US TOO! PROSTATE CANCER EDUCATION & SUPPORT — KNOW YOUR PSA

PROSTATE CANCER HOT SHEET

Us Too! INTERNATIONAL — AUGUST 2003

A STRONG MAN'S FEAR

Sheree Harris Frede
Mrs. Colorado International 2003
*Prostate Cancer & **Us Too!** Advocate*

After waiting several long days to get he results of Norman's biopsy, we got the phone call and I knew by the look on his face that our lives were about to change - and maybe forever! My husband did indeed have prostate cancer. We were scared but determined to find the best treatment in the world. Fortunately some of the best doctors in the world were right at our back door - Houston Texas. Even better news was that Norman's cancer was caught early and was not an aggressive form of the disease. We chose surgery as our treatment option.

After only five wonderful years of marriage it just didn't seem fair that we would be challenged with this life threatening disease. However, after good research, faith, prayers, and experience, it brought us to a place in our lives of thankfulness, gratitude and relief. It has now been five years since his surgery and we have mentored and counseled with numerous couples going through the same experience. It never fails, the men just don't want to talk about it, so it looks like we women are going to have to take the bull by the horns and pull them along!

Norman has been a Chevrolet dealer in the Bay Area of Houston for 36 years. He has two beautiful daughters and six grandchildren that live close-by. He has had a profound, positive impact on many employees, customers and acquaintances. They often tell him how much he has touched their lives in some way. He is also an alcoholic that has been sober now for twenty-five years who has mentored, guided and encouraged countless others through their recovery. Norman and I met on an airplane in 1989 where he thought I was his flight attendant, but I was actually his pilot. Needless to say he was very taken aback when I went to take my seat in the cockpit. However, after a 'grease job' for a landing I had his respect and the rest is history. Oh, I can't forget to mention Dexter, our eight-year-old Jack Russell Terrier that lights up our day with his vivacious personality. So you see, we have a very full life.

Since Norman's surgery I have felt called on several occasions to do more for men and this disease. For several years I have prayed that God would continue to bless me and expand my territory. Well, you had better be careful what you pray for because God may just drop the world in your lap.

Different layering of events led me to compete for the Mrs. Colorado International title. What appealed to me about the pageant was their mission for married women ages 21

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FINASTERIDE (PROSCAR) AND PROSTATE CANCER.

The Merck drug was found to prevent prostate cancer in an National Cancer Institute (NCI) study. In fact it appeared to work so well that the NCI, which was conducting the trials, altered the study protocol so that all participants could be administered the drug.

In the trials, finasteride seemed to reduce prostate cancer by 25%. Appearing in the New England Journal of Medicine, the results also showed that 18% of men taking one Proscar pill per day went on to develop prostate cancer, whereas some 24% of those on placebo went on to develop the disease.

"These are very important results. This is the first intervention that has proved to reduce a man's risk of prostate cancer," said Dr Ian Thompson of the University of Texas Health Sciences Center, in an interview with Reuters.

Finasteride, branded as Proscar, is indicated to prevent BPH, or benign prostatic hyperlasia (enlargement). In lower doses, finasteride, branded as Propecia, has become a best-selling treatment for baldness after it was found to prevent hair loss.

- THE QUESTION: Does finasteride (Proscar) prevent prostate cancer?

- PAST STUDIES: have shown that finasteride can reduce benign prostate growth and relieve the frequent urination symptoms associated with it.

- *THIS STUDY*: involved 18,882 men aged 55 or older who were randomly assigned to take five milligrams of finasteride a day or a placebo for

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PROSTATE CANCER NEWS YOU CAN USE

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EXPERIMENTAL IMAGING TECHNIQUE DETAILS CANCER'S SPREAD TO LYMPH NODES

A study conducted at Massachusetts General Hospital and University of Nijmegen hospital in the Netherlands indicates that an investigational advanced magnetic resonance imaging (MRI) technique may be able precisely to identify the spread of prostate cancer to lymph nodes.

Published in the June 19, 2003, New England Journal of Medicine, the report details how high-resolution MR studies using an iron-oxide-containing contrast agent produced very accurate localization of tumor metastases, information that could be key in guiding the treatment of men with prostate cancer. The imaging agent currently is being evaluated for U.S. Food and Drug Administration approval.

"These imaging techniques allow us to clearly distinguish between benign and malignant nodes and to construct three-dimensional maps to guide surgical planning," says lead author Mukesh Harisinghani, MD, of the abdominal imaging division of the MGH Department of Radiology.

"This approach relies on advanced high-resolution MR imaging, detailed and computerized image analysis, and the novel contrast agent - a lymph-node-seeking magnetic nanoparticle," explains Ralph Weissleder, MD, PhD, director of the MGH Center for Molecular Imaging Research, a professor of Radiology at Harvard Medical School, and the report's senior author. "The experimental aspects of this technique have been tested and validated at MGH over the last decade, and we believe it has the potential of revolutionizing the way we do cancer staging [determining how advanced a tumor is]."

Almost 200,000 men in the U.S. are diagnosed with prostate cancer annually, and more than 30,000 die. The course of the disease varies widely, with some men living for years with slow-growing tumors and others needing more aggressive treatment - including surgery, radiation, and testosterone-reduction therapy - to control the spread of their cancer. Being able to identify which patients need aggressive treatment could improve the care of many patients, and a key factor in that identification is finding metastases, tumors that have spread beyond the prostate.

Standard practice in treating prostate cancer has been for lymph nodes adjacent to the prostate gland to be removed and analyzed for the presence of cancer, but it is not uncommon for metastases to first appear in nodes beyond the usual area of analysis. Standard MRI and computed tomography (CT) scanning cannot detect metastases, so the use of imaging has been limited to identifying enlarged nodes that may contain tumor cells. But some enlarged nodes prove benign, and metastases can occur in very small nodes.

The researchers at MGH and University Medical Center (UMC) in Nijmegen set up a study to examine whether a protocol developed at the MGH could identify prostate cancer metastases in abdominal lymph nodes. Each institution enrolled 40 patients who had been diagnosed with prostate cancer. The patients had preliminary high-resolution abdominal MR studies done before receiving intravenous infusions of the iron-containing contrast agent. A second set of MR studies was taken 24 hours later. A total of 334 lymph nodes were imaged in the 80 study participants.

The study was designed to allow careful comparison of the imaging studies with the surgical findings for all patients. After the MR studies, the participants received standard prostate cancer treatment, which for most was removal of the prostate gland. Patients had the usual lymph nodes removed for pathologic analysis; however, nine patients had additional nodes removed based on results of the MR studies.

The MR studies indicated that 272 of the imaged nodes were benign. Detectable metastases were found in 63 nodes from 33 patients. All of these diagnoses were confirmed by pathological examination of the removed nodes. And of the 63 malignant nodes, more than 70% were so small they would not have been identified as malignant by current imaging techniques.

"The high accuracy and less invasive nature of this method will allow us to stage our prostate cancer patients more efficiently," says Shahin Tabatabaei, MD, an MGH urologist who is a coauthor of the current report. "This technique may revolutionize the diagnosis and treatment of prostate cancer and probably other genitourinary malignancies."

The researchers note that a large-scale,

controlled clinical trial is needed to assess this technique's impact on patients' outcomes, and they hope to embark on such a study in the near future. But if the study's results hold up, this approach, which uses equipment found at most MR centers, has the potential to significantly improve patient care and to reduce costs by eliminating unnecessary procedures.

"This approach also has the potential to be applied to a wide variety of malignancies," says Harisinghani, who is an instructor in Radiology at HMS. "And eventually we could go beyond staging the disease to offering treatments using lymphotrophic [attracted to lymph-nodes] agents that could attack the metastases without the systemic effects of other chemotherapy drugs."

The research was supported by a U.S. National Cancer Institute grant and funds from the radiology departments at both hospitals. The experimental contrast agent was supplied at no cost by U.S. and French manufacturers of the agent.

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FAILED BRACHYTHERAPY IS NOT A TECHNICAL IMPEDIMENT TO SALVAGE THERMAL THERAPY

According to a study from the United States, "Thermal therapy is an experimental treatment to destroy solid tumors by heating them to temperatures ranging from 55 degrees C to 90 degrees C, inducing thermal coagulation and necrosis of the tumor.

"We are investigating the feasibility of interstitial microwave thermal therapy as a salvage treatment for prostate cancer patients with local recurrence following failed brachytherapy. Due to the electrical and thermal conductivity of the brachytherapy seeds, we hypothesized that the seeds could scatter the microwave energy and cause unpredictable heating," wrote C. McCann and colleagues, Los Alamos National Laboratory.

"To investigate this, a 915 MHz helical antenna was inserted into a muscle-equivalent phantom with and without brachytherapy seeds. Following a 10 W, 5 s input to the antenna, the temperature rise was used to calculate absorbed power, also referred to as specific absorption rate (SAR)," the researchers stated.

"Plane wave models based on Maxwell's equations were also used to characterize the electromagnetic scattering effect of the seeds. In addition, the phantom was heated with 8 W for 5 min to quantify the effect of the seeds on the temperature distribution during extended heating. SAR measurements indicated that the seeds had no significant effect on the shape and size of the SAR pattern of the antenna," the researchers wrote.

"However, the plane wave simulations indicated that the seeds could scatter the microwave energy resulting in hot spots at the seed edges. Lack of experimental evidence of these hot spots was probably due to the complex polarization of the microwaves emitted by the helical antenna," they added.

The researchers concluded: "Extended heating experiments also demonstrated that the seeds had no significant effect on the temperature distributions and rates of temperature rise measured in the phantom. The results indicate that brachytherapy seeds are not a technical impediment to interstitial microwave thermal therapy as a salvage treatment following failed brachytherapy."

McCann and colleagues published the results of their research in Physics in Medicine and Biology (Feasibility of salvage interstitial microwave thermal therapy for prostate carcinoma following failed brachytherapy: studies in a tissue equivalent phantom. Phys Med Biol, 2003;48(8):1041-1052).

For additional info, contact C. McCann, Los Alamos National Laboratory, POB 1663, Los Alamos, NM 87545

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ZINC SUPPLEMENTS "INCREASE PROSTATE CANCER RISK"

A team from the National Cancer Institute found that men who take more than 100mg of zinc supplements a day are at twice the risk of being diagnosed with advanced prostate cancer than those who do not take the supplements.

The researchers studied nearly 50,000 men between 1986 and 2000 who were taking part in the Health Professionals Follow-Up Study.

Over the 14-year period of the study, 2,901 cases of prostate cancer were diagnosed, of which 434 were advanced cases of the disease.

After comparing zinc supplement use among the men, the researchers found that doses of up to 100mg a day were not associated with prostate cancer risk. However, men who took more than 100mg had more than double the risk of being diagnosed with advanced prostate cancer.

In the UK the recommended daily intake for men is between 5.5 and 9.5mg a day.

The researchers concluded that, while other factors such as extra calcium intake or some other unknown aspect of taking zinc supplements could have influenced their results, their findings "that chronic zinc oversupply may play a role in prostate carcinogenesis" warranted further investigation.

Commenting on the findings, Dr Chris Hiley, head of policy and research at The Prostate Cancer Charity in the UK, said it was clear that altering diets could considerably reduce the risk of many cancers, which had led some people to seriously consider various supplements.

"Many men are interested in reducing the risk of prostate cancer developing and have heard that zinc may help, even though a medical scientific standard of evidence for this does not really exist," he said.

"[The research] does raise concerns about the doses that men are taking. As the lead researcher in this study points out, more research is needed to generate definitive evidence based advice for men on how to manage their risk of developing this all too common cancer."

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PROSTATE CANCER RISK SKYROCKETS FOR SMOKERS

Longtime, frequent smokers significantly increase their risk of prostate cancer, Seattle researchers have found.

Middle-aged men who smoke a pack a day for 40 years increase their risk for prostate cancer by 60 percent. They're twice as likely to suffer an aggressive form of the cancer.

Even those who haven't smoked that long face, on average, a 40 percent higher risk

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of prostate cancer, according to the study.

The study adds weight to previous findings that link smoking to cancers of the prostate as well as the bladder, cervix, kidney, esophagus and lung. It appears in the July issue of Cancer Epidemiology, Biomarkers and Prevention.

"It should be another message for why men should quit smoking," said Janet Stanford, the paper's senior author and director of prostate cancer research at Fred Hutchinson Cancer Research Center.

"Current smoking and high-dose exposure are associated with a high risk of prostate cancer," she said. "That risk seems to be strongest for the most aggressive, life-threatening forms of prostate cancer."

Stanford was encouraged, however, to discover that men who stopped smoking for a decade lowered their risk to the level of non- smokers.

The study recruited about 1,450 King County residents, both prostate cancer survivors and men with no history of the disease, ages 40 to 64.

Among cancers, prostate cancer kills the most men in this country after lung cancer. This year there will be about 220,900 new cases and 28,900 deaths, the American Cancer Society estimates.

Several theories exist on how smoking leads to prostate cancer. It possibly alters steroid hormone levels, stimulating the growth of regular and malignant prostate cells. Another reason is that cigarettes contain cadmium, a toxin that has been linked to the cancer.

Identified risk factors for prostate cancer are advanced age, family history and being African American. Previous research also has indicated the role of poor nutrition.

The National Cancer Institute, which funded the study, recently started a "9 A Day" campaign to encourage black men to eat more fruits and vegetables.

Stanford and her colleagues, who included University of Washington researchers, collected detailed smoking and cancer histories and accounted for such lifestyle variables as diet. Previous research results are mixed, Stanford said, but recent findings from researchers at Johns Hopkins and Harvard universities also back the connection between smoking and prostate cancer.

REDUCE YOUR PROSTATE CANCER RISK

- Stop smoking.

- Eat more vegetables. Tomatoes contain the cancer-fighting nutrient lycopene. Members of the crucifer family, such as cabbage, broccoli and cauliflower, also lower risk.

- Limit fat to no more than 30 percent of your daily caloric intake.

Source: Janet L. Stanford, director of prostate cancer research at Fred Hutchinson Cancer Research Center.

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RESEARCHERS TEST NEW TYPES OF PROSTATE CANCER DETECTION

Three new non-invasive diagnostic tests now in the research pipeline promise to detect prostate and other cancers earlier and tell whether the tumors are the aggressive kind that should be treated or if they are unlikely to spread and can be left alone.

The tests, one of which could be available to the public within two years, are seen as being more accurate than the current PSA test and could spare patients unnecessary biopsies and, in many cases, unneeded treatments.

"There's a coming revolution in the early diagnosis of cancer," said Dr. Lance Liotta of the National Cancer Institute. "This way patients won't have to be put through things they don't need or won't do them any good."

Data on the new tests, being evaluated now for the detection of prostate cancer, were presented yesterday at the annual meeting of the American Association for Cancer Research.

Dr. William Nelson of Johns Hopkins Hospital said the PSA, or prostate specific antigen, test can only suggest the presence of prostate cancer. Often, levels of the protein are elevated for other reasons. But most men with PSA levels over 4 nanograms per milliliter of blood are referred for invasive biopsies.

The new tests look for patterns of proteins that have been found to be common in men previously diagnosed with cancer, for a very specific form of PSA or for genetic abnormalities that not only suggest cancer but can tell if it is the kind that is likely to kill.

One of the tests, now in development by the FDA, has been shown accurate in diagnosing disease in from 85 to 100 percent of cases. Only men with a positive finding would be referred for biopsies.

"We don't want to pin-cushion these patients to death," said Dr. Emanuel Petricoin of FDA.

The test also has been able to detect ovarian cancers in high-risk women.

Another blood test being developed by Beckman Coulter Inc. looks for a specific form of PSA known as pro-PSA and could be available in two years, said Stephen Mikolajczyk of the firm. He said the test is able to determine whether slightly elevated PSAs - those in the 4 to 10 "gray" zone - should be biopsied.

He also said a coming study in the New England Journal of Medicine will show that the gray zone should be extended below the level of 4. With current PSA technology, that could mean many more unnecessary biopsies.

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INTERMITTENT TAXOTERE/CALCITRIOL CHEMOTHERAPY FEASIBLE

Advanced prostate cancer can be successfully treated with intermittent chemotherapy with no loss of disease control, according to a study conducted by Oregon Health & Science University scientists.

The study was presented at the American Society of Clinical Oncology's annual meeting in Chicago, Illinois.

Breaks - or "holidays" - in chemotherapy potentially allow prostate cancer to be managed as a chronic condition, rather than as an acute or life-threatening disease. Participants in a phase II study reported significant improvements in their quality of life as a result of chemotherapy holidays.

"Our data, while preliminary, suggest that intermittent chemotherapy is safe and that the cancer retains its sensitivity to treatment," said Tomasz M. Beer, MD, an oncologist at the Oregon Health & Science University (OHSU) Cancer Institute in Portland, Oregon, and lead investigator of the study.

Prostate cancer is the most common malignancy among men and the second leading cause of cancer death in men in the United States. Overall, roughly one in six American men will develop prostate cancer during his lifetime.

The optimal duration of chemotherapy treatment for patients with androgen-independent prostate cancer (AIPC) is unknown. In many studies of newer chemotherapy drugs, patients are treated until the disease progresses or until the side effects become intolerable. For patients who are responding to the chemotherapy, however, continuous treatment may be exposing them to unnecessary toxicity.

"Newer chemotherapy drugs are effective, but side effects accumulate when these drugs are used for prolonged periods of time. It is unrealistic to continue the treatment indefinitely," Beer said. "This study sought to answer the question: Is it feasible to stop and start chemotherapy for patients who are responding well to the treatment?"

In the context of a phase II study of calcitriol plus docetaxel (Taxotere) for AIPC, Beer developed and tested an intermittent chemotherapy protocol. A primary criterion for inclusion in the study was a positive response to treatment measured by a prostate-specific antigen (PSA) of less than 4 ng/ml. PSA is a protein made only by prostate cells. Certain prostate conditions, including prostate cancer, can cause high levels of PSA in the blood. PSA blood levels are monitored to help predict the presence and progression of prostate cancer.

These patients were then given the option to select intermittent chemotherapy or to continue the existing treatment protocol. For patients electing chemotherapy holidays, the study protocol required resumption of treatment if a patient's PSA measurement rose by 50% or more and at least 1 ng/ml, or if other key indicators of disease progression were observed.

Of the 37 patients enrolled in the phase II study, 11 responded to chemotherapy to the degree necessary to meet criteria for inclusion in the study. Median treatment length for these men was 45 weeks. Eight of the 11 eligible men, ranging in age from 46-82, chose to suspend their chemotherapy. Of these 8 men, the median length of the treatment holiday was 20 weeks with individual lengths ranging from 13-43 weeks.

Chemotherapy treatment was resumed for seven patients, while one patient remains on the initial treatment holiday after 43 weeks. Of the seven patients who resumed chemotherapy treatment, three remain on an intermittent therapy protocol, mixing chemotherapy treatment with holidays. In all cases, PSA levels stabilized or dropped once chemotherapy resumed.

"Our data suggest that giving chemotherapy intermittently is safe because there was no loss of disease control in any of the patients," Beer said.

Analysis of quality of life data collected during the study revealed that the chemotherapy holiday was associated with improvement of fatigue as well as a trend toward improvement of shortness of breath, increased appetite, and decreased diarrhea, although there was a slight worsening of pain reported by some study participants.

"Instead of treating patients continuously, we can reduce their exposure to chemotherapy to allow them to have a better quality of life," Beer said. "This study suggests that a follow-on clinical trial with more patients to further investigate intermittent chemotherapy for the treatment of AIPC is warranted."

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MISO SOUP INHIBITS BREAST, PROSTATE CANCER

Nichimo Co. has confirmed in joint research with Harvard University that fermented soybean extract inhibits the progress of breast and prostate cancer.

Nichimo, a Japanese diversified fishery and foods-related company, reported the findings at the AACR Conference.

Nichimo's findings come on the heels of a recent report by a Japanese Health Ministry research unit that consumption of Japanese miso soup, made of fermented soybeans, can reduce the risk of breast cancer.

The joint team found that the growth of experimentally cultured cancer cells was substantially reduced when isoflavone, an antibacterial component of the soybean extract, was applied.

The group used an enzyme to make aglycon, or sugar-free, isoflavones to help absorption by the cells. Isoflavones are usually conjugated with sugar, making absorption difficult.

According to Nichimo, Japanese miso, or soybean paste, contains isoflavones in the form of aglycon, due to the workings of malt, but isoflavones in tofu or natto, the two other traditional Japanese foods made from soybeans, stay conjugated with sugar.

Nichimo has sold dietary supplements that contain aglycon isoflavones since 2001.

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TREND IN ONCOLOGY MOVES TOWARD TAILORING TUMOR THERAPIES

The Orange County Register, Calif.

The smartest approach to fighting cancer might just be... to fight cancer.

Doctors at the American Association for Cancer Research conference in Washington, D.C., heard about a new approach to an old and disparaged form of cancer treatment: customizing medicine directly to an individual tumor.

The idea is to target treatment directly to the tumor cells, often sparing healthy cells the worst of chemotherapy's damage. This is one of several approaches to "designer" therapies expected to be discussed at the conference. It highlights a push in oncology toward protecting patients against drugs and treatments that — though successful for some people — won't work for others.

Oncologists say they often prescribe patients one standard chemotherapy regimen after another, until they find the one that works. This can expose patients to the side effects of chemotherapy — hair loss, vomiting, weakness — without showing any cancer-killing results.

Research led by Dr. Robert Nagourney of Long Beach Memorial Hospital suggests that the guesswork can be done in a laboratory instead.

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"Once you've figured out what makes the cancer tick, it's a lot easier to kill it," said Nagourney, who is also an adjunct associate professor of pharmacology at the University of California, Irvine.

Nagourney's lab essentially takes pieces of tumor tissue, applies different chemotherapy treatments to it and examines the results to see which drug or combination of drugs does the best job killing the tumor cells. The tactic of using biopsied cells to predict which cancer treatments will work best for a patient is 30 years old. But Nagourney says those older tests failed because scientists looked to see which drugs inhibited the cancer cells' growth, not which chemotherapies actively killed the tumor cells.

"We had an erroneous understanding of cancer biology," Nagourney said. "Cancer isn't growing faster than other cells, it's just dying slower. We realized, 'Why don't we connect drugs to patients by what kills their cells, not by what slows them down?'" *Killing Cancer Kindly* - This new twist of an old approach appears to be working.

In a study published last year in the journal Gynecologic Oncology, for instance, a team of researchers tested how well women with relapsed ovarian cancer would respond to a combination of a pancreatic cancer drug and an ovarian cancer drug. They found the combination worked on a number of women, and that Nagourney's approach to testing cells in petri dishes predicted which women would respond to the drugs and which wouldn't.

"At first I was pretty skeptical, but we had patients who I thought were going to die, and suddenly they're walking into my office" months later, said Dr. Philip J. DiSaia, director of the division of gynecologic oncology at UCI, who participated in the ovarian cancer clinical trial.

"The other techniques haven't been terribly successful because they tell you which drugs are definitely not good. But this was a prediction of what would work," he said.

Mike Cook, 51, of Brea was diagnosed in January with metastatic pancreatic cancer, a disease that kills 96 percent of its victims. He was sure the diagnosis was a death sentence. A few months later, he was on the road to remission, hanging new windows in his home and taking vacations with his wife and kids. Nagourney is treating Cook with a combination of drugs commonly used to fight lung, pancreatic, breast and colorectal cancers.

'A rational therapy' "I started to feel better almost immediately. I didn't have the throwing up, the hair loss," said Cook, who has had more than eight rounds of treatment. "It is taxing, but it's not nearly the image of chemotherapy we've all seen so many times. It feels like it's a rational therapy, and I'm not buckling under the strain of it."

Nagourney isn't the only researcher trying to find gentler, more targeted approaches to killing cancer. UCI urologist Dr. David Ornstein's work on proteomics, or the analysis of blood proteins, will also be presented at the AACR conference today. His work focused on detecting prostate cancer by looking at protein patterns in the blood.

Men who are suspected of having prostate cancer often undergo needle biopsies of their prostate to check for the disease. Researchers tested the blood of men who had had needle biopsies and found that the blood test could have saved 67 percent of the men who didn't have cancer from having to undergo the painful biopsy.

While this study focused on diagnosis, Ornstein said proteomics might also be used to predict which treatments would work for individual cancer patients.

Researchers at the University of North Carolina have started a clinical trial to test the technology in finding fitting therapies for ovarian cancer patients.

"If you use targeted therapy, meaning you're only treating patients who will benefit from the treatments, you'll eliminate patients from having undue side effects without any benefit," Ornstein said. "The problem with standard chemotherapy is that it's like taking a machine gun and shooting everything in the way and hoping you get the cancer cells along with that."

While doctors seek the best way to match existing drugs to individual tumors, they also believe that emerging technologies will help find better, safer drugs to kill cancer.

Comparing current chemotherapy with the arsenic treatments once given for syphilis, Nagourney said, "Up until now, we've been indiscriminately poisoning healthy cells. Once you could identify a unique aspect to the (syphilis) bacteria, you could come up with penicillin," he said. "We are on the verge of developing penicillin for cancer."

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GENETIC TEST SHOWS PROMISE FOR EARLY PROSTATE CANCER DETECTION

Results of a study in the July 2003 issue of European Urology suggest that a non-invasive genetic test could soon aid the diagnosis of prostate cancer.

Early detection of prostate cancer, the second largest cause of cancer deaths among men in western countries after lung cancer, is essential for effective treatment. A blood test that detects prostate-specific antigen (PSA) is limited as up to 70% of subsequent biopsies of prostate tissue are negative. Genetic tests could provide more specific indications of malignant disease.

Various genes are implicated in the development of prostate cancer. The gene DD3PCA3 is the most prostate cancer-specific gene, and is strongly overexpressed in more than 95% of primary prostate cancer specimens and in metastatic prostate cancer (cancer that has spread to other parts of the body).

Jack Schalken from the University Medical Center Nijmegen, the Netherlands, and colleagues investigated whether assessment of DD3PCA3 in urinary sediments could provide a more reliable indicator of prostate cancer than PSA testing.

After confirming that detection of DD3PCA3 was a reliable indicator of malignant disease, the investigators studied 108 men with a PSA value suggesting possible prostate cancer. Prostate cancer was confirmed in 24 men after biopsy; 16 of these had urinary sediments positive for the DD3 PCA3 gene - a test sensitivity of 66%. The genetic test was also found to be nearly 90% reliable in confirming negative results.

"This genetic test offers great promise as a non-invasive diagnostic tool for the detection of prostate cancer, and its high

negative predictive value should reduce the need for biopsy," said Schalken. "Future multi-center studies using this test should provide the first basis for the use of molecular diagnostics in clinical urological practice to aid the diagnosis of prostate cancer."

In an accompanying editorial, Zoran Culig from the University of Innsbruck, Austria, concluded, "For a practicing urologist, the most important repercussion of the data from this study is the fact that, on the basis of a non-invasive diagnostic DD3 test, the number of repeated biopsies in patients with PSA levels >3 ng/ml might be considerably reduced."

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ANTI-PROLIFERATIVE EFFECTS OF D-LIMONENE ON HUMAN PROSTATE CARCINOMA CELLS

AACR - Abstract Number: 4773

Prostate cancer is clinically diagnosed in 1 of every 11 men in the United States and one-third of those diagnosed will eventually develop metastatic form of the disease. Prostate cancer often progress from a hormone-sensitive, non-metastatic phenotype to a hormone-insensitive and chemotherapy-resistant phenotype with highly invasive and metastatic growth properties. Most prostate cancers respond initially to androgen ablation however, the residual androgen-insensitive cells recolonize, expand and ultimately establish hormone-resistant state. Also, at the time of clinical diagnosis most prostate cancers represent a mixture of androgen-sensitive and androgen-insensitive cells. Therefore, the key to the control of prostate cancer appears to lie in the elimination of both types of cells through mechanism-based preventive or therapeutic approaches. D-limonene, a plant-derived monocyclic monoterpene commonly present in orange and other citrus peel oil has shown promise in the prevention or therapy of some cancer types. D-limonene is probably present in high levels in the Mediterranean diet and may be an important component in putative cancer-preventive effect of such diet. Employing LNCaP as androgen-sensitive and DU145 as androgen-insensitive human prostate carcinoma cells, specifically we first established the anti-proliferative effects of D-limonene and then determined the mechanism of its action. D-limonene (1-10 mM) treatment resulted in dose- and time-dependent (i) inhibition of cell growth, (ii) decrease in mitochondrial activity, (iii) induction of necrosis in both cell types. D-limonene treatment (1-10 mM) showed minimal signs of apoptosis in both cell types and did not significantly affect the distribution of cells among different phases of the cell cycle. These effects were found to correlate with a shift in Bax/Bcl2 ratio towards cell death in both cell types irrespective of the androgen association. Taken together, this is the first study suggesting that D-limonene could be developed as an anti-cancer agent against prostate cancer.

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SULFORAPHANE, A NATURALLY OCCURRING AGENT IN CRUCIFEROUS VEGETABLES, INHIBITS PROLIFERATION OF HUMAN PROSTATE CANCER CELLS BY INDUCING APOPTOSIS AND CAUSING CELL CYCLE ARREST

AACR - Abstract Number: 972

Sulforaphane is a member of the isothiocyanate (ITC) family of chemopreventive agents that are abundant in cruciferous vegetables, such as broccoli, watercress and so forth. ITCs, including sulforaphane, are highly effective in affording protection against chemically induced cancers in experimental animals. Moreover, epidemiological studies have indicated that increased consumption of cruciferous vegetables is associated with a statistically significant reduction in the risk for cancers of various anatomical sites, including prostate cancer. We, therefore, hypothesized that sulforaphane may inhibit proliferation of prostate cancer cells. In the present study, we tested this hypothesis by determining antiproliferative effects of sulforaphane against PC-3, LNCaP and DU-145 human prostate cancer cells. Proliferation of all above mentioned cell lines was significantly retarded in the presence of sulforaphane in a dose-dependent manner. Sulforaphane was more or less equally effective against androgen-dependent (LNCaP) and androgen-independent (PC-3 and DU-145) cells. A 24 h exposure of PC-3 and DU-145 cells to 40 _ M sulforaphane resulted in accumulation of cells in G2/M phase, which was accompanied by a decrease in G0/G1 phase cells. In contrast, sulforaphane treatment of LNCaP cells resulted in G0/G1 phase arrest. Sulforaphane-mediated growth inhibition of all 3 cell lines was associated with apoptosis induction that was characterized by an increase in Annexin V positive cells and increased formation of histone-associated DNA fragments. While the mechanism(s) for sulforaphane-mediated G2/M arrest and apoptosis induction in LNCaP or DU-145 cells remains to be elucidated, a 24 h exposure of PC-3 cells to 40 _ M sulforaphane resulted in a marked decrease in the expression of several proteins that are critical for G2/M progression, including cyclinB1, Cdc25B, and Cdc25C. The expression of Cdk1 was not affected by sulforaphane treatment. Western blot analysis using lysate from sulforaphane treated (40 _ M) PC-3 cells indicated a significant reduction in the expression of anti-apoptotic protein Bcl-2 compared with controls. In addition, the expression of pro-apoptotic protein Bax was increased significantly in sulforaphane treated PC-3 cells relative to DMSO treated controls. Activation of caspase-3 was also observed in sulforaphane treated PC-3 cells. In conclusion, the results of the present study indicate that sulforaphane is an effective inhibitor of the proliferation of human prostate cancer cells irrespective of their sensitivity to androgen. It is conceivable that sulforaphane, and possibly other naturally occurring ITCs, may be used for prevention and/or treatment of human prostate cancer.

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PROSCAR & PROSTATE CANCER

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seven years. About 18 percent of those who took the drug developed prostate cancer, compared with about 24 percent of those who took the placebo. However, 6.4 percent of those in the finasteride group developed high-grade prostate tumors, compared with 5.1 percent of those taking the placebo. Men taking finasteride also had more sexual side effects, such as impotence and decreased libido. The study was stopped ahead of schedule and its findings published early because of their potential implications for large numbers of men.

- WHO MAY BE AFFECTED BY THESE FINDINGS? Men 55 or older

- CAVEATS The prevalence of prostate cancer in the placebo group (24.4 percent) was higher than the lifetime risk in the general population (16.7 percent), possibly because participants in the study were examined more often than is common.

- BOTTOM LINE Men with benign prostate growth, especially those at elevated risk of prostate cancer, may wish to discuss finasteride with their doctor. While the drug may lower the overall risk of prostate cancer, this benefit may be outweighed by the increased likelihood of high-grade tumors and side effects.

- FIND THIS STUDY July 17 issue of the New England Journal of Medicine; available online at www.nejm.org.

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A STRONG MAN'S FEAR

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to 56 years old committed to marriage, family values and community service. It's not just a beauty pageant because only 25% is evening gown, poise and style; 25% is physical fitness (no 'swimsuit' competition - Can you imagine a 48 year old women competing against a 21 year old in a swimsuit?). The remaining 50% is based on an interview focusing on a chosen platform or charity. This was the door that opened for me to do more for prostate cancer. It really is amazing that with a title of Mrs. Colorado International how my territory is expanding - and FAST!

I have been making personal appearances at several 'Relay for Life' events, golf tournaments, meeting with top prostate cancer researchers, attending symposia, helping with fundraising efforts for several non-profit groups and research hospitals and working with ***Us Too!*** **INTERNATIONAL** to help expand their support programs nationally and internationally. On September 5th and 6th - in Pigeon Forge Tennessee - I will compete for the *Mrs. International* title. I am so excited about the thought of representing this great country while promoting prostate cancer awareness and support. You can find out more about the pageant on the Internet at www.mrsinternational.com

What next? Well, I am just walking through every door that opens and I can't wait to see what the future will bring. All I know is that to whom much is given, much is expected. I was given Norman's life. Much is still needed in prostate cancer awareness, support and research. Ultimately I would like to end fear of this disease through better awareness, so a man can have a successful therapy through early detection or better yet - that this disease can be PREVENTED! I encourage everyone I meet to learn more about prostate cancer, get involved and encourage the men in their lives to start thinking about early detection of prostate cancer in their 40's - so that they have a baseline well before the age of 50! Your involvement just might save a life that is special to YOU!

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