



# Newsletter

## Prostate Cancer 101, Inc.

March, 2005

The Prostate Cancer Information and Support Group of the Mid-Hudson

### Dr. Howard Scher, PCa 101 Distinguished Lecturer, Mar. 15

Prostate Cancer 101 is most fortunate to have the distinguished **Dr. Howard Scher** speaking to us regarding “**Recent Developments in the Treatment of Recurring and Refractory Prostate Cancer**” at our Tuesday, March 15 program scheduled to begin at 4:30 P.M. in the Hurley Reformed Church Hall. For the past thirteen years Dr. Scher has been Chief, Genitourinary Oncology Service, Department of Medicine, Sidney Kimmel Center for Prostate and Urologic Cancers at Memorial Sloan Kettering Cancer Center. In addition he is a Professor of Medicine of Weill Medical College, Cornell University, NY, NY.

He is board certified in both Internal Medicine and Medical Oncology and received his education at Bates College (undergraduate) and his MD in 1976 from NY University School of Medicine. He did his internship and residency at Bellevue Hospital NY, NY with a fellowship in Medical Oncology in Memorial Sloan Kettering.

Dr. Scher's many awards and honors are too numerous to mention here but in his busy schedule he has found time to train many prominent physicians that are



Dr. Howard Scher

now either doing research or actively involved in the treatment to further the cause of curing prostate cancer. He has had the honor of receiving “The Memorial Sloan-Kettering Teaching Excellence Award” over a six-year period. Two of his prominent “trainees” are the notable Dr. Daniel Petrylak of Presbyterian Hospital and Dr. Susan Slovin, Assistant Attending, Genitourinary Oncology, MSKCC.

A recent grant from CaPCure enabled Dr. Scher to research *Targeted Therapy for Prostate Cancer Preclinical and Clinical Investigations for Improving Therapeutic Outcomes*.

While many of us complain about the high cost of drugs and the huge profit margin that the

pharmaceutical companies generate, no one can dispute the good that these companies contribute in the form of grants and clinical trials for research. In the early 90's Dr. Scher participated in many Phase II trials of drugs such as Casodex (Zeneca Pharmaceuticals) that are now a first-line drug in the treatment of advanced or recurring PCa.

From 1982 to the present Dr. Scher has either written or co-authored 312 manuscripts with the most recent being *The Influence of PSA Doubling Times on the Incidence of Distance Metastases in Prostate Cancer Patients with Established Biochemical Recurrence after Radiotherapy*. Hopefully, he will address this during his presentation to our group!

Recently Dr. Scher was the guest lecturer at the 4<sup>th</sup> Annual Clinical Cancer Update, University of California, San Francisco School of Medicine – “*Who Should Get Chemotherapy for Prostate Cancer*”.

Please join us on Tuesday, March 15<sup>th</sup> at 4:30 P.M. at the Hurley Reformed Church Hall for this important lecture. Bring your questions and concerns, as a question and answer period will follow

Arlene Ryan, PCa 101

## TREATING RADIATION CYSTITIS AND RADIATION PROCTITIS

Dr. Yoram Beer, one of our January DISTINGUISHED LECTURERS, briefly mentioned treating men suffering from radiation cystitis or radiation proctitis with a specially formulated suppository or with the Hyperbaric Oxygen Therapy. Our February Prostate Cancer 101 seminar –the first seminar we encouraged previously treated men who had “concerns” to attend — was attended by several men expressing concern about rectal bleeding – possibly radiation proctitis.

I invited Dr. Beer to write a few paragraphs expanding the information about these treatments for our Newsletter. Ellen Briggs, his office manager, developed this information which might be helpful to men with these problems:



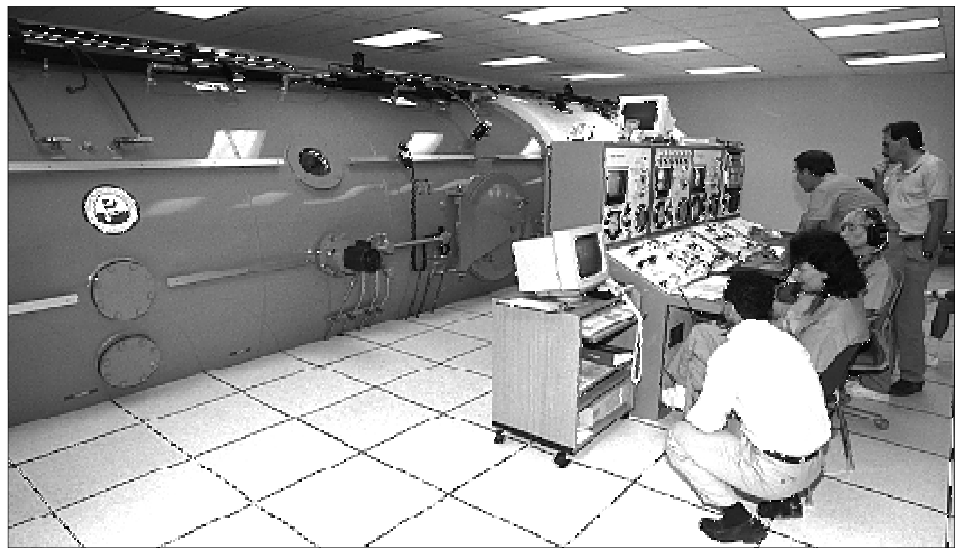
Well known complications of radiation administered therapy for prostate cancer are radiation cystitis and radiation proctitis. Radiation cystitis symptoms range from blood in urine, urinary urgency and frequency accompanied with pain. Radiation proctitis may find blood in the stool, frequent movements, loose stools, with rectal pain. Quality of life is compromised though these are not serious medical problems.

Dr. Beer can prescribe a 1 gram Sucralfate rectal suppository which is inserted three times daily. The main ingredient is carafate which is an ulcer drug com-

pounded in a suppository base. The effect is that it binds to injured tissue. This suppository must be prepared by a compounding pharmacy. Dr. Beer’s office has used this compounding pharmacy to prepare the suppository, which requires a prescription:

Fallons Pharmacy  
1057 Troy Schenectady Road  
Latham, New York 12210  
518-220-2005

*(I called Nekos Pharmacy in Kingston to determine whether they were a compounding phar-*



Hyperbaric Oxygen Chamber

*macy, and found that they are a compounding pharmacy. However, when I mentioned the Sucralfate rectal suppository, they immediately referred me to the Fallons Pharmacy. Nekos Pharmacy does not compound this type of suppository. RonKoster )*

Most patients are able to have their symptoms managed with medications, etc. However, a

small percentage has no resolution of their symptoms and fail all other treatment modalities such as bladder irrigation, instillation of medication into the bladder or rectum, or urinary diversion to give the bladder a rest. With the new technology for radiation treatment we are finding fewer patients with significant complaints. However, for that small majority, we have found hyperbaric oxygen therapy to be effective.

Hyperbaric oxygen therapy is limited to patients who fail conservative measures. It involves placing the patient in a special hyperbaric pressure chamber.

100% oxygen is given at high pressures under the guidance of a trained attendant. The treatment is for 90 minutes for 5 days a week until endpoints are achieved. An average of 30-40 treatments is the standard of care to see improvement in symptoms. This treatment delivers approximately 15 times more oxygen to tissues to promote formation of new capillaries to wound areas and sufficient oxygen to meet the needs of ischemic tissues.

What the patient can expect is that once inside the chamber, the patient will hear the air beginning to circulate. Patients are able to see and talk with the chamber staff attendant, who will tell them when the gradual increase in pressure is begun. This is called compression and may take anywhere from 5-10 minutes. The recurring fullness in the ears will stop and then patients may rest or sleep during their treatment. Patients may also read or do handwork during the treatment which lasts about 90 minutes. Near the end of the treatment, the chamber attendant will gradually decrease the chamber pressure. This is the decompression phase, which usually lasts about 7 minutes. During this phase the patient will experience an automatic popping sensation in their ears similar to what is felt in an airplane.

While Hyperbaric Oxygen Chambers may be available in other area locations, Dr. Beer has sent patients to chambers at Albany Memorial Hospital in Albany and Amsterdam Hospital in Amsterdam.



If you wish to consult with Dr. Beer (Latham, NY) about a radiation cystitis or radiation proctitis problem, call Ellen Briggs at 518-786-9135.



Patients of Dr. Dattoli, Sarasota FL, have had success with Carafate, Trental and Canasa suppositories he prescribes for radiation proctitis.

***If You Want to Help:***

***Prostate Cancer 101 Seminar***

**Fred Bell**

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**2005 Program Committee**

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**Yavuz Birturk**

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**Other PCa 101 Activities**

**Ron Koster**

Phone: 845-338-8005  
E-Mail: RKoster@hvc.rr.com

***March Birthdays***



<i>Name</i>	<i>Date</i>
St. Julian Fishburne	2-Mar
Donald E. Carney	3-Mar
Harold Shorr	4-Mar
Shay Morey	5-Mar
Joseph Sullivan	6-Mar
Frank R. Allen	8-Mar
Gary W. Johnston	8-Mar
Robert F. Winne	8-Mar
Chester W. Cunningham	10-Mar
Howard Nickerson	10-Mar
Milton Schedivy	14-Mar
Walter J. Krein	15-Mar
Tjongtik Goei	18-Mar
Frank Becker	21-Mar
Edwin C. Thompson, Jr.	21-Mar
William H. Williams	25-Mar
Robert A. Hargrave	31-Mar

Birthdays are announced on Kingston radio stations between 7:15 and 7:25 a.m. on WKNY (1490 am) and between 7:40 and 7:50 a.m. on WGHQ (920 am) each day on the early morning shows. Listen for Birthday Greetings from "The Gang".

Each station also draws a name from all the men, women, and children celebrating birthdays each day for the award of "special gifts." Many of our members have been selected as winners.

Celebrate your birthday at Mariner's Harbor at the Rondout, where you will receive a free Lobster or Prime Rib Dinner on your actual birth date. One of our members is an owner of Mariner's and they have been generous with their support.

## NIH slated for 0.7% raise in 2006: Research advocates 'disappointed' over meager increases, cuts in White House proposal Ted Agres

President Bush yesterday (February 7) sent to Congress a \$28.8 billion budget request for the National Institutes of Health (NIH) in fiscal year (FY) 2006, a virtually flat 0.7% increase of \$196 million over the current year's funding and far below the projected biomedical inflation rate of 3.5%. If enacted, it would be the first time since 1964 that NIH received an annual increase of less than 1%.

The Centers for Disease Control and Prevention (CDC) would be cut by 12.1% to \$4 billion, a reduction of \$555 million. The National Science Foundation (NSF) would receive a 2.4% increase of around \$132 million to \$5.6 billion, which is still \$47 million less than its FY 2004 funding level. NIH's proposed budget for 2006, before transfers from other sources and agencies, totals \$28.5 billion, a 0.5% increase of \$146 million over the current year's appropriation.

The president's overall budget request for the fiscal year beginning October 1 totals \$2.57 trillion. Still, it is one of the most austere in recent history with overall non-defense discretionary funding cut by an average of 1%. Nine of 15 cabinet-level depart-

ments would receive less money next year than they do this year.

In the past, the NIH has benefited from supporters in Congress who had managed to boost the agency's final budget beyond that which the president proposed. Research advocates hope that will again happen this year.

"We understand the reality of the [fiscal] environment we are living in," said Paul Kincade, president of the Federation of American Societies for Experimental Biology (FASEB). "But it's very serious if we erase the [gains made from] doubling the NIH budget, which will happen in fiscal year '07 if present trends continue," he told *The Scientist* yesterday. FASEB, the American Society for Microbiology, and other research organizations had urged that NIH receive a 6% increase to \$30.07 billion.

Because NIH's budget is so large, even a small percentage increase translates into "significant number of dollars when you're trying to freeze discretionary spending," said Dave Moore, associate vice president for government relations at the Association of American Medical Colleges.

"On the one hand, 0.7% is very disappointing, but compared to the rest of the Public Health Service, where you're seeing actual cuts, a \$196 million increase certainly is nothing to be sneezed at," Moore told *The Scientist*.

The proposed NIH budget would provide \$15.5 billion for new (competing) and continuing (non-competing) research project grants, a 0.4% increase of \$56 million. This would fund about 38,746 total projects, 402 less than this year. The average new research project grant would be funded at \$347,000, about the same amount as in FY 2005.

Most NIH institutes and centers would receive increases of less than 1%. The National Institute of Allergy and Infectious Diseases (NIAID), which funds most of NIH's bioterrorism-related research, is once again the agency's biggest gainer at \$4.5 billion, a 1.8% increase of \$57 million.

"If we had an unlimited budget, we would spend more on many programs," said Mike Leavitt, secretary of the Department of Health and Human Services yesterday. "Since we don't, we have focused money on the most urgent priorities that will make the biggest difference in the health and well being of Americans."

Bioterrorism-related funding, including the Strategic National Stockpile and environmental biosurveillance, would increase by 3.6% to \$1.6 billion. A reduction of \$240 million in CDC's budget results from no new

buildings and facilities construction being planned in fiscal 2006.

In NSF's budget, research and related activities would grow by \$113 million or 2.7% to \$4.3 billion, while the major research equipment and facilities construction account would increase to \$250 million, a 44% increase of \$76 million.

Funding for NSF's biological sciences directorate would increase by \$5 million (0.9%) to \$582 million. Minimal funding for planning and designing the National Ecological Observatory Network also would continue, bringing the total to \$6 million.

"At least it's a positive number compared to last year's omnibus," said Moore, referring to NSF's 1.9% loss of \$106.7 million in the FY 2005 budget approved last November. *Source: The Scientist*

## Prostate Cancer: New studies of combination therapy

Doctors have finally begun to understand prostate cancer. Geneticists have identified abnormal genes that increase a man's vulnerability to the disease. Epidemiologists have discovered that a diet high in saturated fat is linked to an increased risk, while tomatoes, whole grains, fish, soy, and the mineral selenium appear to be protective. Urologists are learning how to use the PSA test to detect the disease. Radiologists are developing new ways to obtain images of the elusive gland, and oncologists have honed their understanding of what makes prostate cancers grow and what slows the multiplication of malignant cells.

It's important progress that has resulted from teamwork. Every man stands to benefit from these new insights, but men with prostate cancer have an additional urgent need. Fortunately, there have been important gains here, too. In fact, each of the standard therapeutic options has registered major improvements:

Surgical removal of the gland, the radical prostatectomy, has become safer and requires a shorter hospital stay. In addition, the nerve-sparing operation can help preserve potency, and laparoscopic surgery can reduce postoperative pain, at least for some men.

Radiation treatment has improved in two ways. Three-dimensional conformal therapy has made external beam radiation better than ever, allowing radiation oncologists to deliver more cancer-killing x-ray energy with fewer side effects. In addition, brachytherapy, a newer approach, allows doctors to place radioactive seeds directly into the gland, eliminating the need for daily trips to the hospital.

Hormonal treatment has benefited from new drugs that can dramatically lower levels of testosterone, the male hormone that fuels the growth of prostate cells.

Watchful waiting — close observation without active therapy — has also been refined. Doctors have learned that this option is best suited to older men with less aggressive tumors, and they have improved their ability to follow the disease and initiate therapy if it becomes necessary.

Even as these standard options are improving, new approaches are being developed. Cryotherapy, for example, freezes the prostate to kill malignant cells. These developments are all for the good, but they have made it harder than ever for a man with prostate cancer to choose among the different therapies. And to make matters even more confusing — but even better — some



*No Computer?*

Go to your  
Public Library  
They will  
Teach you to do  
PCa research  
On their computers!

studies suggest that combination treatments may outperform individual methods, at least for some men.

For treating prostate cancer, as for understanding the disease, teamwork is best.

### **The Hormone Connection**

Male hormones, androgens, are required for the growth of prostate cells, both benign and malignant. When prostate cells are deprived of these hormones, their growth is halted, at least for a time. Androgen-deprivation therapy has been used since the 1940s, but it has changed dramatically since.

Androgen production depends on a lengthy chain of events. It begins in the brain, where the hypothalamus produces the hormone that sets the wheels in motion. It's a single protein, but it has two names: to urologists it's luteinizing hormone-releasing hormone (LHRH), but to endocrinologists it's gonadotropin-releasing hormone (GnRH). By either name, the hormone acts on a nearby part of the brain, the pituitary, which responds by producing two additional hormones.

One of these pituitary products, luteinizing hormone (LH), carries the chain further by traveling to the testicles, where it stimulates the Leydig cells to produce testosterone. About 95% of a man's testosterone is made in his testicles, the rest in his adrenal glands. Whatever its source, testosterone

undergoes a final transformation in the prostate itself, where the enzyme 5-alpha reductase turns it into dihydrotestosterone (DHT).

### **The Androgen Cascade Blocking the Androgen Cascade**

Prostate cells depend on androgens for growth; they can be deprived of androgens in several ways: estrogens and LHRH agonists inhibit the release of LH (steps 1 and 2); Abarelix suppresses LH production; orchiectomy eliminates testicular testosterone (steps 2 and 4); finasteride blocks testosterone's conversion to DHT (step 5); and antiandrogens block the binding of DHT to cellular receptors (step 6).

### **Breaking the Chain**

The oldest method of androgen deprivation is also the fastest; testosterone levels plummet within hours after an orchiectomy, the surgical removal of the testicles, and they stay low. Permanence may be an advantage to men with advanced prostate cancer, but it makes orchiectomy useless for combination therapy, which relies on temporary androgen deprivation to enhance the effect of other treatments. Although estrogens could be used to temporarily lower testosterone levels, they have not been studied in combination treatment. And while the 5-alpha reductase inhibitors finasteride (Proscar) and dutasteride (Avodart) can help some men with benign prostatic hyperplasia, they do not have a role in prostate cancer. But two other hormonal

approaches have been useful in combination therapy.

LHRH agonists are synthetic drugs that resemble LHRH. Unlike the real thing, however, they block the release of LH by the pituitary, thus reducing testosterone production by the testicles. After a brief surge, testosterone levels decline dramatically, and they stay low as long as the drug is injected every one to four months, depending on the preparation. The major LHRH agonists are goserelin (Zoladex), leuprolide (Lupron, Eligard, Viadur), and triptorelin (Trelstar). They are equally effective and equally likely to produce side effects such as fatigue, breast pain and enlargement, hot flashes, loss of bone calcium, anemia, and sexual dysfunction. They are also equally expensive.

The GnRH antagonist is a newer medication for advanced prostate cancer. Abarelix (Plenaxis) suppresses the production of LH and follicle-stimulating hormone (FSH), thus reducing testosterone levels. Unlike the LHRH agonists, it does not cause an early surge in testosterone, but it can produce allergic reactions that may be serious. As of 2005 Abarelix is approved only for certain men with advanced prostate cancer.

Antiandrogens don't reduce the body's production of hormones, but they block the hormone's ability to stimulate cells. Antiandrogens act against both testosterone and DHT, and they also block the effects of the weaker andro-

glands. The major preparations include bicalutamide (Casodex), flutamide (Eulexin), and nilutamide (Nilandron). All are taken orally, and all are expensive. Antiandrogens can cause breast enlargement, but they don't usually provoke hot flashes, and they are less likely to cause sexual dysfunction than LHRH agonists.

### **Teaming Up**

A similar tactic to combination therapy for prostate cancer has proven its worth in another hormonally responsive malignancy, breast cancer. Doctors have learned that the antiestrogen drug tamoxifen can improve the results of surgery or radiation in women with estrogen-responsive breast cancer.

Some studies of prostate cancer revealed that a combination of androgen-deprivation therapy and external beam radiation could help men with locally advanced cancer by reducing its progression more effectively than radiation alone. In contrast, men treated surgically did not appear to benefit from antiandrogen therapy. But three newer studies extend the reach of combination therapy. Two found that it can prolong survival in men receiving radiation, and the third reported that it could reduce the progression of disease in men treated with radiation, surgery, or watchful waiting.

### **The EORTC Trial**

The European Organization for Research and Treatment of Cancer (EORTC) conducted the first study. Between 1987 and 1995, 415 men volunteered to be ran-

domly assigned to receive either external beam radiation alone or similar radiation combined with androgen deprivation (an LHRH agonist for three years with an antiandrogen for the first month). All of the men had locally advanced prostate cancer, but none had been previously treated. Scientists tracked the men for an average of 66 months, evaluating three factors: freedom from prostate cancer, survival from prostate cancer, and overall survival. At the end of five years, combination therapy was better than radiation alone in all three respects; it improved overall survival (79% vs. 62%), survival from cancer (98% vs. 88%), and survival without any evidence of cancer (67% vs. 30%). The study did not describe the side effects of either treatment, but it did note that 6% of the men in the combination group did not complete the full three years of LHRH treatment because of adverse symptoms.

### **A Harvard Study**

The EORTC trial demonstrated that three years of androgen-deprivation therapy can improve the results of radiation treatment. But long-term hormonal treatment is expensive, and it often produces unpleasant side effects. To find out if short-term androgen treatment is beneficial, Harvard researchers studied 206 volunteers with clinically localized but high-grade prostate cancer. Half the men received standard external beam radiotherapy; the others received the same doses of radiation plus six months of androgen deprivation with an

LHRH agonist and an antiandrogen. After an average follow-up of more than four and a half years, the men who received combination therapy enjoyed a higher overall survival rate (88% vs. 78%), a lower risk of dying from prostate cancer, and a lower risk of requiring additional cancer treatment. However, combination therapy produced more breast enlargement and impotence.

### **The Casodex Trial**

The Casodex Early Prostate Cancer Trialist Group, a consortium of scientists in Europe and the United States, conducted a much larger trial. A total of 8,113 men volunteered to be randomly assigned to receive either standard treatment plus a placebo or standard treatment plus 150 mg a day of the antiandrogen bicalutamide. The patients had localized or locally advanced prostate cancers. The patients and their doctors selected the standard treatments, which included surgery, radiotherapy, and watchful waiting. The scientists tracked patients for an average of three years. They were unable to detect any differences in survival between the two groups, at least in part because there were so few deaths from prostate cancer (less than 2%). But combination therapy did reduce the risk of local recurrence from 14% to 9%. However, it did produce more side effects, including breast enlargement in 73% and breast pain in 66% of the men. In all, 26% of the men in the bicalutamide group withdrew

*(continued on page 8)*

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from the trial because of adverse symptoms, while only 8% of the placebo group dropped out.

The Casodex trial — still in progress in 2005 — will hopefully determine if this form of combination therapy prolongs survival in addition to reducing the risk of recurrences. It is also important to evaluate the quality of life in both groups. The FDA has approved bicalutamide only for the treatment of advanced prostate cancer in combination with an LHRH agonist.

### What's Best?

The EORTC trials showed that long-term combination treatment can offer real advantages to men with locally advanced prostate cancer, and the Harvard study found similar benefits from short-term androgen deprivation in men with clinically localized but high-grade disease. The Casodex trial is less convincing, demonstrating a reduced risk of recurrence but no effect on survival.

Despite these encouraging results, the new trials leave some questions unanswered. Doctors don't know if combination therapy will help men with low-risk disease, and they don't know the best time to start androgen deprivation or how long to continue it.

Finally, the research on combination therapy does not address the \$64,000 question: Which primary treatment (surgery, external radiation, brachytherapy, watchful

waiting) is best? That crucial answer depends on still other randomized clinical trials.

When it comes to prostate cancer, every new answer seems to trigger still more questions. But those queries, too, will be resolved — and in the meantime, the cycle of questions and answers has already improved the outlook of prostate cancer patients.

*Source: Harvard Medical School Newsletter*

### February, 2005 Donations

**Stephen Altschuler  
John & Lois Brewer  
Stanley & Martha Cruden  
Jay Dorin  
Donald Droulette  
Keith Johnson  
J. & D.E. Metzelaar**

### **Ulster Federal Credit Union**

Our thanks to the Ulster Federal Credit Union for their donation to help support our organization. Cheers to Don Droulette for donating his winnings from the 50/50 drawing at the excellent lecture given by Dr. Hugh Fisher on February 15.

If you wish to contribute financially, mail your check, made payable to

**Prostate Cancer 101**

To:

*Prostate Cancer 101  
c/o Diane Sutkowski,  
Treasurer*

*8 Alcazar Avenue  
Kingston, NY 12401-4302*

## **Federal Agency Adds X-Rays to Carcinogen Warning List**

Ionizing radiation has been listed for the first time as a known human carcinogen in a report prepared by the National Toxicology Program, an interagency group coordinated by the U.S. Department of Health and Human Services. The report has been published every two years for more than two decades.

According to the "Report on Carcinogens, Eleventh Edition" released on Jan. 28, studies show that exposure to x-rays and gamma rays causes many types of cancer. Childhood exposure is linked to an increased risk for leukemia and thyroid cancer, while exposure during reproductive years increases the risk for breast cancer. Exposure later in life increases risk for lung cancer.

The report cites evidence that exposure to ionizing radiation is linked to cancer of the salivary glands, stomach, colon, bladder, ovaries, central nervous system, and skin.

The American College of Radiology will petition the NTP to have ionizing radiation removed from the list. The ACR fears that patients will be inappropriately alarmed.

"We tried to caution them not to include diagnostic imaging on a

## Study Says Obesity May Hinder Prostate Cancer Screenings

Continued from page 8

report like this," said Dr. James Borgstede, chair of the ACR board of chancellors.

X-rays and gamma rays are not substances that the general public has access or exposure to, and they do not belong on a list of substances that pose a risk to people in the course of their normal daily lives, Borgstede said.

"This report could lead patients to mistakenly believe that they are being placed at undue risk by undergoing a radiological procedure and cause many who may desperately need care to avoid seeking appropriate medical attention," he said.

Radiologists were concerned that inclusion of ionizing radiation on the list without a strong statement of the benefits would be misleading, said Christopher Portier, Ph.D., associate director of the NTP. The report's introduction states that the purpose of the information is only to identify hazards and not to address potential benefits.

"We tell people to talk to their physicians if they have concerns about medical x-rays. We point them to the FDA Web site, which does a good job of explaining the risks versus benefits in more detail than we could," Portier said.

A formal process exists for individuals or organizations such as

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A new U.S. study suggests a man's weight may affect the accuracy of a common test to detect prostate cancer, leading researchers to warn that doctors could be missing the dangerous cancer in obese men.

Researchers at the University of Texas Health Science Center in San Antonio studied 2,779 men without prostate cancer between 2001-04. In the study released online January 24, 2005, in the journal *Cancer*, they reported finding that the more obese the men were, the lower their levels of prostate-specific antigen or PSA. A PSA of 4.0 or lower usually means no cancer.

Previous studies have shown that prostate cancer is more aggressive in obese men than in men of average weight. The researchers wanted to see if the cancer's detection was somehow being delayed in obese men.

The Texas study found that the most morbidly obese men had about 30% lower PSA levels than men of normal weight.

"That tells us it's likely or it's possible that prostate cancer detection may be delayed in overweight or obese men," said Jacques Baillargeon, associate professor of epidemiology at the health science center.

The research may encourage many doctors to take a closer look at the tests of obese men.

"For sure, I will be more vigilant in my patients who are obese in evalu-

ating their PSA," said Nelson Stone, MD, of Mount Sinai School of Medicine, who was not involved in the study. "We may be losing some of the sensitivity of the test in the obese patient in our ability to detect prostate cancer. We may have to set our sights lower."

*"For sure, I will be more vigilant in my patients who are obese in evaluating their PSA."*

*Nelson Stone*

The antigen used in the screening test is made by normal prostate cells and is measured in blood. The higher the antigen level, the more likely the chance of prostate cancer, as the cells multiply uncontrollably, according to the American Cancer

Society.

But having high PSA levels is not a definitive diagnosis of cancer, which is why the Atlanta-based society recommends men with high PSA levels have a biopsy.

The latest study builds on previous research released in May, 2004, in the *New England Journal of Medicine* that found that men with a "normal" PSA actually had cancer 15% of the time and that two-thirds of those men with cancer had aggressive cases.

The Texas study did not explain why obese men have lower PSA levels. But doctors believe obese men produce more estrogen, which drives down testosterone levels and could affect cells that produce the antigen used in the test.

*Prostate Cancer News/  
Prostate Cancer Foundation*

The ACR to petition the NTP for removal of an agent. In case of ionizing radiation, the evidence — both human and animal — is strong, according to Portier.

"The ACR can make the petition and we will seriously review it. But my gut feeling is that it would not happen, certainly not in the next review, unless there was a dramatic change in the evidence," he said.

Dr. David Brenner, a radiobiologist at Columbia University and coauthor of the seminal 2001 American Journal of Roentgenology study that exposed the dangers of routine pediatric CT scans, said it's really an issue of dose.

"I'd be surprised that anyone would argue against x-rays and gamma rays being carcinogens at high doses. At extremely low doses, it's still a controversial issue. The question that we are talking about is somewhere in between," Brenner said.

The report does not specify a dose range. Setting standards of safe exposure is the job of other government agencies, such as the FDA and the U.S. Environmental Protection Agency, Portier said.

Brenner said that making a statement of carcinogenic risk without reference to dose is vague and misleading.

Virtually every group worldwide lists ionizing radiation as a known

human carcinogen, Portier said. In 1999, the World Health Organization's International Agency for Research on Cancer published a monograph detailing the carcinogenic evidence of x-rays and gamma rays. The International Commission on Radiological Protection long ago established the three principles of dose: justification, optimization, and limitation. The FDA in the last several years has cautioned against receiving medically unnecessary x-ray procedures.

Ionizing radiation had been an obvious omission from the toxicology report for several years, Portier said. This was more as a matter of cost than evidence. The NTP can add only six to eight new agents per year, and each agent is subject to a rigorous two-and-a-half-year review process.

"We believed that ionizing radiation was so well known as a carcinogen that we decided early on to concentrate on other less well-known agents," he said. "But the time had come to finally include it."

The NTP is located at the National Institute of Environmental Health Sciences (NIEHS), which is part of the National Institutes of Health. Most nominations for agents to be added to the list come from within the various governmental bodies associated with the NTP, including the Centers for Disease Control and Prevention, FDA, EPA, and Occupational and Safety Health Admini-

stration. Nominations can also come from individuals.

The nomination for x-rays came from within the NIEHS, Portier said. Panels that discuss the nominations consist of scientists who are toxicologists, exposure experts, medical physicians, public health experts, epidemiologists, statisticians, and physicists. The panel that deliberated the final report on carcinogens was composed mostly of epidemiologists.

"The human evidence is very important," Portier said.

Four other agents were also added. For the first time, viruses made the list of known human carcinogens: hepatitis B and C (liver cancer), and some human papillomaviruses that cause common sexually transmitted diseases (cervical cancer in women). Neutron radiation causes genetic damage similar to that of x- and gamma radiation and thus can cause the same cancers, according to the report.

Eleven substances that can be reasonably anticipated to cause cancer have been added as well. They include compounds found in grilled meats and a host of substances used in textile dyes, paints, and inks. The NTP report now contains 58 known human carcinogens and 188 "reasonably anticipated" carcinogens.

The full report is available at the NTP Web site National Toxicology Program.

*Source: Diagnostic Imaging.com*

## Mutations in Mitochondrial DNA

Mutations in mitochondrial DNA (mtDNA) play an important role in the development of prostate cancer, according to research by scientists at Emory University School of Medicine and the University of California, Irvine. The findings are published online this week in the Proceedings of the National Academy of Sciences (PNAS). Mitochondrial DNA, which is separate from nuclear DNA, is found in the hundreds of mitochondria located in the cytoplasm outside of each cell's nucleus. The mitochondria often are called the "powerhouse" of the cell because they produce about 90 percent of the body's energy.

John A. Petros, MD, associate professor of urology and pathology at Emory University School of Medicine and the Winship Cancer Institute, and Douglas C. Wallace, PhD, director of the Center for Molecular and Mitochondrial Medicine and Genetics at the University of California, Irvine, sequenced segments of mtDNA from prostate cancer patients and found a variety of mutations, including various mutations in the mtDNA cytochrome oxidase subunit (COI) gene. They then sequenced the COI gene in 260 prostate cancer tissues samples or blood cells from patients with confirmed cancer who had undergone radical prostatectomies between 1995 and 2002, and 54 tissue samples from patients who had prostate biopsies but were found to be cancer free. Twelve percent of all the prostate cancer samples had

mutations in the COI gene, while less than 2 percent of the samples from patients found to be cancer free harbored mutations in this gene. In a control sample of 1,019 individuals from the general population, 7.8 percent had mutations in the COI gene. The researchers found both germ-line (inherited) and somatic (acquired) mutations in the prostate cancer samples.

Because COI mutations are known to be more common in individuals of African descent, the scientists also analyzed a group of patients and controls of European ancestry. In this group they found the COI mutations in 11 percent of the prostate cancer specimens, in 0 percent of the no-cancer group and in 6.5 percent in a general population sample of 898 Europeans.

To determine whether mtDNA mutations are causally related to prostate cancer, the researchers introduced into a prostate cancer cell line mtDNAs harboring a known disease-causing mtDNA mutation and, as a control, the same mtDNA but without the disease mutation. They then injected these modified prostate cancer cells into mice to assess their tumor-forming ability. The prostate cancer cells with the mutant mtDNAs generated tumors that were on average seven times larger than the prostate cancer cells with normal mitochondria. Hence, the deleterious mtDNA

mutation greatly enhanced prostate cancer growth.

Since mitochondria make oxygen radicals as a by-product of making energy, and oxygen radicals can stimulate cell growth, the researchers then tested the tumors for oxygen radical production. The tumors with the mutant mtDNAs generated significantly more oxygen radicals than those with normal mtDNAs, suggesting that this may be an important contributory factor in the mitochondrial enhancement of prostate cancer tumor growth.

Because the study found that COI mutations were common in the general population (7.8 percent), but very infrequent (<2 percent) in men without prostate cancer, the investigators noted that men harboring these mutations are at increased risk for developing prostate cancer.

"We believe this study provides convincing evidence that mitochondrial mutations play an important role in prostate cancer," said Dr. Petros.

The research was funded by the Emory Urology Trust for Urologic Research, the U.S. Department of Defense, the National Institutes of Health and an Ellison Medical Foundation Senior Investigator Grant.

*Source: Emory University*

Prostate Cancer 101, Inc.  
75 Florence Street  
Kingston, NY 12401-3017

**1<sup>st</sup>**

**Tuesday**

**3<sup>rd</sup>**

**Tuesday**

4:30 p.m. monthly

Seminar for  
Newly Diagnosed  
& Treated Men with  
Concerns

**Distinguished  
Lecturer  
Series**

Hurley Reformed Church Hall, Hurley, NY

## Notes from Ron Koster

As the number of newly diagnosed men attending our monthly **Prostate Cancer 101 Seminars** dwindled, and with the recognition that the Question and Answer periods following our **DISTINGUISHED LECTURE** presentations were inadequate, I took the liberty of inviting treated men who have “concerns” to bring their concerns to the February seminar.

This seminar had only one newly diagnosed participant. “Mickey”, a friend of another of our members, was able to attend the Beer/Puranik lecture in January. He’s continuing to seek additional opinions, but seems to be most interested in IMRT and Brachytherapy.

Most of the “previously treated” participants shared the same concern: rectal bleeding – probably caused by radiation proctitis. The issue was so predominant; it prompted me to request Dr. Beer to expand on his brief comments on this problem for the Newsletter. Ellen Briggs,

his office manager, prepared information about the specially compounded suppositories he prescribes, and provided information about Hyperbaric Oxygen Therapy.

Bruce, a previously treated member, came to share his story of serious problems after IMRT and Brachytherapy. His problems (radiation damage to the urethra and bladder) have been resolved and he has added this name to our list of “Special Purpose” doctors: **Dr. Jerry Blaivas**, MD, FAS, Medical Director, URO Center of New York, 445 East 77th Street, New York, NY 10021, 212-772-3900.

The seminar reminded me of our earlier meetings and we’ll continue to invite previously treated men with “concerns” to our Prostate Cancer 101 seminar regularly scheduled on the first Tuesday of each month.

### **Membership Update**

In January, Prostate Cancer 101 included an envelope with a blank “Update” form requesting your coop-

eration in updating our records. I am delighted to inform you that many members updated the membership information and gave us some guidance regarding future meetings and this Newsletter. I am, however, disappointed that many members did not respond to this request. If your name is highlighted in “yellow” on the mailing label, thank you. If it is not highlighted, we are including another copy of the membership update form. Please complete the form and return it to: Ron Koster, 75 Florence Street, Kingston, NY 12401-3017. Your failure to complete and return this form **MAY** result in the removal of your name from the membership.

### **Planning Ahead**

Another world-class medical oncologist, **Dr. Daniel Petrylak**, will be our April 19 **DISTINGUISHED LECTURER**. His topic: “Recent Developments in the Treatment of Advanced Prostate Cancer.”