels of PSA in men immediately following treatement should be undetectable, Pantuck said. If PSA can be detected, it's an indication of an aggressive cancer that is likely to progress. The men in Pantuck's study all had detectable PSA following treatment. Of the 50 men enrolled, more than 80 percent experienced improvement in doubling times.



Conventional treatment for men with recurrent prostate cancer includes hormonal therapy, a chemical castration which removes testosterone from the system. Men treated with hormonal therapy can experience hot flashes, osteoporosis, fatigue, depression, muscle wasting, loss of libido and erectile dysfunction. If drinking pomegranate juice can delay or prevent the need for hormonal therapy, patients would experience a better quality of life for a longer time, Pantuck said.

The patients in Pantuck's study experienced no side effects and none of the participants had cancers that metastasized during the study.

Pantuck, along with UCLA colleagues including Dr. Arie Belldegrun, professor and chief of urologic oncology, and Dr. David Heber, professor and director of the Center for Human Nutrition, first began research on pomegranate juice in prostate cancer about six years ago, conducting preclinical research in cell cultures and in animals. Those studies showed pomegranate juice slowed the growth of prostate cancer, Pantuck said.

The data was impressive enough to test pomegranate juice in clinical trials, Pantuck said. To confirm their findings, a larger Phase III study, headed up by UCLA, will be conducted at ten centers across the county. UCLA is the only Southern California center involved in the study. For more information on the Phase III trial, call (310) 825-5538.

Pantuck said he has men on the study more than three years out who are not being treated for prostate cancer other than drinking pomegranate juice and their PSA levels continue to be suppressed.

"The juice seems to be working," he said.

The study, performed at the Clark Urology Center, was funded by the Stewart and Lynda Resnick Trust. The Resnicks own POM Wonderful, which provided the juice from the Wonderful variety of pomegranate for the study.

Adapted from materials provided by University of California