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“This is only the second study showing that allium vegetables are associated with reduced (prostate cancer) risk,” said lead researcher Ann W. Hsing, an epidemiologist at the National Cancer Institute in Bethesda, Md.

“The point is not that people should increase their intake of garlic and not pay attention to other components of their diet,” Hsing told United Press International. “The best advice is still a balanced diet, regular exercise and to try to avoid obesity — to have a healthy lifestyle.”

Allium vegetable consumption is significantly higher in China than in the United States, she added.

Hsing interviewed 238 men with prostate cancer and 471 men without the condition about their diet five years prior to the interview, in order to avoid reporting changes in diet due to the development of the disease. She recommends further, prospective studies to follow men over time to determine which ones develop prostate cancer and whether there is an increased risk of the disease.

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Patterns of proteins found in patients’ blood serum may help distinguish between prostate cancer and benign conditions, scientists from the National Cancer Institute (NCI) and the Food and Drug Administration (FDA) report in the Journal of the National Cancer Institute.

The technique, which relies on a simple test using a drop of blood, may be useful in deciding whether to perform a biopsy in men with elevated prostate specific antigen (PSA) levels.

Using a test that can analyze the patterns of small proteins in blood serum samples in just 30 minutes, researchers were able to differentiate between samples taken from patients diagnosed with cancer and those from patients diagnosed with benign prostate disease. The technique proved effective not only in men with normal and high PSA levels, but also in those whose PSA levels were marginally elevated (4-10 ng of antigen per mL of fluid), in whom it is difficult to rule out cancer without a biopsy.

Although the technique is still under evaluation, researchers believe the analysis of protein patterns will be a useful tool in the future for deciding whether men with marginally elevated PSA levels should undergo biopsy. PSA levels are commonly used as a preliminary screen for prostate cancer, but 70-75% of men who undergo biopsy because of an abnormal PSA level do not have cancer. The new proteomic approach has a higher specificity - that is, of the samples the test identifies as cancer, a large percentage are in fact cancer, rather than some other benign disease.

“For men with marginally elevated PSA levels, the specificity of the test is 71%, as opposed to a very low specificity for

Researchers at The Cleveland Clinic have discovered a relatively common gene mutation that could double a man’s risk for developing prostate cancer.

Results of the study - published in the journal Nature Genetics - suggest that up to 13% of prostate cancer cases are attributable to a mutation of the RNASEL gene known as R462Q, making R462Q one of the most frequent genetic alterations in any of the common cancers. In comparison, mutations of the widely known BRCA1 gene account for less than 5% of breast and ovarian cancers.

The study was authored by Graham Casey, Ph.D, of the Cleveland Clinic Lerner Research Institute’s Department of Cancer Biology; John Witte, Ph.D., of Case Western Reserve University; and a team of collaborating scientists from The Cleveland Clinic, Washington University, and the National Institutes of Health.

Nearly 60% of the 877 men in the study possessed at least one copy of the R462Q variant. Men who inherited only one copy of the mutation from a parent had a 50% increased risk of prostate cancer, while those who inherited two copies of the gene - one from each parent - had a two-fold increased risk of the disease.

“This means that while the effect of carrying the R462Q variant may be relatively small for a given individual, the effect on men’s health overall is very large because of the frequency of the R462Q variant in the population,” said Dr. Casey. “These findings suggest that screening men for this mutation may be justified in future risk assessment of prostate cancer.”

RNASEL is a protein produced by normal cells that can lead to cell death, in

(continued on page 7)
Infection With C. Trachomatis May Protect Against Prostate Cancer

Men with Chlamydia trachomatis infection appear to have a reduced risk of prostate cancer, according to findings presented at the 42nd annual meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy. Overall, chlamydia infection was associated with a 31% lower risk of prostate cancer, according to the report. In addition, the risk of prostate cancer steadily decreased as antibody levels increased. The findings are not an endorsement for avoiding chlamydial treatment in an effort to ward off the malignancy, Dr. Anttila emphasized. Furthermore, additional studies are needed to confirm and, possibly explain, the current findings.

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TREATING SEXUAL DYSFUNCTION REQUIRES OPEN DISCUSSION, SPECIAL MANAGEMENT

Bob Dole may have been the first person to discuss erectile dysfunction openly on TV, but family physicians are the ones who need to talk openly and routinely about sexual activity and sexual dysfunction with their patients in everyday practice. Many patients, especially men, rarely initiate clinical conversations about such sexual concerns as low libido, arousal difficulties, and problems with early ejaculation or lack of orgasm. But studies show that most patients want to talk about these problems with their physicians. Satisfying sexual activity, it has been shown, enhances quality of life and self-esteem. “Family physicians need to be proactive in discussing sex. Satisfying sexual activity can enhance relationships, and good relationships are good for overall health,” Richard Sadovsky, M.D., associate professor of family practice at the State University of New York Health Science-Downstate Medical Center, Brooklyn also indicated that sexual dysfunction may provide family physicians with a clue to associated medical problems, such as endothelial dysfunction in the form of coronary artery disease. Some types of sexual dysfunction, especially erectile dysfunction, are associated with depression. Sexual dysfunction is common in men and women. Sadovsky said. About 31 percent of men have some form of sexual dysfunction. The most common complaint is premature ejaculation (21 percent), followed by erectile dysfunction and low sex drive. The major causes of sexual dysfunction include comorbidities, such as cardiovascular disease, diabetes and cancer; psychotropic medications for depression and anxiety; antihypertensive medications; hypogonadism; and alcohol abuse. Low libido may be associated with psychosocial issues, such as misconceptions about sex, cultural or religious taboos, relationship issues, and loss of job or income. FPs should advise patients that improved communication between sexual partners about their needs and difficulties will likely improve sexual satisfaction and resolve some problems, Nusbaum and Sadovsky said. Healthy lifestyle choices, especially exercise, will also improve sexual function.

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NEW FINDINGS ILLUSTRATE EFFECTIVENESS OF PALLADIUM-103 BRACHYTHERAPY IN TREATMENT OF AGGRESSIVE PROSTATE CANCER

The findings, revealed in several presentations at the October 6-10, 2002, ASTRO (American Society of Therapeutic Radiology and Oncology) meeting in New Orleans, also reinforce the effectiveness of Palladium-103 (Pd-103) treatment for localized cancer. “The scientific data presented at this year’s ASTRO meeting. The results presented in the following studies confirm the effectiveness of Pd-103 brachytherapy in low- and intermediate-risk patients, as well as in high-risk patients. This study demonstrates that patients who received Pd-103 therapy with or without external beam radiation show a faster resolution of side effects than patients who receive I-125 therapy with or without external radiation. The morbidity scores returned to baseline levels within six months after brachytherapy in the Pd-103 patient group, while the I-125 group still had elevated levels 12 months after the procedure was performed.**********

MAGNETS COULD BE CANCER KILLERS

One day, removing a cancerous tumor might be almost as simple as placing a magnet on the refrigerator. Los Alamos National Laboratory is developing a method that will use a magnetic field and tiny bacteria-sized magnetic beads to zap tumors in the body without surgery. Work is in the very early stages.

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NEW STATISTICS SHOW INCREASE IN CANCER RATES

The National Cancer Institute will release a report today showing that the incidence of some forms of cancer that has been assumed to be in decline or holding steady has actually been rising. New NCI figures reveal that rates for breast cancer in white women have been rising 0.6% annually since 1987, while lung-cancer rates have been increasing 1.2% since 1996. The
and found they had fewer radiation-related suppress tumor growth. The researchers turmeric its yellow color and has been Radiology and Oncology. The substance his findings at a recent conference of the Although their study was conducted on may protect cancer patients from the burns Turmeric, a principal ingredient of curry, moderate intensity, for approximately 30 risk of cancer, people should aim to importance in keeping cancer at bay. The moderate activity of at least moderate intensity, for approximately 30 minutes on three or more days a week throughout their lifetime.”

**Exercise Helps Fight Against Cancer**

Researchers at Britain’s University of Bristol have found regular exercise can help people avoid developing cancer. They also found that exercise aided a more successful recovery among cancer sufferers. The combined results of 15 studies on physical activity and found that people taking this as part of their job or as a leisure pursuit could substantially cut their risk. Regular exercise reduced the change of developing bowel cancer by between 40% and 50%. In other results, the effect on breast cancer was a 30% reduction in risk, with stronger effects in post-menopausal women. The study also concluded that the quality of life of leukemia, breast, bowel and prostate cancer patients was improved by exercise. Professor Ken Fox, from the department of exercise and health sciences at the University of Bristol, said: “Physical activity is a crucial component of a healthy lifestyle and we have found a growing body of evidence that indicates its importance in keeping cancer at bay. The evidence of beneficial effects is the strongest for colon cancer. To reduce their risk of cancer, people should aim to engage in physical activity of at least moderate intensity, for approximately 30 minutes on three or more days a week throughout their lifetime.”

**To Radiation Regimen, Add Spice**

Turmeric, a principal ingredient of curry, may protect cancer patients from the burns and blisters they often suffer from radiation therapy, researchers report. Although their study was conducted on mice, the researchers, from the University of Rochester Medical Center, suggested that patients undergoing radiation might want to try eating foods with curry. The lead researcher, Dr. Ivan Ding, presented his findings at a recent conference of the American Society for Therapeutic Radiology and Oncology. The substance studied was curcumin, which gives turmeric its yellow color and has been shown to have anti-inflammatory benefits. Evidence also suggests it may be able to suppress tumor growth. The researchers gave mice differing regimens of curcumin and found they had fewer radiation-related skin problems in all cases. It also appeared to enhance the benefits of the treatment. Dr. Paul Okunieff, the university’s radiation oncology chief, said the group looked at curcumin in part because turmeric has long been used to treat burns in India. Turmeric supplements are available at health food stores, but Dr. Okunieff said it was unclear how much would be needed. “It would be more or less equivalent to somewhere between half a teaspoon and a tablespoon,” he said. He rejected the notion of turmeric as an alternative medicine. “Alternative medicine becomes standard medicine when it is proven true,” he said.

**Misonix Announces Focus Surgery’s Positive Prostate Cancer Results Using High Intensity Focused Ultrasound**

Misonix, Inc. announced that Focus Surgery has released outstanding interim results for the treatment of prostate cancer using the Sonablate(R) High Intensity Focused Ultrasound (HIFU) device. Results have been obtained in both Japanese clinical trials of approximately 100 patients at 10 locations, and 15 patients in the U.S. clinical trials at Indiana University School of Medicine in Indianapolis, Indiana. Misonix currently owns approximately 20% of Focus and has the right to produce its products. The Sonablate(R) system, developed by Focus Surgery, Inc. of Indianapolis, IN, is capable of killing deep-seated cancer tissue by rapidly elevating the temperature in a precise focal zone, without affecting the intervening tissue, and without side effects such as ionization or radiation. The treatment is precise, bloodless and has minimal complications. The treatment is guided by ultrasound imaging that also combines HIFU technology. Dr. Toyoaki Uchida, MD in Tokyo, Japan released results at the September Societe Internationale d’Urologie (SIU) Meeting in Stockholm, Sweden indicating that patients in a 50 patient study with pre-treatment prostate specific antigen (PSA) scores of less than 20ng/ml have a 95% success rate and a 100% negative biopsy. Narendra Sanghvi, President of Focus Surgery, said, “Patients in the 10 to 20ng/ml PSA range represent much higher risk patients and we were still able to get good results. Even more encouraging is the low rate of complications for the patients after the treatments. Adverse effects of most prostate cancer treatments include significant blood loss, incontinence and total impotency. With HIFU, we have a bloodless, outpatient procedure.” Mike McManus, President of Misonix, said, “It is encouraging to know that our results in the United States are similar to Dr. Uchida’s in Japan. Currently, the 15 patients treated in the U.S. are experiencing a quick PSA drop and a mean PSA level of 0.44ng/ml at 180 days for an outpatient treatment with no blood loss or incontinence.”

**New Drug Could Help Target Cancer Cells With Deadly Accuracy**

A new drug that could revolutionize the impact of radiotherapy on cancer and make treatment much more effective, has been developed by Cancer Research UK scientists at Newcastle University. The drug, developed by the charity’s clinical unit at the University, has been designed to destroy the protection enjoyed by cancer cells. Radiotherapy kills cancer cells by causing damage to DNA. But the DNA damage in the patients in each body’s Sir Lancelot which is present in all cells - rides to the rescue of the beleaguered cells and can get in the way of effective treatment.

**Three Prostate Cancer Monotherapies Provide Equivalent Relapse-Free Survival**

Three monotherapies for treating T1/T2 adenocarcinoma of the prostate provide similar rates of five-year biochemical relapse-free survival, suggesting that side effects, not efficacy, should be the main consideration in selecting a therapy. Dr. Louis Potters, chief of radiation oncology at Memorial Sloan-Kettering Cancer Center’s Mercy Hospital, New York, United States, and colleagues presented their findings at the American Society for Therapeutic Radiology and Oncology (ASTRO) 44th Annual Meeting, in New Orleans, Louisiana. The researchers reviewed the biochemical relapse-free survival in 1,866 consecutive patients receiving permanent seed implantation (PI), external beam radiotherapy (EBRT) to a minimum 70 Gy, or radical prostatectomy (RP). All patients had clinically localized stage T1/T2 prostate cancer treated between 1992 and 1998. Three and forty eight of the patients were treated with EBRT, 783 were treated with RP, and 735 were treated PI. Over 90 percent of the patients in each treatment group were stage T1-T2a, and the rest were T2b. About three-fourths of the patients in each treatment group had an initial prostate-specific antigen (PSA) level of 10 ng/ml or less and a Gleason score of six or less. Median follow-up time was 54 months for all cases. Biochemical relapse was defined as any detectable PSA value greater than 0.2 ng/ml for patients receiving RP, or three consecutive PSA value rises for those receiving EBRT or (continued on page 4)
NEWS You Can Use (continued from page 3)

Pl. The 5-year biochemical relapse-free survival rates for cases treated with Pl, EBRT, and RP were 82 percent, 77 percent, and 83 percent, respectively (p=0.082); the 7-year biochemical relapse-free survival rates were 74 percent, 77 percent and 79 percent, respectively. Multivariate analysis identified initial PSA (p<0.001), Gleason score (p<0.001), and clinical T-stage (p=0.035) as independent predictors of biochemical relapse-free survival. In contrast, treatment modality, age, and race were not predictors. “We are encouraged that our results confirmed that of these other studies,” Dr. Potters told Doctor’s Guide. “Further, our study examined only monotherapy so that the results are unencumbered by adjuvant therapies or the addition of radiation,” he added. Dr. Potters continued to say that the treatment decision for a man with prostate cancer may be better based on side effects rather than that of biochemical outcome. “Further, the results imply excellent biochemical control regardless of which therapy is chosen,” he added.

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MEN WITH OSTEOSPOROSIS OFTEN OVERLOOKED
Men are far less likely than women to receive treatment for bone loss after suffering a hip fracture, an injury that could be potentially fatal, a new survey released Sunday reveals. Researchers led by Gary M. Kiebzak of Baylor College of Medicine analyzed the medical records of 110 men and 253 women who were hospitalized for hip fractures and found men with osteoporosis were overlooked repeatedly. Bone mineral density among men was “just one of those things that we didn’t look at before,” Kiebzak told United Press International.

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SCIENTISTS TAKE NEW APPROACH TO FIGHT CANCER
British scientists are trying to develop a drug that mimics the action of a natural protein in the body, which could pave the way for a new approach to fighting cancer. Unlike chemotherapy drugs, which kill cancerous and healthy cells and produce serious side effects, the new drug would selectively destroy only the diseased cells.

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VITAMIN D FOR PROSTATE CANCER
Though studies are not conclusive, researchers say vitamin D deficiency may play a role as a potential risk factor for prostate cancer. In fact, massive doses of the vitamin may help treat the disease. In a study out of Oregon Health & Science University, 25 percent of patients showed dramatic drops in their PSA levels. Most had their levels drop by 50 percent. Oncologist Tomasz Beer, M.D., tells Ivanhoe, “Taxotere alone works in about 40 percent of patients, we saw over 80 percent of patients respond to the combination, so we’re very encouraged by those earlier results.” In the next phase of the study, researchers are recruiting more than 200 patients at about 20 medical centers in the United States.

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KOREAN RED GINSENG MAY TREAT IMPOTENCE
Korean red ginseng, a herb considered an aphrodisiac in some Asian countries, seems to be an effective treatment for erectile dysfunction, according to the results of a small study from Korea. SOURCE: The Journal of Urology 2002;168:2070-2073.

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CANCER TEST SHOWS 100% SENSITIVITY AND SPECIFICITY
The results of multisite clinical trials have shown that a new blood test for cancer detection, based on molecular fingerprinting, correctly identified 177 patients known to have lung, breast, gastrointestinal, or prostate cancer; and also correctly ruled out cancer in each of the 72 control patients. The data were performed at Karolinska Institute (Solna, Sweden) by Dr. Toomas Neuman, chief scientific officer of CeMines, Inc. (Evergreen, CO, USA), which developed the test. Based on the data, Karolinska has initiated a 4,500 patient study of the cancer-detection technology. CeMines noninvasive molecular fingerprinting technology is extremely promising, and the idea behind this approach is brilliant, said Dr. Madis Metsis, principal investigator of the study now under way at Karolinska. The next step will be systematic and well-defined analyses of tumors in order to reach the ultimate goal of molecular fingerprinting — deciphering the molecular structure of individual tumors that will help us design specific diagnostic methods and drugs to treat cancer.

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GENES EYED TO FIGHT PROSTATE CANCER
Researchers at the Baylor College of Medicine in Houston confirm that they are looking at the possible effects of a newly discovered gene in the fight against prostate cancer. The school, in its monthly newsletter, says that the gene was found to not only kill cancer of the prostate, but to create a long-lasting resistance to related cancers. Within the next year the research team doing the study says it wants to test the gene (RVTP-1) on a human patient. So far tests have only been conducted on animals, but the doctors associated with the study say they are heartened by the fact they have found a rare case of a gene that produced therapeutic results. Additionally, if the tests continue to show that use of the gene will treat not only cancer within the prostate but cancer that has spread outside it, it could mark the first time that this kind of advanced cancer might fall into the category of “treatable.” Baylor doctors also intend to make use of conventional radiation treatments in conjunction with the new gene therapy during part of their testing.

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LATEST ABSTRACTS FROM SCIENTIFIC JOURNALS

ELASTOGRAPHY IN THE DETECTION OF PROSTATIC CANCER
Cochlin, D. Li. et al. Clinical Radiology - p 1014-1020. Volume 57, Number 11, November 2002 We describe a simple, practical technique for producing elastography images of the prostate. Our standard technique for the detection of prostatic cancer is ultrasound guided systematic biopsy of the prostate, with extra targeted biopsies of any abnormal areas detected by grey-scale ultrasound. The aim of this study to determine whether adding elastography imaging with targeted biopsies of abnormal areas detects more cancers. The results of elastography imaging were evaluated against grey-scale images and biopsy data in 100 patients. Elastography detected an additional 5 cancers in the 100 patients and detected an extra 3 patients with cancer at the expense of 8 extra biopsies. This represents a significant improvement in the detection rate of prostatic cancer.

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RADIOTHERAPY AFTER RADICAL PROSTATECTOMY: IMPROVED OUTCOMES WHEN COMBINED WITH TRANSIENT ANDROGEN SUPPRESSION
C.R. King et al. Int J Radiat Oncol Biol Phys - Volume 54, Issue 2 (Supp 0). Pages 63-64. Radiotherapy combined with short-course TAS after radical prostatectomy appears to confer both a PSA relapse-free survival
advantage and an overall survival advantage when compared with RT alone. These results will need to be confirmed by current randomized trials now underway.

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SERUM PROTEOMIC PATTERNS FOR DETECTION OF PROSTATE CANCER
E. F. Petricoin et al
Journal of the National Cancer Institute, Vol. 94, No. 20, 1576-1578, October 16, 2002

Pathologic states within the prostate may be reflected by changes in serum proteomic patterns. A predicted diagnosis of benign disease or cancer was rendered based on similarity to the discriminating pattern discovered from the training set. The proteomic pattern correctly predicted 36 (95%, 95% confidence interval [CI] = 82% to 99%) of 38 patients with prostate cancer, while 177 (78%, 95% CI = 72% to 83%) of 228 patients were correctly classified as having benign conditions. For men with marginally elevated PSA levels (4-10 ng/mL; n = 137), the specificity was 71%. If validated in future series, serum proteomic pattern diagnostics may be of value in deciding whether to perform a biopsy on a man with an elevated PSA level.

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PROSTATE SPECIFIC ANTIGEN BOUNCE PHENOMENON AFTER EXTERNAL BEAM RADIATION FOR CLINICALLY LOCALIZED PROSTATE CANCER.
Rosser CJ et al

Of men with prostate cancer treated with external beam radiation therapy 12% experienced a transient increase in PSA (PSA bounce) followed by a return to pre-bounce levels after radiation. The PSA bounce phenomenon was not predictive of time to biochemical recurrence.

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MASPIN IS UP-REGULATED IN PREMALIGNANT PROSTATE EPITHELIUM
C. R. Pierson et al

An up-regulation of maspin (a novel serine protease inhibitor, has been shown to inhibit prostate tumor cell motility and invasion in vitro and to inhibit prostate tumor growth and metastasis in vivo.) expression precedes, rather than occurs at, the critical transition from premalignant prostate lesion of HGPIN to PC. Our data suggest maspin may mark an important transitional phase and play an important role in the premalignancy of the prostate gland.

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ASSOCIATION BETWEEN PROSTATE CANCER AND SERUM TESTOSTERONE LEVELS
P. L. Zhang et al

Findings show that serum total and free testosterone levels in patients with prostate cancer are altered, supporting the possibility that prostate cancer may inhibit serum testosterone levels.

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FACTORS INFLUENCING MEN'S INTEREST IN GENE TESTING FOR PROSTATE CANCER SUSCEPTIBILITY
D.D. Callier et al

Interest in genetic testing for inherited cancer susceptibility is high in the general population. Women at risk for BRCA1 and BRCA2 mutations represent the best studied populations undergoing genetic testing for cancer susceptibility. However, it is unclear whether factors influencing interest in genetic testing in women are directly applicable to men. We designed a study to examine factors associated with men’s interest in genetic testing to identify prostate cancer susceptibility. Our sample consisted of 267 men present in waiting rooms of a urology clinic in an urban area. We examined whether the concept of “monitoring” could be used to predict the interest of men in a genetic test for prostate cancer susceptibility. Our results indicated that “monitoring” trait was positively associated with interest in genetic testing in these men, but primarily for patients rather than nonpatients. Moreover we found that monitoring was associated with over estimation of risk in those men with prostate cancer. Other factors found to influence interest in genetic testing included recommendation by a doctor, family history of prostate cancer, and cost. This study indicated that interest in genetic testing and estimation of risk is influenced by a complex interaction between both psychological factors (monitoring) and nonbehavioral factors (such as patient status, cost, and doctor recommendation).

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PHASE III TRIAL OF CONFORMAL RADIOTHERAPY FOLLOWING NEOADJUVANT HORMONE TREATMENT IN EARLY PROSTATE CANCER
D. DeLarue et al
Int J Radiat Oncol Biol Phys - Volume 54, Issue 2 Supp 0, Pages 134-135

In patients treated with conformal radiotherapy following 3, 18 months of hormonal deprivation for early prostate cancer, this pilot trial confirmed low levels of acute and late toxicity and suggested improvement in biochemical control with increased radiation dose. No benefit was detected for the larger planning target volume margin. The pilot was developed into a national trial (MRC RTO1) which will compare the two dose levels in 850 patients.

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NEOADJUVANT THERAPY BEFORE RADICAL PROSTATECTOMY FOR CLINICAL T3/T4 CARCINOMA OF THE PROSTATE: 5-YEAR FOLLOWUP, PHASE II SOUTHWEST ONCOLOGY GROUP STUDY 9109.
Powell II et al

Neoadjuvant hormonal therapy followed by radical prostatectomy is reasonable and appropriate for clinical stage T3 prostate cancer. A prospective trial of patients with clinical stage T3 prostate cancer randomly assigned to neoadjuvant hormonal therapy followed by radical prostatectomy or radical prostatectomy alone has shown improved biochemical control and a survival benefit for neoadjuvant therapy followed by radical prostatectomy.

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SEQUENCING HORMONAL ABLATION AND RADIOTHERAPY IN PROSTATE CANCER: A MOLECULAR AND THERAPEUTIC PERSPECTIVE (REVIEW).
Hill B et al
Oncol Rep 2002 Nov-Dec;9(6):1151-6

Current therapeutic modalities for advanced prostate cancer are palliative in nature, with no effective treatment increasing survival in patients with metastatic prostate cancer. Apoptosis as a molecular process of genetically regulated cell death has a critical endpoint that coincides with the goal of successful treatment of prostate cancer. Expression of key regulators of the apoptotic pathway such as bcl-2 and caspases within individual prostate tumors appear to correlate with the prostate cancer cell’s sensitivity to traditional therapeutic modalities, including androgen ablation and radiotherapy. Androgen-dependent prostate tumors undergo apoptosis in response to androgen-ablation. Cancer regression after radiation occurs by disruption of the reproductive integrity of the tumor cells and via activation of the apoptotic pathway. Increasing the sensitivity of prostate tumor cells to die via apoptosis increases the efficacy of fractionated therapy by reducing tumor cell survival. Thus signaling interaction between androgen ablation and radiotherapy may be synergistic in maximally activating the apoptotic potential of prostate cancer cells. The role

(continued on page 6)
of molecular technology in identifying apoptosis regulation in association with combination hormonal ablation and radiotherapy for the treatment of advanced prostate cancer holds tremendous promise, as any approach significantly decreasing the apoptotic threshold may lead to total synergistic killing of tumor cells. This review is an attempt to summarize the current knowledge of the clinical consequences of sequencing androgen ablation and radiotherapy in the treatment of prostate cancer patients and the molecular parameters underlying a potential optimization of such a combination strategy.

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Cyclooxygenase-2 Promotes Prostate Cancer Progression
H. Fujita et al

Data demonstrate that Cyclooxygenase (COX)-2, an inducible isofrom of COX - contributes to prostate cancer progression and suggest that it mediates this effect, in part, through increased VEGF.

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Reduced Risk of PCA Among Patients With Diabetes Mellitus
Weiderpass E et al

Although diabetes mellitus is associated with an increased risk of several malignancies, a negative association with prostate cancer is biologically most plausible. The epidemiologic evidence is, however, inconsistent, limited and based mostly on small studies. We present results from a large, population-based cohort study in Sweden, where we assessed prostate cancer risk among patients hospitalized for diabetes mellitus. We found no consistent trends in risk related to age at first hospitalization or to duration of follow-up. We did find a small, but significantly decreased risk of prostate cancer among men who had been hospitalized for diabetes mellitus.

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Brachytherapy Causes Iatrogenic Shedding of Prostate Cancer Cells
Urology 2002;60:270-275

Brachytherapy can result in the iatrogenic shedding of prostate cancer cells, which may increase the risk of metastatic deposits and systemic failure, researchers report. Dr. Mansoor M. Ahmed from the University of Kentucky, Lexington reported “Our results suggest for the first time in published reports that a substantial number of patients undergoing brachytherapy have iatrogenic dissemination of prostate cancer cells in peripheral blood caused by the insertion of needles in the prostate gland,” the researchers conclude. “The detection of PSA mRNA in the peripheral circulation appears to have a significant correlation with biochemical failure after interstitial brachytherapy and needs additional study in a larger patient population.”

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The Percentage of Free Prostatic-Specific Antigen Is Also Useful in Men With Normal Digital Rectal Examination and Serum Prostatic-Specific Antigen Between 10.1 and 20 ng/ml
J. Morote et al
European Urology / Volume 42 , Issue 4 , Pages 333-337

This prospective study demonstrates that the percentage of free PSA seems to have similar utility when serum PSA levels are between 4.1 and 10 ng/ml and between 10.1 and 20 ng/ml at the time of the first prostate biopsy indication.

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Screening: With Low PSA Cutoff Values Results in Low Rates of Positive Surgical Margins in Radical Prostatectomy Specimens
A. P. Berger et al

As tumor stage and surgical margin status after radical prostatectomy are important predictors of the likelihood of PSA recurrence, which necessitates additional therapy, these findings support the concept of PSA screening by using low PSA cutoff levels.

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Algorithm Helps Predict Lymph Node Metastases in Prostate Cancer
Cancer 2002;95:1016-1021

The biopsy-based Hamburg algorithm is a valid means of predicting lymphatic spread in patients with clinically localized prostate carcinoma, researchers from Germany and the US report in the September 1st issue of Cancer. Dr. Alexander Haese, who is currently at the University Clinic Hamburg-Eppendorf, and colleagues point out that the algorithm is based on the Gleason grade of a systematic sextant biopsy and uses classification and regression tree analysis. Patients are deemed as being of low, intermediate or high risk for lymph node involvement. To investigate the validity of the algorithm at a center other than the one where it was developed, the researchers applied it to a cohort of 443 men who underwent systematic sextant biopsy and radical retropubic prostatectomy with staging lymphadenectomy at the Johns Hopkins University Medical Institution, Baltimore. Overall, 20 of the patients (4.5%) had lymph node metastases. Metastases were seen in 44.4% of the 9 patients classified as being in the high-risk group, 20.0% of the 30 patients in the intermediate-risk group and 2.47% of the 404 patients in the low-risk group. For the low-risk group, the negative predictive value of the algorithm was 97.52% and the specificity was 94.14%. Thus, Dr. Haese told Reuters Health, “the Hamburg Algorithm has been shown to withstand external validation as a tool to predict the likelihood of lymph node metastases in an individual patient. Furthermore, it can reduce expense and provide additional criteria on which to base treatment decisions.”

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Carcinoma Extent in Prostate Needle Biopsy Tissue in the Prediction of Whole Gland Tumor Volume in a Screening Population
J. S. Lewis, Jr et al

Increasing prostate tumor volume has been shown to correlate with numerous adverse prognostic indicators for patients with prostate carcinoma. The ability to predict tumor volume from pretreatment parameters is potentially critical in the stratification of patients for different management strategies. Findings highlight the importance of reporting quantitative measures of tumor amount in prostate needle biopsy specimens; several measures of tumor extent (vs 1 measure) provide maximal information on prostate cancer size.

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Value Of Contrast Ultrasonography In The Detection Of Significant Prostate Cancer: Correlation With Radical Prostatectomy Specimens
J.P.M. Sedelaar et al

Three-dimensional contrast-enhanced power Doppler ultrasonography (3D-CE-PDU) improves the detection of prostate cancer in this group of prostate cancer patients. Use in the clinic is questionable as indications are still unclear.
GARLIC & HERBS FIGHT PCA
(continued from page 1)

For example, prostate cancers are historically rare among Asians who live their entire lives in Asia, Nelson said, but Asians who immigrate to the United States often develop the same risk for the disease as American and western European men.

Allium vegetables are rich in flavonols and organosulfur compounds, which have been shown to fight tumors in laboratory studies.

“It may be more practical to focus future research on identifying the active anti-cancer components in these vegetables and using concentrated forms ... in future clinical trials for prostate cancer prevention and treatment,” urologist William Aronson of the Jonsson Comprehensive Cancer Center at University of California, Los Angeles, told UPI.

A second study appearing in JNCI focused on a patented product called PC-SPES, which consists of eight herbs, seven of them from China. Although some studies have shown PS-SPES can reduce prostate cancer indicators — even when the disease has metastasized — this is the first study to identify the mechanism at the cellular level, researcher Peter Nelson told UPI.

“A some component in PC-SPES inhibited the synthesis of structures within cells called microtubules that are involved with the cell’s support scaffolding structure,” said Nelson, an oncologist at the Fred Hutchinson Cancer Research Center in Seattle. “Inhibiting the synthesis results in cancer cell death,” he said.

However, the study also found PC-SPES can interfere with the therapeutic effects of paclitaxel, a commonly used drug for prostate cancer, so researchers concluded PC-SPES and paclitaxel should not be taken together.

Although the eight-herb mixture — which includes chrysanthemum, licorice, saw palmetto and panax pseudo-ginseng — has been shown to be effective, researchers still want to know how it works.

“Ultimately, what needs to be done is separate all the active PC-SPES components ... and then test them for anti-cancer activity,” said H. Phillip Koeffler, chief of hematology-oncology at Cedars Sinai Medical Center in Los Angeles and also a member of the Jonsson Comprehensive Cancer Center. “Then the components would need to be combined in different mixtures to see which works best.”

PC-SPES, which is associated with some increase in blood clotting, was taken off the market earlier this year when low levels of prescription blood thinners and certain hormones were found in the product. Other manufacturers now are producing a variation claimed to be similar in effect. Nelson said he would like to see PC-SPES come back on the market in an uncountaminated version.

“While we have now demonstrated that combining proteomic technology with artificial intelligence based bioinformatics can be a powerful tool, and is a new paradigm in the detection and diagnosis of both ovarian and prostate cancers,” said Lance Liotta, MD, PhD, the senior investigator on the study from NCI’s Center for Cancer Research. “We are extremely optimistic that this new approach will prove useful in detecting and diagnosing many other cancers and diseases in the future.”

PROTEIN PATTERN PREDICTS DIAGNOSIS
(continued from page 1)

PSA in this range,” said Emanuel Petricoin III, PhD, of the FDA’s Center for Biologics Evaluation and Research, the first author of the study. “We hope that by using proteomic pattern analysis screening in combination with other screening methods, we can reduce the number of unnecessary biopsies for prostate cancer in the future.”

The diagnostic test relied on computer software that detects key patterns of small proteins in the blood. Researchers analyzed serum proteins with mass spectroscopy, a technique used to sort proteins and other molecules based on their weight and electrical charge. Then they used an artificial intelligence program developed by Correlogic Systems, Inc., in Bethesda, Maryland, to train a computer to identify patterns of proteins that differed between patients with prostate cancer and those in which a biopsy had found no evidence of disease. These patterns were identified using serum samples from 56 patients who had undergone a biopsy and whose disease status was known.

Once established, the protein patterns were then used to predict diagnosis in a separate group of patients, whose biopsy results were not known by the researchers. From this group, researchers were able to correctly identify 36 of 38 (95%) cases of prostate cancer and 177 of 228 (78%) cases of benign disease.

The study follows up on the recent finding by the same research group that protein patterns in serum can be used to detect ovarian cancer.

“ ‘We have now demonstrated that combining proteomic technology with artificial intelligence based bioinformatics can be a powerful tool, and is a new paradigm in the detection and diagnosis of both ovarian and prostate cancers,’ ” said Lance Liotta, MD, PhD, the senior investigator on the study from NCI’s Center for Cancer Research. “ ‘We are extremely optimistic that this new approach will prove useful in detecting and diagnosing many other cancers and diseases in the future.’

GENE MUTATION DOUBLES PCA RISK
(continued from page 1)

cluding the death of cancer cells. When RNASEL is mutated, one of the brakes to uncontrolled cell growth is removed, which in turn leads to the development of cancer.

Studies from the laboratory of Robert Silverman, Ph.D., of the Cleveland Clinic Lerner Research Institute indicate that the R462Q variant cripples the normal function of RNASEL, but does not stop it from working altogether. As a result, its effectiveness in preventing uncontrolled cell growth is weakened, thereby increasing the chances of a cell turning cancerous.

In a study published earlier this year in Nature Genetics involving Dr. Silverman and colleagues, the RNASEL gene was associated with increased risk of prostate cancer in families with a history of the disease. In Dr. Casey’s study, a specific common alteration in the RNASEL gene was identified as being crucial to increased risk in all men who carry the R462Q variant, not just in those with a family history of prostate cancer.

The study involved collaborative efforts by doctors from the Cleveland Clinic Lerner Research Institute; Case Western Reserve University; Washington University; and the National Human Genome Research Institute.

SOURCE The Cleveland Clinic
rates are atypical because its patients are younger and healthier than most prostate cancer patients.

In the latest study, lead author Leslie R. Schover, a psychologist at Houston’s M.D. Anderson Cancer Center, and doctors at the Cleveland Clinic analyzed demographic characteristics of patients and treatments to determine which factors were related to better sexual outcomes.

Schover’s team found that age was strongly associated with a return to potency: The younger the man, the better the outcome. The average age of men in the study was nearly 69, older than men in previous studies of the sexual side effects of prostate cancer.

Men who underwent nerve-sparing prostatectomy or brachytherapy fared better sexually than those who opted for conventional external beam radiation or hormonal treatments, the researchers found. Patients who took hormones fared poorest, possibly because the drugs suppress testosterone, the male sex hormone.

The researchers found that the men who underwent surgery, especially those who had nerve-sparing prostatectomy, reported more success using Viagra than the brachytherapy group.

And men who chose treatment based in part on its effect on sexual function fared better than those who did not consider potency to be important.

**Breast Gene Fault Increases PCA Risk**

A genetic fault that makes women more susceptible to breast and ovarian cancer also raises a man’s risk of developing prostate cancer, a British scientist said.

Dr. Ros Eeles, a medical geneticist at The Institute of Cancer Research in southern, England, told a medical conference that men with an inherited defect in the BRCA 2 gene have a five-to-seven-fold increased risk of prostate cancer than those without the fault. She announced plans to launch a European-wide study of 500 men who have four or more close relatives who have developed breast cancer before the age of 60. They may have inherited the mutation and would be more likely to develop prostate cancer.

“We are trying to see if you can identify a high-risk group (of men) that you can target for screening.” Eeles told the first annual meeting of the medical charity Cancer Research UK.

Forty percent of early onset, aggressive prostate cancers are linked to inherited factors. Some are due to alterations in the BRCA 2 gene, according to Eeles.

The trial, which is due to begin in December or January, will be among the first to use genetic screening to target men in this way.

“The crucial thing about screening for prostate cancer is to identify those men with a high risk of an aggressive form of the disease,” Eeles added. “At the moment it is the best test we’ve got.

The BRCA 2 gene mends damage to DNA. Mutations in the BRCA 1 and BRCA 2 genes increase breast cancer risk. Eeles and her colleagues will screen the men with the BRCA 2 mutation with the PSA test for five years and offer biopsies to men with raised levels of the antigen.

They will compare the number of men who develop the illness with results from a randomized PSA trial of men being done in the Netherlands. “As scientists’ understanding of cancer genetics improves, pressure on screening programs will increase dramatically and it will not be possible to screen every man — we need a more targeted approach,” Eeles added.

**Latest News From Scientific Journals**

(continued from page 6)

**Gleason Score on Biopsy: Is It Reliable for Predicting the Final Grade on Pathology?**

J.-B. Lattouf et al

BJU International - Volume 90 Issue 7

Page 694 - November 2002

Gleason grading of the prostate biopsy remains a poor predictor of pathological outcome. Assessment by the same pathologist reduces the discrepancy but over half the patients are under- or overgraded on final pathology. Clinicians should be aware of these limitations when using the biopsy Gleason grade in decision making.

**Survival Prospects After Screen-Detection Of Prostate Cancer**

P.W. Nicholson et al

BJU International - Volume 90 Issue 7

Page 686 - November 2002

Screening detects prostate cancer a mean of 9 years before clinical presentation. The prognosis of screen-detected prostate cancer is considerably better than that of conventionally presenting localized disease. The advice given to patients with early prostate cancer should take account of this.