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PROSTATE CANCER
EDUCATION & SUPPORT

HOTSHEET

February 2010

ERSPC STUDY SHOWS PSA SCREENING REDUCED PROSTATE CANCER DEATHS BY 20 PERCENT

The effectiveness of PSA (prostate-specific antigen) screening on reducing prostate cancer mortality has been given a boost with new data from the European Randomized Study of Screening for Prostate Cancer (ERSPC). This shows the true impact to be much higher than what was previously reported – up to a 31 percent reduction in mortality.

Preliminary ERSPC findings showed that screening reduced prostate cancer deaths by 20 percent. This latest ERSPC analysis corrects for non-attendance and contamination to assess the true effectiveness of PSA testing in men actually screened (see <www.erspc.org.com> for the update to the ERSPC study).

From 1992, the ERSPC study randomized 162,000 men, aged 55 to 69, in seven European countries to either a screening arm or a control group. Those screened were given a blood test to detect PSA levels: if it was 3.0 ng/ml or more, they were offered a biopsy. Screening took place on average every four years. Mean followup was nine years.

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PSA VELOCITY MAY HELP IDENTIFY INSIGNIFICANT PROSTATE CANCER

PSA velocity (PSAV), increasingly recognized as a marker of potentially lethal prostate cancer, can also predict the likelihood that a given patient's cancer is insignificant, researchers say.

"A controversy of current PSA-based prostate cancer screening is the over detection of potentially insignificant prostate cancer," Dr. William J. Catalona, of Northwestern Feinberg School of Medicine, Chicago, and colleagues write. "A promising marker is prostate specific antigen velocity (rapidly increasing PSA)."

The 2010 National Comprehensive Cancer Network Guidelines recommend a PSAV threshold of about 0.35 to 0.4 ng/mL per year for prostate cancer screening protocols. Dr. Catalona and his co-authors sought to determine "whether this PSAV threshold is associated with...histologically insignificant prostate cancer at radical prostatectomy (RP)."

As they report in the January issue of the *Journal of Urology* (Vol. 183, pp. 112-7, 2010), their study focused on 1073 men who underwent RP between 1992 and 2008. Insignificant prostate cancer was defined (on the basis of the

(Continued on page 8)

NCCN PROSTATE CANCER GUIDELINES STRESS CAREFUL CONSIDERATION OF ACTIVE SURVEILLANCE

The National Comprehensive Cancer Network (NCCN) recently updated the NCCN Clinical Practice Guidelines for Oncology™ for Prostate Cancer to reflect new recommendations regarding active surveillance, also referred to as watchful waiting, for men with low risk prostate cancer.

A significant change incorporated into the updated NCCN Guidelines for Prostate Cancer is the recommendation for active surveillance and only active surveillance for many men diagnosed with prostate cancer. Men with low risk prostate cancer who have a life expectancy of less than 10 years should be offered and recommended active surveillance.

In addition, a new "very low risk" category has been added to the updated NCCN Guidelines using a modification of the Epstein criteria for clinically insignificant prostate cancer. Only active surveillance is offered and recommended for men in this category when life expectancy is less than 20 years.

"The NCCN Prostate Cancer Guideline Panel and the NCCN Prostate Cancer Early Detection Panel remain concerned about over-diagnosis and

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AN UPDATE OF THE GLEASON GRADING SYSTEM

Epstein JI

J Urol [Epub ahead of print]

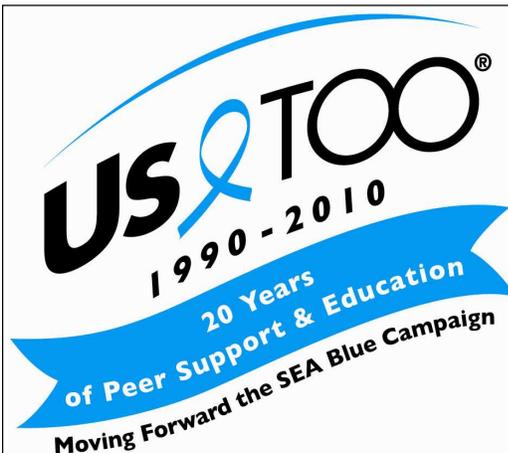
PURPOSE: An update is provided of the Gleason grading system, which has evolved significantly since its initial description.

MATERIALS AND METHODS: A search was performed using the MEDLINE(R) database and referenced lists of relevant studies to obtain articles concerning changes to the Gleason grading system.

RESULTS: Since the introduction of the Gleason grading system more than 40 years ago many aspects of prostate cancer have changed, including prostate specific antigen testing, transrectal ultrasound guided prostate needle biopsy with greater sampling, immunohistochemistry for basal cells that changed the classification of prostate cancer and new prostate cancer variants. The system was updated at a 2005 consensus conference of international experts in urological pathology, under the auspices of the International Society of Urological Pathology. Gleason score 2-4 should rarely if ever be diagnosed on needle biopsy, certain patterns (i.e. poorly formed glands) originally considered Gleason pattern 3 are now considered Gleason pattern 4 and all cribriform cancer should be graded pattern 4. The grading of variants and subtypes of acinar adenocarcinoma of the prostate, including cancer with vacuoles, foamy gland carcinoma, ductal adenocarcinoma, pseudohyperplastic carcinoma and small cell carcinoma have also been modified. Other recent issues include reporting secondary patterns of lower

and higher grades when present to a limited extent, and commenting on tertiary grade patterns which differ depending on whether the specimen is from needle biopsy or radical prostatectomy. Whereas there is little debate on the definition of tertiary pattern on needle biopsy, this issue is controversial in radical prostatectomy specimens. Although tertiary Gleason patterns are typically added to pathology reports, they are routinely omitted in practice since there is no simple way to incorporate them in predictive nomograms/tables, research studies and patient counseling. Thus, a modified radical prostatectomy Gleason scoring system was recently proposed to incorporate tertiary Gleason patterns in an intuitive fashion. For needle biopsy with different cores showing different grades, the current recommendation is to report the grades of each core separately, whereby the highest grade tumor is selected as the grade of the entire case to determine treatment, regardless of the percent involvement. After the 2005 consensus conference several studies confirmed the superiority of the modified Gleason system as well as its impact on urological practice.

CONCLUSIONS: It is remarkable that nearly 40 years after its inception the Gleason grading system remains one of the most powerful prognostic factors for prostate cancer. This system has remained timely because of gradual adaptations by urological pathologists to accommodate the changing practice of medicine.



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COFFEE MAY CUT RISK OF PROSTATE CANCER

Drinking coffee regularly may help lower the risk of advanced prostate cancer, a study shows. The study, presented this week at a conference of the American Association for Cancer Research in Houston, TX shows men who drank the most coffee were nearly 60% less likely to develop advanced prostate cancer than non-coffee drinkers.

In the study, researchers analyzed information from the Health Professionals' Follow-Up Study, which included data on the coffee-drinking habits of nearly 50,000 men from 1986 to 2006. During that time period, 4,975 of the men developed prostate cancer. The results showed men who drank the most coffee (six or more cups per day) had a 59% lower risk of aggressive prostate cancer (fatal or advanced disease) compared to non-coffee drinkers.

But researchers say it's not just caffeine that's responsible for the prostate cancer prevention benefits. The study showed men who drank decaffeinated coffee also had a similar reduction in aggressive prostate cancer risk. Researchers say coffee also contains many other potentially beneficial compounds such as antioxidants and minerals that may play a role in preventing prostate cancer and more research is needed to confirm these results.

"Coffee has effects on insulin and glucose metabolism as well as sex hormone levels, all of which play a role in prostate cancer," says researcher Kathryn M. Wilson, PhD, a postdoctoral fellow at the Channing Laboratory, Harvard Medical School and the Harvard School of Public Health. But, she added that it's too early to recommend men start drinking coffee to help prevent prostate cancer.

WebMD Health News, 8 December 2009

Want to learn more about local prostate cancer support group activities? Read the

CHAPTER NEWS!

at www.ustoo.org

PSA SCREENING REDUCED PROSTATE CANCER DEATHS

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In any randomized trial, some in the screening arm do not attend and some in the control group inadvertently receive a PSA test (contamination).

Contamination makes it difficult to detect differences. This is believed to be one reason why the Prostate Lung, Colon and Ovarian (PLCO) study failed to detect any significant reduction in mortality.

PSA cut off level of 3 ng/ml is safer threshold for reducing biopsies

Using retrospective data from the Dutch arm, the ERSPC has shown that using a screening algorithm – an individual risk assessment - alongside PSA testing can reduce the number of unnecessary biopsies. PSA testing is

sensitive but not specific, so elevated levels do not necessarily imply cancer. Approximately 30 percent of detected cancers are non-aggressive (indolent) or slow growing.

Their findings, published online in the January 2010 issue of *European Urology* suggest a PSA cut off of 3 ng/mL combined with an individual risk assessment would reduce biopsies by 33%. The majority of cancers potentially missed would be indolent, so no risk would occur from non-treatment. Increasing the PSA cut-off level from 3 to 4 ng/ml may save a similar number of biopsies, but will miss more clinically significant cancers.

*<www.news-medical.net>
8 December 2009*

RADIOFREQUENCY ABLATION SAFE AND EFFECTIVE FOR REDUCING PAIN FROM BONE METASTASES

Image-guided radiofrequency ablation (RFA), a minimally invasive cancer treatment which can be performed in the outpatient setting, significantly reduced the level of pain experienced by cancer patients with bone (osseous) metastases, limiting the need for strong narcotic pain management, and supporting improved patient frame of mind, according to results of an American College of Radiology Imaging Network (ACRIN) study published online in the journal *Cancer*.

RFA uses heat to kill, or ablate, tumor cells. This study, sponsored by the National Cancer Institute (NCI), part of the National Institutes of Health (NIH), demonstrated that RFA, often used to treat liver, kidney and lung cancer tumors, is also a safe and effective pain management tool for patients with bone metastases.

"It is clear that improved palliative treatments must be identified to address the needs of these great many patients. RFA is widely available, covered by most insurance, can be performed in a single outpatient session and often allows patients enhanced interaction with loved ones by reducing use of strong narcotics which can leave them in a medicated state. Also, unlike many other cancer pain man-

agement treatments, RFA can be repeated and maintain similar results," said Damian Dupuy, MD, principal investigator of the study, director of ablation services at Rhode Island Hospital, and professor of diagnostic imaging at The Warren Alpert Medical School of Brown University.

The researchers studied 55 patients who had a single painful bone metastasis. Each received computed tomography (CT) guided RFA of the tumor. Patients evaluated their pain prior to treatment, then daily for two weeks following the procedure, and again at one month and three months after RFA. The study results showed statistically significant pain reduction at the one and three-month follow-ups for all pain assessment measurements: pain relief, intensity and severity. In all cases, improvement was seen for each measurement, including patient mood, with the most improvement at the one-month interval.

"We know that RFA is a highly effective cancer treatment when surgery is not an option. RFA offers potential advantages over other methods in that cell death is immediate, lesion size can be accurately controlled, lesion tem-

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ASK DR. SNUFFY MYERS

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Dear Dr. Myers:

Many men would love to use second line hormone treatment but cannot find a local doctor who has the background and ability to monitor the patient for side effects and prostate health. How do we find doctors who are able to monitor our health using second line hormone treatment?

The first question is what qualifications are needed to administer second line hormonal therapy properly. Initial hormonal therapy using Lupron and/or Casodex is commonly done well by both urologists and medical oncologists. Additionally, many radiation oncologists have experience using hormonal therapy in combination with radiation therapy. Things can be much different when it comes to second line hormonal therapy.

Estrogens

Perhaps the second line hormonal therapy is estrogen, the female sex hormone. There are many estrogen-like drugs available. Diethylstilbestrol (DES) is a synthetic drug that acts like estrogen and can be given orally. In the past, oral administration was associated with significant cardiovascular side effects, such blood clots, swollen ankles and high blood pressure. However, when given at a lower dose and along with modern diuretics, blood pressure drugs and anticoagulants DES is a much more useful agent.

More recently, estradiol, the normal human estrogen, has come to the fore. One attractive form is estradiol skin patches, which have been widely studied in women to manage menopausal symptoms. A major attraction is a reduced risk of cardiovascular complications compared with oral therapy. While this has been well documented in postmenopausal women, there are only two papers that report this advantage in men with advanced prostate cancer. In addition, no studies have

directly compared the efficacy of the two drugs against prostate cancer. Nonetheless, in clinical practice they do appear to be roughly equivalent.

Both urologists and medical oncologists often have extensive experience in the use of these various forms of estradiol. In most large communities, it should not be difficult to find someone who understands and is comfortable with the use of these agents.

Ketoconazole

Another second line hormonal therapy is ketoconazole, first shown to have activity against prostate cancer in 1982. Virtually all practicing urologists and medical oncologists have had some experience using this drug during medical training. Principally used as an antifungal agent, it is available as a generic and usually covered by prescription insurance. Used correctly, its response rate can approach 50% in patients that develop a rising PSA on Lupron and/or Casodex treatment.

Unfortunately, it is not optimally utilized in the community setting for a number of important reasons. In addition it has drug interactions with several commonly used prescription drugs. The Prostate Forum website has a nice discussion of the issues to consider when you consider using this drug – you can read the full article at <www.prostateforum.com>.

The final issue with ketoconazole is that it is best absorbed when the stomach contents are acid. Many men have low stomach acidity because of aging or because they are on medications to decrease stomach acid. We recommend taking ketoconazole with an acid beverage such as fruit juice or a carbonated beverage. Vitamin C 200-500 mg taken with each dose of ketoconazole will also improve absorption.

So, it may be easy to find a physician to prescribe ketoconazole, but you may have difficulty getting the drug delivered to you in an optimal manner. So, it is very important that you have a good relationship with your physician that allows discussion of these details.

To submit a question to Dr. Myers, please email it to ustoo@ustoo.org.

GAT'S HYPOTHESIS FOR THE CAUSE OF MOST PROSTATE CANCERS

In the May 2009 issue of *Andrologia*, Gat et al reported the discovery of a previously unrecognized route of flow of free testosterone to the prostate via the testicular and prostate venous drainage systems. They showed that varicocele caused deviation of the testicular venous flow from its normal route to the prostate. Measured levels of free testosterone in the venous blood was 130 times higher than the normal physiological concentration.

In the first part of the study, the authors tested 72 men with localized prostate cancer and found that all of them had varicoceles in one or both of their internal spermatic veins. In the second part of the study, they treated 6 men with varicoceles and biopsy-proven prostate cancer with an interventional radiological procedure to correct abnormal venous blood flow.

Results appear in the table below:

Parameter	Before procedure	6 month afterwards
Prostate volume	65.3 mL	36.0 mL
Serum PSA	8.89 ng/mL	5.95 ng/mL
# with + biopsies	6 of 6	1 of 6

The authors refer to the microsurgical varicocelectomy procedures they did as “super-selective intraprostatic androgen deprivation” although it is not clear to what extent the free testosterone concentrations in the internal spermatic veins declined.

The authors present some of the unresolved biological enigmatic questions associated with prostate cancer and discuss how they may relate to their hypothesis. Gat and colleagues conclude that the “backflow” of androgen from the testes to the prostate might possibly be a mechanism for the development of prostate cancer.

The hypothesis proposed by Gat and his colleagues may seem completely “off the wall” to many. However, some advocates such as those with the “New”

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PSA VALUE AT TWO YEARS POST-TREATMENT CAN PREDICT LONG-TERM SURVIVAL IN PROSTATE CANCER PATIENTS

Prostate cancer patients having a PSA value less than or equal to 1.5 ng/mL at 2 years after external beam radiation therapy (EBRT) are less likely to have a cancer recurrence and cancer-related death, according to a study in the 1 December 2009 issue (Vol. 75, pp. 1350-6) of the *International Journal of Radiation Oncology*Biophysics*Physicists*, the official journal of the American Society for Radiation Oncology.

PSA levels after a successful course of EBRT should decline gradually over the following 18 to 24 months. A continued rise in PSA can indicate relapsing disease. Prior studies attempted to categorize PSA response patterns, but most did not use a fixed point after RT to predict outcomes.

Researchers at the Memorial Sloan-Kettering Cancer Center Department of Radiation Oncology and Epidemiology and Biostatistics in New York sought to determine the significance of a patient's reaching a certain PSA level at a specific point in time after EBRT.

The study authors found that patients with a PSA value of less than or equal to 1.5 at two years had a 2.4 and 7.9 percent incidence of distant metastases at 5 and 10 years after treatment respectively. Patients with a PSA value higher than 1.5 experienced a significantly higher rate of metastases at 5 and 10 years after treatment (10 percent and 17.5 percent, respectively).

"In the past, patients with a relapsing cancer after receiving radiation were not identified until several years after treatment and at that point it may be too late to effectively salvage their recurrence," Michael Zelefsky, MD, lead author of the study and a radiation oncologist at Memorial Sloan-Kettering Cancer Center, said.

"If we can catch these future instances of cancer recurrence earlier in prostate cancer patients, then we have a much higher chance of reducing the mortality associated with the cancer."

Science Daily, 2 December 2009

NANOSENSORS USED TO MEASURE CANCER BIOMARKERS IN BLOOD

For the first time, Yale University researchers used nanosensors to measure cancer biomarkers in whole blood. Their findings, appearing online 13 December 2009 in the journal *Nanotechnology*, could dramatically simplify the way physicians test biomarkers of cancer and other diseases.

The team – led by Mark Reed, Yale's Harold Hodgkinson Professor of Engineering & Applied Science, and Tarek Fahmy, an associate professor of biomedical and chemical engineering – used nanowire sensors to detect and measure concentrations of two specific biomarkers: one for prostate cancer and the other for breast cancer.

To overcome the challenge of whole blood detection, the researchers developed a novel device that acts as a filter, catching the biomarkers – in this case, antigens specific to prostate and breast cancer – on a chip while washing away the rest of the blood. Creating a buildup of the antigens on the chip allows for detection down to extremely small concentrations, on the order of picograms per milliliter, with 10 percent accuracy. This is the equivalent of being able to detect the concentration of a single grain of salt dissolved in a large swimming pool.

"This new method is much more precise in reading out concentrations, and is much less dependent on the individual operator's interpretation," Fahmy said. Many current tests can also be labor intensive and can take hours to days to provide results. The new device is able to read out biomarker concentrations in a just a few minutes.

"Doctors could have these small, portable devices in their offices and get nearly instant readings," Fahmy said. "They could also carry them into the field and test patients on site."

The new device could also be used to test for a wide range of biomarkers at the same time, from ovarian cancer to cardiovascular disease, Reed said.

"We've brought the power of modern microelectronics to cancer detection."

ScienceDaily, 14 December 2009

ACTIVE SURVEILLANCE

(Continued from page 1)

over-treatment of prostate cancer," says James L. Mohler, MD, of Roswell Park Cancer Institute and chair of the NCCN Guidelines Panel for Prostate Cancer. "Growing evidence suggests that over-treatment of prostate cancer commits too many men to side effects that outweigh a very small risk of prostate cancer death."

The updated NCCN Guidelines now recommend active surveillance for men with very low risk prostate cancer and life expectancy estimated at less than 20 years or men with low risk prostate cancer and life expectancy estimated at less than 10 years.

"Although the NCCN Guidelines Panel stresses the importance of considering active surveillance, ultimately this decision must be based on careful individualized weighting of a number of factors including life expectancy, disease characteristics, general health condition, potential side effects of treatment, and patient preference," notes Dr. Mohler. "It is an option that needs to be thoroughly discussed with the patient and all of his physicians which may include his urologist, radiation oncologist, medical oncologist, and primary care physician."

The updated NCCN Guidelines stress that active surveillance involves actively monitoring the course of the disease with the expectation to intervene if the cancer progresses. Patients under active surveillance must commit to a regular schedule of follow-up, which includes a prostate exam and PSA, and which may include repeat prostate needle biopsies. The most recent version of this and all the NCCN Guidelines are available free of charge at <www.NCCN.org>.

The NCCN Clinical Practice Guidelines in Oncology™ are developed and updated through an evidence-based process with explicit review of the scientific evidence integrated with expert judgment by multidisciplinary panels of physicians from NCCN Member Institutions. The NCCN is a not-for-profit alliance of 21 of the world's leading cancer centers and is dedicated to improving the quality and effectiveness of cancer care.

BUSINESS WIRE, 7 January 2010

DOC MOYAD'S WHAT WORKS & WHAT IS WORTHLESS COLUMN, ALSO KNOWN AS "NO BOGUS SCIENCE" COLUMN

"Hot off the press! Hot off this Hot Sheet! Most men do not ask their doctor for conventional treatment for their hot flashes! Why is this so important?"

Mark A. Moyad, MD, MPH,
University of Michigan Medical Center, Department of Urology

Editors' note: In the spirit of information sharing, we have invited certain physicians and others to provide comments and opinions for Us TOO's *HotSheet*. It is our desire to enrich the content of the *HotSheet* to empower the reader. Each piece contains the opinions and thoughts of its author and is not necessarily those of Us TOO International.

Bottom line:

Hot flashes are not fun for men on androgen deprivation treatment (ADT)! However, a recent large study¹ suggests that most do not need or request conventional treatment for hot flashes, but if they do need prescription medication, the progesterone medications work really, really well!

Ohio State wins a BCS bowl game!
Michigan does not make a bowl game!
Tiger Woods gets into trouble! Wow!
These were some of the hot off the press stories of 2009.

Another hot subject – hot flashes – received a fabulous study at the end of 2009 that did not seem to get much attention. The drug venlafaxine (75 mg daily) went up against progesterone pills (medroxyprogesterone acetate, 20 mg daily) for 12 weeks and the winner was the progesterone pill!

In fact, about 20% of the men had their hot flashes almost completely go away! Now, that is the good news for men because they can get medroxyprogesterone as an injection or they can take it as a progesterone pill (megesterol acetate is also an option). Also, for those that do not like progesterone, they can still take venlafaxine because that also worked well, but just not as well as progesterone.

So, Doc Moyad, what is the catch!? I am glad I asked myself this question. The catch is that in this large study, only about 20% of men on ADT for at least 6 months actually requested hot flash medication! In other words, most men did not even ask for it despite the researchers believing that most would

ask for medication after 6 months of LHRH treatment.

So, that either means that men are shy or tough guys, or most men do not need more medication for a medication side effect. I tend to think that most men do not need medication for a medication side effect, but perhaps I am biased because I want to see more men consuming flaxseed, soy, doing paced breathing exercises, keeping a hot flash diary, limiting spicy and hot foods, exercising more, using acupuncture if needed, wearing loose fitting clothing... to avoid medication for hot flashes.

But, if your personal hot flash diary reveals to the doctor that most of your hot flashes are moderate to very severe, chances are a prescription medication will work very well in your case. Or, if your hot flash diary shows that most of the hot flashes you are experiencing are mild to moderate, you probably would not want to go on another medication. Even progesterone has side effects such as weight gain, reduces libido, and may even reduce your good cholesterol. And venlafaxine can cause gastrointestinal side effects like constipation or diarrhea.

Hey, everything comes with a catch (except reading the Hot Sheet – that comes with no catch! What a beautiful statement on my part....time for a group hug)!

Reference

1. Irani J, Salomon L, Oba R, Bouchard P, Mottet N. Efficacy of venlafaxine, medroxyprogesterone acetate, and cyproterone acetate for the treatment of vasomotor hot flushes in men taking gonadotropin-releasing hormone analogues for prostate cancer: a double-blind, randomised trial. *Lancet Oncol* 4 December 2009, e-pub ahead of print.

FOUND, THE SUPER MOLECULE TO KILL PROSTATE CANCER CELLS

Scientists have discovered a super-molecule which targets and destroys prostate cancer cells, giving hope to men in the final stages of the disease. The antibody – known as F77 – attacks the disease directly and helps the immune system identify and destroy cancer cells in patients with advanced, treatment-resistant tumors. However, it could also be used for patients in the early stages of the disease, doubling its benefits.

F77 is a monoclonal antibody which can be mass-produced in the laboratory by copying a single type of immune system protein. Like natural antibodies made in the body, they help identify and neutralize invaders or sources of danger, such as cancer cells. This is done by latching on to a specific target molecule, or antigen.

In the case of F77, the target is a fatty sugar only found on prostate cancer cell surfaces. Researchers, led by Dr. Mark Greene from the University of Pennsylvania in Philadelphia, said F77 had "promising potential."

The antibody was tested on mice injected with highly aggressive human prostate cancer cells, reported the journal *Proceedings of the National Academy of Sciences*. Tests found that it wiped out 85 percent of one type of highly aggressive prostate cancer.

Large prostate tumors grown in the laboratory were dramatically reduced in size when treated with the antibody. Tagging F77 antibody with a radioactive tracer could theoretically be used to detect any spread of prostate cancer.

Initially, tumors which have spread can be controlled using therapies to block androgen male hormones, which fuel its growth. But, eventually, most prostate cancers stop responding.

Dr. Sarah Cant, head of policy and campaigns at The Prostate Cancer Charity, said it was "potentially significant" that F77 could be used to treat early and late stages of prostate cancer. However, more research is needed, she added.

Mail Online (UK), 29 December 2009

THE DOCTORS NOTE – GERALD CHODAK, MD

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Starting with this issue of The Doctors Note, each article discussed will end with "the Bottom Line" to make it easier for the reader to take away a simple message.

Screening is again in the news. The European prostate cancer screening study was reevaluated omitting those men who did not follow their assigned screening protocol because if a man was suppose to be screened and did not comply, he could not have a chance of benefiting. Using this approach, they concluded that the drop in mortality from screening was really about 30% rather than the 20% in the original report. Is this conclusion valid? Unfortunately, probably not. Randomized studies must analyze all the individuals enrolled to each arm, regardless whether they followed their assigned protocol. It is called an "intention to treat" analysis. Unfortunately, omitting those not compliant is highly likely to overestimate the benefit because it assumes that all the men omitted would have benefited had they followed the protocol which is not correct. The issue is less about whether the drop in mortality is 20%, 30% or something in between. Rather it is that methods are needed to help reduce the number of men being over treated after being diagnosed through screening.

The Bottom Line – Screening saves lives but results in considerable over treatment. Better ways are needed to identify who should be treated aggressively.

A report by Catalona and associates attempts to do that by looking at the change in PSA over time, called the PSA velocity or PSAV. If the velocity was greater than 0.4 ng/ml per year men were more likely to progress than if they had a lower velocity. They used certain criteria to define "insignificant" cancer and applied it to more than 1000 men who had a radical prostatectomy. With this approach they conclude that only 6% of the treated men

had insignificant cancer. The idea of defining clinically insignificant cancer has been used for some time but those criteria have never been properly documented. One has to conclude that the data from this uncontrolled study must be greatly overestimating the number of men benefiting from treatment. By concluding that only 6% of men who undergo radical prostatectomy have insignificant cancer, it would mean that 15 out of every 16 men having surgery is benefiting. This is a completely different conclusion than was reached in the European randomized screening study which found that only 1 out of every 24 to 48 men who was screened and treated was benefiting.

The Bottom Line – Uncontrolled trials can greatly exaggerate the percentage of men benefiting from radical prostatectomy.

Another report with implications about treating men properly is the reevaluation and modification of the Gleason scoring system as reported by Epstein. A consensus conference concluded that a biopsy should no longer be assigned a Gleason pattern 1 or 2 which means that a Gleason score of 2-5 is no longer valid. Furthermore, criteria for Gleason pattern 4 have been modified making many cancers previously diagnosed with a Gleason score of 6 now assigned to Gleason 7 or 8. That would explain the marked increase in Gleason 7 cancers in the United States. This change has tremendous implications for deciding how to manage newly diagnosed cases. It means that many of the men who were diagnosed with Gleason 3+3 were under graded and should have been called either Gleason 7 or Gleason 8. What does this mean when older studies of watchful waiting are reevaluated? If many of the men thought to have Gleason 6 really had Gleason 7 then it would mean that many of the Gleason 7 cancers diagnosed today pose a smaller risk than people think. The reason is that the watchful waiting studies found the odds of dying in 10-20 years was very low for those previously diagnosed with Gleason 6 disease.

The Bottom Line – Changes in the criteria for defining Gleason scores

on biopsies mean that active surveillance may still be a good option for some of the men diagnosed with Gleason 7 disease.

For those men treated by radiation therapy, a report from Sloan Kettering attempts to predict which patients may need additional therapy by looking at the PSA value 2 years after treatment. They observed that the risk for disease progression was low if the total PSA was less than 1.5 ng/ml two years after radiation but it was significantly higher if the PSA was over that value. The problem with this study is that it would not be useful for an individual patient to make a decision about treatment.

The Bottom Line – Treating all men who have a PSA over 1.5 ng/ml two years after radiation therapy is likely to result in considerable over treatment. The PSA doubling time combined with the time after radiation that the PSA begins to rise might be a better way to identify who needs additional treatment.

Another report with uncertain validity is the study on coffee suggesting that its intake reduces aggressive cancer. This is yet another example of trying to draw conclusions from uncontrolled studies.

The Bottom Line – Uncontrolled studies do not permit valid conclusions. Their only value is to help design a properly controlled trial that can truly determine if there is a cause and effect relationship.

Lastly, a report on an antibody that was effective in killing prostate cancer cells in mice is encouraging but one must be very cautious before jumping to the conclusion that it will be effective for men with prostate cancer. Too often, laboratory findings have given many patients false hope only to find out later that they do not produce similar results when tested in patients. Let us hope that forthcoming studies will demonstrate it has real value for men suffering from advanced disease.

The Bottom Line – Patients should use caution in becoming prematurely excited about results obtained in laboratory experiments because most do not come to fruition when tested in patients.

PSA VELOCITY

(Continued from page 1)

Ohuri criteria) as confined to the prostate, with a tumor volume 0.5 cc or less and no Gleason pattern 4 or 5. The patients' mean age was 62 years and their median PSA level at diagnosis was 4.3 ng/mL, and most had a clinical stage T1c disease with a Gleason score of 6.

Preoperative PSAV greater than 0.4 ng/mL per year was significantly associated with positive surgical margins (19% versus 12%, p = 0.003) seminal vesicle invasion (4% vs. 1%, p = 0.007), a Gleason score of 7 or greater (p = 0.008), and greater tumor volume.

Sixty-nine men (6%) had pathologically insignificant cancer. Insignificant disease was significantly more likely in men with preoperative PSAV less than 0.4 ng/mL per year (10%, vs. 5% for PSAV greater than 0.4 ng/mL per year, p = 0.003).

“These results suggest that PSAV may be useful in conjunction with other variables to help enhance the specificity of prostate cancer screening to detect clinically significant prostate cancer,” the authors conclude.

Reuters Health, 21 December 2009

RFA FOR BONE PAIN

(Continued from page 3)

perature can be monitored, and it can be performed under local anesthesia and conscious sedation in the outpatient setting. This is a significant step forward in the pain management of these patients,” said Dupuy.

The procedure was found to be safe with few adverse events. RFA can be an alternative for patients who previously received radiation therapy and have reached their maximum radiation dose, but are still experiencing pain.

“Despite advances in radiation technology and development of new medical manipulations, too many cancer patients still experience pain associated with their disease. This study demonstrates the palliative benefits of RFA with minimal treatment-related morbidity. Oncologists have another tool for the management of cancer pain,” said Thomas DiPetrillo, clinical director of radiation oncology at Rhode Island Hospital and associate professor of radiation oncology at The Warren Alpert Medical School of Brown University.

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GAT'S HYPOTHESIS

(Continued from page 4)

Prostate Cancer InfoLink thinks that their hypothesis makes some sound physiological sense – and they feel that the hypothesis is supported by Gat's initial experiments.

Us TOO feels that some aspects of Gat's hypothesis are hard to swallow. There is no evidence of a cause of effect relationship between high serum testosterone levels and prostate cancer. So it is difficult to accept that androgen receptor overstimulation by a “flood” of free testosterone causes cancer.

What is clear is that Gat's results need to be confirmed (or disproved) in repeat experiments using a larger study population. Varicocele is considered a major cause of infertility and treatments such as those used by Gat are not successful in all cases and varicoceles can recur.

The “New” Prostate Cancer InfoLink acknowledges that radically new theories that propose “off the wall” causes for common disorders take time to filter their way into the medical mainstream – even when those theories are right and are later confirmed by relatively compelling data. Until then we will have to wait and see.

**US TOO INTERNATIONAL:
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Be the leading prostate cancer organization helping men and their families make informed decisions about prostate cancer detection and treatment through support, education and advocacy.



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