



PROSTATE CANCER *HOT SHEET*

Us Too! INTERNATIONAL

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BIOCHEMICAL RELAPSE IN PROSTATE CANCER: Is PSA PROMOTING STRESS AND ANXIETY? Susan Slovin, MD, PhD

Introduction

Standard therapies for the primary treatment of localized prostate cancer routinely include surgery (prostatectomy), radiation therapy through brachytherapy (interstitial seed implants), or 3-dimensional conformational radiation therapy. In patients treated with surgery, prostate-specific antigen (PSA), a biomarker detected in the blood, should decline to undetectable levels, compared with a nadir value of < 0.5 for patients who are treated with radiation therapy. Although “cure” is the word that most patients want to hear at the end of their therapy, depending on the level of aggressiveness of the tumor (Gleason grade), pretreatment values of PSA, and the extent of disease at time of diagnosis, it is not uncommon for prostate disease to recur anytime (from several months to even a decade later) in the form of a rising PSA — an event called biochemical relapse.

Recent Surveillance, Epidemiology, and End Results (SEER) program data^[1] have shown that there is a decline in mortality due to early disease detection through PSA screening and digital rectal exams. However, we are now identifying large numbers of previously treated patients at earlier time points and at even younger ages (sometimes in their thirties) who come to observation with rising PSA values in the absence of disease at conventional radiographic exams, such as bone scan and computed axial tomography (CAT) scan. This

new subgroup of men who have rising PSA values are the most difficult to treat, as there is no standard management strategy for patients who have only a rising biomarker.

PSA: Promoting Stress and Anxiety?

The detection of rising PSA values months or years following primary treatment causes significant stress among patients. They often run from physician to physician, seeking suggestions, only to realize that there is not a solution. When asked what a rising PSA means, many patients will say that it means that the disease has returned and that they are “on a timer” toward disaster, with the PSA heralding disease acceleration. Others are of the opinion that if the PSA goes from 2 to 4, it corresponds to a doubling in the number of cancer cells. Either way, this population suffers from high levels of anxiety, with many people claiming that PSA stands for “Promotes Stress and Anxiety!”

Observation

How does a physician address this problem, and how does a patient know what to do when there is no accepted standard of care? Patients are often confused about how to proceed, and there is true discordance as to how to approach this clinical condition. Prostate cancer is a dynamic process in which the disease evolves from one clinical state to another; that is, from localized disease to a stage where it is treated, then in some cases to relapse or to clinical progression in soft tissue or bone.^[2] There are statistical models^[2] that can predict the likelihood of

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EARLY PROSTATE CANCER TREATMENT SAVES LIVES

A large, rigorous study shows that treating early prostate cancer with surgery rather than waiting to see if it grows reduces the chance of dying from the disease.

The issue of treatment is controversial because diagnostic tests cannot tell which tumors will grow so slowly that they never become lethal. Furthermore, while surgery is the most common form of treatment, removing the prostate often causes incontinence and impotence.

In the latest study, published in the September 12, 2002 issue of the *New England Journal of Medicine*, Scandinavian researchers followed 695 patients under age 75 for an average of six years though the year 2000. About 9 percent died of prostate cancer in the “watchful waiting” group, compared to 5 percent in the group that had surgery — so surgery cut the mortality risk almost in half.

Surgery also reduced the risk of metastases, or distant spread, of the cancer. Metastases developed in 35 treated men, compared to 54 in the monitored group.

“This shows, loud and clear, that treatment saves lives,” said Patrick Walsh, director of urology at Johns Hopkins University. In an editorial in the same journal, he called the study a “landmark.”

“The key finding is that prostate cancer mortality is cut in half,” says Dr. Tomasz M. Beer, assistant professor of medicine at Oregon Health and Science University.

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PROSTATE CANCER NEWS YOU CAN USE

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NEW TEST HIGHLIGHTS PROSTATE CANCER AWARENESS WEEK

The prostate specific antigen (PSA) test, already the standard for determining whether a man is predisposed toward contracting prostate cancer, has a new, improved version. It's the complexed PSA test (cPSA), and it was used on thousands of U.S. men during the week of Sept. 15-22, 14th Annual National Prostate Cancer Awareness Week, an event in which it was hoped that more than 100,000 men would be given the cPSA test at 500 hospitals free or at a nominal charge. The event is organized by the the Prostate Cancer Education Council, a non-profit umbrella organization whose goal is providing information about the dangers of prostate cancer. The cPSA test was developed in clinical trials during the past two years and is about 4 percent to 5 percent more accurate, the results show. According to an article in the Urology Times, the researchers believe the cPSA test can replace the PSA test at all levels. "cPSA outperforms tPSA over all PSA ranges and can be used as a first-line test for prostate cancer detection," say study co-author Dr. Herbert Lepor, Spatz chairman of urology at New York University School of Medicine.

MORE THAN 70 PERCENT OF ADULTS WITH CANCER USE ALTERNATIVE THERAPIES; NEARLY ALL REPORT IMPROVED SENSE OF WELL-BEING

More than 70 percent of adult cancer patients in western Washington use alternative therapies and almost all report substantial improvements in well-being as a result of using alternative medicine, according to a Fred Hutchinson Cancer Research Center survey. The results of this survey - the first population-based study of its kind to look at predictors, motivators and costs of different types of alternative-medicine use in adults with cancer - appeared in *The Journal of Alternative and Complementary Medicine: Research on Paradigm, Practice and Policy*. To obtain a copy of the paper, "Types of Alternative Medicine Used by Breast, Colon, and Prostate Cancer Patients: Predictors, Motives and Costs" by Patterson et al., *The Journal of Alternative and Complementary Medicine: Paradigm, Practice and Policy*, Vol. 8, No. 4, 2002, pp. 477-485, visit the journal's Web site at www.liebertpub.com/acm or contact Vicki Cohn - vcohn@liebertpub.com

INNOVATIVE MICROSURGERY REDUCES RISK OF INCONTINENCE, IMPOTENCE

Doctors at Jersey Shore Medical Center in Neptune, New Jersey, are among the first in the country to use an innovative new procedure to reduce or eliminate unwanted side effects of prostate removal. "A radical prostatectomy with a sural nerve graft - a procedure being performed at only a few select hospitals like Baylor Medical Center in Texas and Sloan Kettering Cancer Center in New York, and now at Jersey Shore Medical Center - can help reduce certain patients' risk of becoming impotent by 50%," Matthew S. Tobin, MD at Jersey Shore said. Due to the delicate location of the prostate region, the prostatectomy sural nerve grafting procedure is extremely delicate and complex. According to Tobin, it usually takes between 3 and 12 months after prostate cancer surgery to determine the effect of the procedure on erectile function - urinary control often returns sooner.

PRIMARY TUMOUR CONTROL MAY IMPACT ULTIMATE OUTCOME

In metastatic prostate cancer, the main treatment is hormonal cancer and the primary tumour is rarely treated. Research in other cancer types has shown that controlling the primary neoplasm affects survival. Men with a previous history of radical prostatectomy had a 30 per cent decrease in mortality risk compared with those who had no earlier definitive treatment. In comparison, there was a 22 per cent increase in the risk of death among those who had previously received radiotherapy. Researchers said that one possible explanation for the poor prognosis in patients who had prior radiation therapy is that this treatment might change the primary tumour to a higher-grade tumour. A likely explanation for the decrease in mortality risk in those who had a prostatectomy is that metastatic foci can develop from the primary tumour as well as other metastases, said the study authors. Reference: Thompson et al, *Journal of Urology* 2002;168:1008-1012

MAYO CLINIC SURGEONS DIRECT ROBOTIC 'HANDS' TO PERFORM SURGERY

For the first time, surgeons at Mayo Clinic in Rochester, Minn., can

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perform complex, yet minimally invasive surgery by directing robotic "hands" to assist in delicate surgery. The surgeon's finger motions, conveyed through sophisticated joy sticks, direct the minute maneuvers carried out by two robotic hands holding surgical instruments. The surgeon views the surgery on a computer screen, which shows an enlarged and three-dimensional view of the surgical area. The images are transmitted by a tiny camera with multiple lenses, which is attached to a third robotic hand. "This technology enhances a surgeon's skills, making it easier to do more complex surgeries laparoscopically — that is with incisions as small as one centimeter," says Michael Blute, M.D., a urologist at Mayo Clinic. "Patients who have laparoscopic surgery, rather than open surgery, often recover more quickly and return to their normal activities sooner," says Dr. Blute.

BETTER PROSTATE CARE

Urologic oncologist Timothy Wilson, M.D., of City of Hope Medical Center in Los Angeles, says, "If men could find a simple way of testing and screening for prostate cancer that involves really very little pain and discomfort, they'd be much more willing to undergo it." A test is being developed that checks for changes in DNA. In a study

of 30 patients, the DNA test detected one-third of the cancers missed by a biopsy. For patients who are not cancer-free, medical oncologist George Wilding, M.D., hopes the drug Panzem will help. "It could be an alternative for patients that would be less toxic, more convenient, and still control their cancer," says Dr. Wilding, of the University of Wisconsin Medical Center in Madison. Panzem works by cutting

off blood supply to tumors. Researchers at the University of Virginia are hoping to get FDA approval soon for the DNA detection method. The drug Panzem is also being studied for the treatment of breast cancer and multiple myeloma. Note: Researchers are no longer enrolling new patients in the Panzem/prostate cancer trial. For more info: Cancer Connect c/o University of Wisconsin Comprehensive Cancer Center 600 Highland Avenue Madison, WI 53792 (800) 622-8922 uwccc@uwccc.wisc.edu

BASEBALL HALL OF FAME YOGI BERRA TEAMS UP TO PROMOTE PROSTATE CANCER EDUCATION AND AWARENESS

Baseball legend and Hall of Fame member Yogi Berra helped to launch the second annual "Screen, Stage and Support" campaign to promote prostate cancer education and

screened to detect the presence of cancer, the need to gain a clear assessment of the stage of the disease prior to undergoing treatment, and the vital role that support from family, friends and patient organizations plays in recovery. The program highlights the importance of early detection (Screen), proper staging and diagnosis (Stage) and the need to support people living with prostate cancer through education to help them make informed treatment decisions (Support).

ULTRASOUND FOR PROSTATE CANCER

A new procedure could be easier on men being treated for prostate cancer. The procedure uses 3-D technology and doctors say it's painless and bloodless. Urologist Michael Koch, M.D., is studying high intensity focused ultrasound, or HIFU, to treat prostate cancer.

HIFU is 10,000 times more powerful than a regular ultrasound. "HIFU is unique, though, that because it's administered transrectally, it doesn't really cause any discomfort at all," Dr. Koch, of Indiana University in Indianapolis, says. HIFU destroys the tissue by heating it up. European research on HIFU shows promise. Dr. Koch says, "In those studies, they found

that it has an effectiveness that's probably comparable to radiation therapy. It may or may not be comparable to surgery." For more information: Mary Hardin Indiana University School of Medicine 1110 W. Michigan, LO 401 Indianapolis, IN 46202 (317) 274-7722 - www.iupui.edu e-mail: mhardin@iupui.edu



Us Too! at the NASDAQ Promoting Prostate Cancer Awareness

awareness. Berra teamed up with Cytogen, the American Cancer Society, Us Too! International, and Progenics Pharmaceuticals in a special event at the NASDAQ MarketSite. Screen, Stage and Support was first introduced during Prostate Cancer Awareness Month 2001 in an effort to help more people focus on three of the most critical and overlooked components of prostate cancer treatment — the need to be

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HEART DISEASE GENE LINKED TO PROSTATE CANCER

Researchers at Johns Hopkins, Wake Forest, and The National Human Genome Research Institute have implicated mutations in a "heart disease gene" in hereditary prostate cancer. The findings, which offer new evidence that at least some cases of prostate cancer may begin with an infection and inflammatory response, were published online September 16, 2002, in *Nature Genetics*.

The gene, called macrophage scavenger receptor-1 (MSR1), was identified more than 20 years ago as a factor in plaque formation in arteries, a process that contributes to coronary artery disease, or so-called hardening of the arteries. MSR1 helps immune system cells called macrophages clean up cellular debris from bacterial infections and damaged fats or lipids. Macrophage activity has been known to increase in the early stages of prostate cancer, and the Hopkins investigators suspected that some MSR1 mutations might inhibit the ability of macrophages to clean up properly after prostate infections, producing inflammatory lesions that are often markers of prostate cancer.

This is the first time that MSR1 has been linked to cancer, and it may tie infections and similar environmental exposures to cancer of the prostate in a way that we haven't thought about before, says William B. Isaacs, Ph.D., professor of urology and oncology at the Brady Urological Institute and Kimmel Cancer Center at Johns Hopkins.

Hunting for gene mutations that increase one's risk for prostate cancer, researchers screened 159 families with hereditary prostate cancer and found seven different mutations in the MSR1 gene in 13 families or about eight percent of the hereditary prostate cancer families studied.

To compare the impact of this gene in men with non-hereditary sporadic prostate cancer, the researchers screened another 731 men, 365 with prostate cancer and 366 without. Overall, the research team found that

MSR1 mutations were about seven times more common in men with prostate cancer than in those without. Mutations were found in 12.5 percent of African American men with prostate cancer as compared to 1.8 percent without the disease. In men of European descent, 4.4 percent of men with prostate cancer and less than one percent without prostate cancer had MSR1 mutations. "This genetic evidence suggests that MSR1 may play an important role in prostate cancer susceptibility in both African American men and men of European descent," says Jianfeng Xu, M.D., Dr. PH, of the Center for Human Genomics at Wake Forest.

Isaacs and colleagues will conduct additional studies to uncover the pathway that the MSR1 gene controls and confirm the prevalence of MSR1 mutations in larger studies.

The research was funded by the National Cancer Institute, the Department of Defense, CaPCURE, Fund for Research and Progress in Urology, and the William Thomas Gerrard, Mario Anthony Duhon, Jennifer and John Chalsty Professorship in Urology.

NOVEL GENE PRODUCT FACILITATES SUICIDE GENE TRACKING IN MALE CANCERS

Medical researchers at the University of California School of Medicine in Los Angeles have discovered a novel gene product that enables doctors to track prostate cancer suicide gene therapy with a noninvasive imaging technique.

The gene product is sr39tk, a mutant of the herpes simplex virus thymidine kinase (HSV1-tk) reporter gene. Allan J. Pantuck and colleagues in the Departments of Urology and Molecular and Medical Pharmacy say sr39tk is useful for visualizing the by-products of intratumoral suicide gene activity with positron emission tomography, a noninvasive procedure that detects metabolic activity.

The investigators think the molecular imaging model would enable physicians to better evaluate prostate cancer gene therapy dynamics, thus

enhancing treatment regimens and patient safety.

"The androgen independent, metastatic prostate cancer cell lines CL1 and CL1-GFP were stably transfected with the mutant HSV1-tk gene pcDNA3.1/pCMV-sr39tk, which has increased ability to phosphorylate penciclovir," described Pantuck and coauthors.

The researchers examined thymidine kinase enzymatic activity in cultured cells. They also implanted severe combined immunodeficient (SCID) mice with sr39tk-transfected (CL1-SR39) or nontransfected CL1 cells, exploring imaging capacity with a micro-PET rodent PET scanner.

"CL1-SR39 thymidine kinase enzyme activity was greater than twice the activity of the glioma cell line C6-SR39 control and above the threshold necessary for micro-PET detection," the team said.

Both CL1 and CL1-SR39 tumors in implanted mice could be detected with the micro-PET scanning system, and selective monitoring for CL1-SR39 with fluorodeoxyglucose and 18F-penciclovir yielded positive results, according to Pantuck and coauthors (CL1-SR39: A noninvasive molecular imaging model of prostate cancer suicide gene therapy using positron emission tomography. *The Journal of Urology*, September 2002;168(3):1193-1198).

Pantuck's group evaluated the animals for both systemic and tumoral effects of transgene activity by injecting the animals with adenovirus encoded for the sr39tk gene under control of the cytomegalovirus promoter (Ad-CMV-HSV1-sr39tk). They determined that systemic or intratumoral injections of the adenovirus led to transgene leakage and a great deal of sr39TK protein expression within the liver.

Using sr39tk with PET imaging to track prostate cancer suicide gene therapy is a viable option for monitoring therapeutic efficacy and side effects, Pantuck and colleagues indicated. The technique could be extended for use in exploring the effects of new drugs in prostate cancer animal models and for

evaluating the safety and effectiveness of experimental gene therapies used in clinical trials, they predicted.

The corresponding author for this study is Allan J. Pantuck, Department of Urology, University of California School of Medicine, Los Angeles, CA 90095, USA.

Key points reported in this study include:

- * A herpes simplex virus thymidine (HSV1-tk) mutant gene product sr39tk enables selective imaging of prostate cancer cells treated with suicide gene therapy
- * Imaging with sr39tk suggests transgene expression after suicide gene therapy delivery extends to liver cells
- * The new sr39tk molecular imaging model could be used for monitoring experimental drugs used in animals models and gene therapies used in clinical trials.

BIOCHEMICAL RELAPSE

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progression to the next stage.

It is important to note that progression of disease due to prostate cancer will be in competition with other noncancer-related morbidities to which the patient may ultimately succumb. Which will kill the patient first — cancer or other medical problems such as stroke, heart disease, diabetes, or hypertension — is the question. Therefore, for patients who have no demonstrable disease but only a rising PSA, it may be reasonable “to wait and observe” until the PSA increases at a higher rate or clinical symptoms develop, given that the chance of dying from other diseases is much greater than the risk from the cancer itself.

Diagnostic Iter

All patients with rising PSA values following primary therapy should have their PSAs checked to confirm the rise. Confirmatory tests should be done at the same institution to

ensure consistency. In addition, it is reasonable to have a bone and CAT scan of the abdomen and pelvis to look for recurrence of disease. Another instrument to look for recurrent disease, particularly in those patients who have undergone surgery, is magnetic resonance imaging (MRI) with an endorectal probe. This MRI, which focuses on the prostate with a rectal probe, allows visualization of the area of prostate left behind following surgery. This “bed” is a common site for disease recurrence, particularly in those patients whose pathology specimens revealed disease approaching the capsule or disease involving the surgical margins.

The presence of disease at these sites often means that there may have been microscopic extension of the tumor well beyond the prostate. If disease is seen in the prostate bed, radiation therapy is a reasonable option. Other tests, such as ProstaScint scans, are used to look for occult disease. However, the ProstaScint test, which employs a monoclonal antibody directed to a molecule related to PSA called prostate-specific membrane antigen, is often too sensitive and can yield false positive results.

Following the PSA Trend: Risk Prognostication

Once these scans are performed, it is imperative to evaluate the PSA values for a trend. Several studies^[3,4] have sought to clarify the impact of rising PSAs based on pretreatment characteristics (ie, Gleason grade, pretreatment PSA, and time to PSA recurrence after primary therapy). It has been shown that if the Gleason grade is 8 or greater, if the PSA recurs within 2 years of primary treatment, or if the doubling time of the PSA is less than 6 months with a slope of > 0.15 , these patients are at risk of radiographic recurrence. These patients should be identified early and directed to standard therapy such as hormonal treatment, if appropriate. The problem that often occurs is that patients assume that these indicators mean that they will die. It is imperative to note that this is clearly not the case, and that these values tell us who is at high

risk at some unknown time in the future.

Early identification of patients at high risk, known as risk prognostication, should be done at the time of diagnosis. By identifying those patients with high-grade Gleason scores and PSAs > 20 at diagnosis, we can try to treat them with more aggressive regimens so that the interval to either biochemical (PSA) or radiographic recurrence can be delayed. It is also a future goal to find other, more specific indicators that can help to identify aggressive tumors and patients at high risk.

How To Proceed?

So how should we proceed? Let us assume that a patient comes in with a rising PSA after either radiation or surgery, and he has no evidence of disease recurrence on any type of scan. What are the options? Many! It is not unreasonable for a patient to undergo expectant monitoring, with bone and CAT scans or MRI being performed every 4-6 months. There is no added risk of radiation exposure or development of additional malignancies by undergoing scans on a routine basis. It is also important to remember that rising PSA values may not correlate with disease progression as seen on a scan.

If the PSA velocity is greater than 6 months, it is not unreasonable to monitor the patient closely every 4-6 months with routine PSA and digital rectal exam. Inherent in this approach is modification of dietary habits, with avoidance of red meat, ham, pork, veal, hamburgers, hot dogs, and cheese. Fish, chicken, white meat turkey, fruits, vegetables, and low-fat cheeses are fine. Of interest, it is more than anecdotal to see the PSA modulated and stabilized by just a change in diet with accompanying weight loss.

If the PSA is doubling or tripling in less than 6 months with a steep slope, combined androgen blockade or investigational protocols with vaccine or other growth factor inhibitory agents may be

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NEWS YOU CAN USE

(continued from page 3)

AS CANCER PROGRESSES, PROTEIN LEVELS SOAR

A protein with an intriguing connection to the gene for Huntington disease could help physicians diagnose and more effectively treat patients with two of the most common and deadly forms of cancer, according to a new University of Michigan study. Absent in normal prostate and colon epithelial cells, but found in large amounts in prostate, colon and other tumor cells, it is called huntingtin interacting protein or HIP1. The protein has never before been associated with any type of cancer. "Anytime you find a true marker for cancer, it's surprising," said Theodora S. Ross, MD, PhD, an oncologist at U-M's Comprehensive Cancer Center and assistant professor of internal medicine in the U-M Medical School. "But HIP1 also is unusual, because it seems to be such a strong prognosticator, especially for prostate cancer." Results of U-M research on HIP1's relationship to human prostate and colon cancer were published August 2002 in the Journal of Clinical Investigation.

POSSIBLE NEW DRUG FOR CANCER

An experimental drug called 2C4 slows tumor growth in both breast and prostate cancer tumors in mice, according to a new study. As a result of this research, the drug is currently being tested in humans. In one study, researchers found 2C4 blocked signaling activity in prostate tumors grown in mice and significantly reduced tumor growth. Researchers found 2C4 prevented tumor growth in the majority of mice who did not respond to Herceptin. Researchers say if this is proven true in humans, the drug could be beneficial for many breast cancer patients. SOURCE: Cancer Cell, 2002;2:127-137

PESTICIDES LINKED TO

PROSTATE CANCER IN FARMERS

Chemical pesticide use and heredity may work together to increase farmers' risk of developing prostate cancer, a National Cancer Institute (NCI) researcher says. Michael Alavanja of the NCI told a meeting of pest control officials that exposure to certain pesticides increases the risk farmers of developing the disease,

as does a family history of prostate cancer. He also said the preliminary results of the ongoing, long-term study suggest that the two factors may work together to increase risk. Research has established that occurrence of prostate cancer is higher than normal among farmers even though they generally suffer from lower rates of all other types of cancer, says Mr. Alavanja. Now-banned chlorinated pesticides, such as DDT, appear to cause a statistically significant increase in the risk of prostate cancer among the subjects. In addition, the study finds that exposure to high levels of methyl bromide also cause a significant increase in the risk of prostate cancer. Mr. Alavanja says methyl bromide was the only individual chemical of the 50 examined to demonstrate a "significant exposure response pattern." The study also found that farmers with a family history of prostate cancer had an even greater risk of developing the disease when exposed to methyl bromide. Furthermore, he says a family history of prostate cancer "appears to significantly modify the risks among those using several widely used insecticides," including chlorpyrifos, coumaphos, fonofos, phorate and permethrin.

RACE GAP FOR PROSTATE CANCER SURVIVAL CLOSING

Black American men have been less likely than white Americans to survive prostate cancer but the results of a new study suggest that this racial survival gap may be narrowing. In a study of more than 1,000 men with prostate cancer who had their prostates removed during the 1990s, men treated during the second half of the decade were more likely to survive and be cancer-free than those treated before 1996. Survival improved in both races but to a greater degree in blacks than in whites. The study, by the Wayne State University in Detroit, Michigan, is reported in The Journal of Urology 2002;168:479-482.

INTERNAL ILIAC LYMPH NODE DISSECTION "ESSENTIAL" FOR REPRESENTATIVE STAGING

Improvements in prostate cancer detection and in preoperative staging has led to a reduction in the incidence of lymph node metastases diagnosed

in patients with localized prostate cancer. In turn, this has called into question the need for systematic lymph node dissection. Dr Pia Bader and colleagues at the University of Bern aimed to determine the extent of lymph node dissection necessary to avoid under staging prostate cancer. All patients who had undergone radical prostatectomy between 1989 and 1999 and who had clinically organ-confined prostate cancer, had no history of hormonal treatment, negative preoperative staging computerized tomographies and bone scans were evaluated prospectively. The number and location of lymph node metastasis were determined for each of the 365 patients by performing a meticulous dissection along the external iliac vein, obturator nerve and internal iliac vessels. The median number of nodes removed was 21 with 24 per cent of patients found to have node-positive cancer. In 58 per cent of these cases the internal iliac nodes and other lymph nodes were positive, while 19 per cent had positive internal iliac nodes alone. No preferential site of lymph node metastases was found - there were no obvious sentinel lymph nodes and no consecutive pathway for metastasis was found. Based on their findings, Dr Bader and colleagues recommend that the internal iliac nodes always be sampled to ensure adequate staging. "Without dissection of the internal iliac lymph nodes a fifth of the lymph node positive cases would be under staged and more than half would be left with diseased nodes," they explained. Reference: Bader et al, Journal of Urology 2002;168:514-518

OUTSMARTING CANCER WITH FOLATE THE SATURDAY EVENING POST - SEPTEMBER 02, 2002

Q: What forms of cancer does vitamin-based anticancer therapy appear effective in treating?

A: The key is that the cell must express the protein called the folate receptor. In looking at human tissues from tissue banks, we found that greater than 90 percent of ovarian cancers contain this protein. More than 50 percent of kidney cancers also do-the renal cell carcinoma, about 50 percent of all breast, and about one-third of all lung cancers have this protein. In some cancers, such as those of the colon or prostate, we just

don't see any folate receptors there. (according to Christopher Leamon, Ph.D., at his office in West Lafayette, IN)

USING TELEMEDICINE

IN PROSTATE CANCER TREATMENT

Roland J. Gardner, chief executive of the Beaufort-Jasper-Hampton (SC) Community Health Center, hopes telemedicine will help change the way patients are treated. In addition to partnering with Columbia Eye Clinic, the center received a \$1 million grant last year from the American Health Foundation to study prostate cancer in the Lowcountry. The grant allows Gardner and his staff to have biweekly conferences with experts from the New York-based foundation to discuss how to better educate Lowcountry men about their risk for prostate cancer, a disease that is one of South Carolina's top killers. "In small communities, you don't have the number of specialists you need," Gardner said, adding his area has only one endocrinologist and oncologist. "I think telemedicine is a bridge right now until you can get more doctors into rural communities."

CANCER EXPERTS APPLAUD NEW REPORT'S INCREASED EXERCISE RECOMMENDATIONS-CITING CONVINCING EVIDENCE, AICR SAYS "ONE HOUR PER DAY"

RECOMMENDATION GOOD FOR PREVENTING CANCER TOO

Experts at the American Institute for Cancer Research (AICR) welcomed a new health report that recommends increasing the current recommendations for daily physical activity. The AICR researchers pointed to mounting evidence linking physical activity to cancer prevention and increased cancer survival, in addition to improved cardiovascular health. There is also evidence of a probable link between increased physical activity and lower risk for cancers of the prostate.

UCLA OPENS ROBOTIC SURGERY RESEARCH FACILITY

In a unique academic and business partnership, UCLA, Computer Motion, Inc., Karl Storz Endoscopy-America, Inc. and BERCHTOLD Corporation, announce the opening of a new robotic and technology center at UCLA. One of the first of its kind in the country, the new center will help promote clinical, educational and research use of surgical robots and

digital imaging in surgery and medicine. The new center — a minimally invasive surgery think tank — is called CASIT, the Center for Advanced Surgical and Interventional Technology. The partners have created an environment for industry — innovators in minimally invasive surgery and advanced operating room technology — and scientists to work together to fuel robotic and imaging research and development to further define the operating room of the future. The first projects at CASIT include new diagnostic and treatment tools for neuroscience, pulmonology and urology, as well as a new robotic surgical training system. For example, CASIT will help develop an advanced laparoscopic method for removing the prostate gland, a procedure now performed using traditional open surgery.

BENEFITS OF TEA

Both men and women can benefit by drinking tea, according to two studies published in medical journals. First, Oncogene reported that regular tea drinking can help men with prostate cancer. The disease can be stimulated by androgens, the male sex hormones. Some components of tea appear to bind to androgen receptors in the prostate gland, slowing the growth of the cancer. And the American Journal of Clinical Nutrition reported that in a study of 1,256 women, tea drinkers had a higher bone-mineral density than those who didn't drink tea. In other words, tea may protect against osteoporosis.

WILLIAM A. SCHWARTZ COMMUNICATIONS EXECUTIVE NPCC CEO AND CO-CHAIR

William A. Schwartz, a past president and chief operating officer of the Cox Enterprises and Cox Communications media organizations who was the chief executive and co-chair of the National Prostate Cancer Coalition, died of prostate cancer Sept. 9 at a hospital in Atlanta. He also had served as president of the Prostate Cancer Research Political Action Committee and had worked on cancer projects for the Defense Department and the National Dialogue on Cancer. Mr. Schwartz, a Detroit native and Atlanta resident,

worked in the broadcast industry in New York and Cleveland before joining Cox. After leaving Cox, he served as president of Cannell Communications and of First Media Television.

PAPER IN SCIENCE SHOWS BRCA2 CONTROLS DAMAGE TO DNA

Defects in BRCA2, a gene that otherwise suppresses tumors, are responsible for a strong familial predisposition to breast cancer. Carriers of BRCA2 mutations also are at increased risk of ovarian, prostate, pancreatic and male breast cancer. Now a new study, featured in the Sept. 13 issue of Science, reveals that the protein made by BRCA2 is especially important in controlling damage to DNA, the double-strand molecule that houses our genetic blueprints.

RESEARCHERS CONFIRM TELOMERASE AS AN ANTIGEN FOR CANCER IMMUNOTHERAPY

The research, published in the September 1, 2002 issue of Cancer Research, shows that RNA encoding the protein component of telomerase (TERT RNA), when introduced into dendritic cells (DCs), is effective in priming telomerase-specific cytotoxic T-lymphocytes (CTLs) to target and destroy malignant tumors. Telomerase is abnormally activated in all human cancer types, including breast, lung, colon, prostate and hematologic tumors. That makes telomerase an attractive candidate for use in a therapeutic cancer vaccine. A phase I study of Geron's ex vivo telomerase vaccine is currently underway in patients with metastatic prostate cancer at Duke University Medical Center. "These experimental results are very important," commented Dr Calvin B Harley, Geron's chief scientific officer, in a statement to the press. "It is widely recognized that telomerase is universally present in cancer cells, and that an effective TERT-based cancer vaccine could be used against a broad range of tumor types." "These results demonstrate again that TERT RNA should function as an effective immunogen in cancer patients, stimulating telomerase-specific immune cells that can destroy cancer cells. They also suggest that the broad immune response stimulated by TERT RNA should lead to tumor cell death without damaging the normal cells that express lower levels of telomerase."

BIOCHEMICAL RELAPSE

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reasonable. There is a fine line as to when to begin treatment, much of it sometimes instigated more by patients' anxiety than by evidence of disease activity.

When to initiate hormone treatment is a topic of little concordance among urologists and medical oncologists. There are conflicting data as to when to initiate it, and patients would be best served by having a thorough discussion with their physicians as to the relative merits of starting hormonal therapy early and in the absence of advanced disease. For some patients, this treatment is the mainstay of their existence; for others, the associated side effects of hot flashes, impotency, weight gain, mood changes, accelerated osteoporosis, anemia, and muscle weakness are too concerning even to consider. Treatment may, however, be indicated for some patients depending on clinical presentation. Of note, hormonal treatment given too early only for a rising PSA may lead to early disease resistance and, thus, should be started only under advisement with healthcare professionals.

Unfortunately, there are numerous herbal preparations that can influence PSA and cause a decline in values. If at any point in time there is underlying disease, it will keep progressing without the patient ever knowing. In addition, many of these so-called natural herbs are really drugs that can be toxic to the liver. It is extremely important for patients to keep their physicians informed of all drugs taken, and for healthcare professionals to ask about alternative medications, as there is always a chance for these substances to interfere with standard treatments for heart disease, diabetes, or hypertension. On the other hand, taking drugs such as selenium, vitamin E, or vitamin C in reasonable amounts may not be harmful and, in some cases, may be helpful. A randomized trial of 32,000 patients, called SELECT, is underway to study the effect of vitamin E and selenium in PCa prevention.

There are probably more treatments available for prostate cancer

patients than they can use in their lifetimes. It is of paramount importance that anxiety not be the trigger of treatment that leads to regret.

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SOURCE: Medscape Hematology-Oncology eJournal 5(4), 2002 - Susan Slovin, MD, PhD, Genitourinary Oncology Service, Memorial Sloan-Kettering Cancer Center, New York, NY

TREATMENT SAVES LIVES

(continued from P. 1)

Because the cancers were diagnosed early, even men who were not treated had a relatively small — 14 percent — chance of dying from the disease during the eight-year study. And the number of deaths from all causes — including prostate cancer — was statistically the same between the men who got surgery and those who did not. The research, led by Lars Holmberg of the Scandinavian Prostatic Cancer Group, involved men in Sweden, Finland and Norway.

Dr. Michael Koch, chairman and professor at Indiana University points out that up until now, there have been no other studies to compare these results to. "Physicians rely on evidence-based methodology to make therapeutic decisions when possible but in localized prostate cancer the data was not previously available. The study is well-done and seems to have clear-cut results," he says.

"I think they will help men," says Dr. Peter Scardino, chief of urology at Memorial Sloan-Kettering Cancer Center in New York. "They will give men stronger evidence that treatment of prostate cancer really has a benefit."

"This is the first well-designed clinical trial that actually shows us that surgical removal of the prostate does something positive," said Dr. Otis Brawley, associate director of cancer control at Emory Univ.

Although those who had surgery were far more likely to suffer incontinence and impotence than those who were merely monitored, the two groups had similar self-assessments of well-being and quality of life, the researchers reported. (In recent years, serious side effects have been reduced with "nerve-sparing" surgery, a refinement that was not part of the study.) "What is very surprising to me is that the article concludes that there is little difference overall in quality of life. I would have thought that a doubling of impotence and incontinence would have a major impact on overall quality of life," says Dr. Derek Raghavan, chief of oncology at the University of Southern California, Los Angeles

While the new study is the first clear evidence that aggressive treatment offers a survival benefit, even the authors say it does not settle the debate surrounding early detection and treatment. About 75 percent of cases in the United States are diagnosed following PSAs, which can detect a tumor too small to be felt by a doctor. In contrast, the Scandinavian men were diagnosed because their tumors were palpable.

This latest research, however, does not address which treatment is best: surgery or different forms of radiation. That kind of controlled study has yet to be done.

SOURCE: New England Journal of Medicine 2002;347: article on pages 790-796, editorial on pages 839-840 - published September 12, 2002.

**Prostate Cancer
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