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◆ **HELPING TO DIRECT PROSTATE CANCER RESEARCH** ◆
by
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As a result of increased public awareness and the advocacy of the cancer support community, Congress directed the Department of Defense to execute targeted biomedical research programs for prostate cancer (PC) research. As a PC survivor and member of the Walter Reed PC support community, in August of 2011, I was given the opportunity to participate in an evaluation process that led to the selection and funding for innovative PC research projects. This article summarizes the program that makes these research grants possible and my experience as a participant in the review process.

Beginning in Fiscal Year 1992, Congress directed the Department of Defense (DoD) to execute targeted biomedical research programs. The U.S. Army subsequently established the Office of Congressionally Directed Medical Research Programs (CDMRP) within the U.S. Army Medical Research and Materiel Command (USAMRMC) to manage Special Interest Medical Research Programs encompassing breast, prostate, lung, ovarian, and other cancers; neurofibromatosis; military health; and other specified areas.

Beginning in FY97, Congress began to provide funding specifically for the DoD Prostate Cancer Research Program (PCRP). Its mission is to eliminate death and suffering from PC, and the specific overarching challenges for the program are the development of effective therapeutics for the advanced disease and the creation of tools for clinicians to distinguish between indolent and aggressive PC. For the last six years, Congress has provided 80 million dollars annually for this research program.

Prospective researchers are invited to submit applications that are subjected to a two-tier review process in order to identify scientifically meritorious and innovative applications and to fund those that best fulfill the program's goals. Applications are first assigned to a Peer Review Panel that completes an evaluation and scoring process. A unique aspect of this review process is that in addition to using experienced scientific reviewers consisting of physicians and research scientists, the process includes so-called Consumer Reviewers.

Consumer Reviewers are individuals invited into the peer process because they provide a unique perspective on the proposed research. They are PC survivors or individuals currently undergoing treatment for PC or family members of persons with the illness. They work alongside the scientist peer reviewers. Consumer Reviewers represent the perspective of those living with the disease, enabling those who are ultimately affected by the proposed research to have a voice in its evaluation. Consumer Reviewers serve as fully voting panel members. Since they are not scientific researchers, they are not expected to evaluate applications on their scientific merits. Rather, they are to assume the application is scientifically sound and to focus on evaluating the potential impact of the proposed research in benefiting the patient community. **(Continued on page 11)**

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◆ FROM THE EDITOR'S DESK ◆

Well, here it is, the first edition of the newsletter to reach you "electronically!" We trust that you found it a convenient way to receive the newsletter, although, no doubt, some readers may prefer to hold a hard copy in their hands. We encourage you to share it with interested friends, and if any are interested in receiving their own notification directly, simply tell them to contact Jane Hudak, at the Center for Prostate Disease Research at Jane.Hudak@med.navy.mil, asking to be included on our email notification list. We also welcome your comments or suggestions about the newsletter and your "electronic experience" with it by contacting the editor as shown to the left on this page.

◆ AUGUST SPEAKER'S REMARKS ◆

Our August program featured Dr. Stacey L. Koff, Department of Urology, Fort Belvoir Community Hospital. Her topic was "Nutrition and Prostate Cancer: Can Diet and Lifestyle Improve Cancer Outcomes." A summary of Dr. Koff's presentation begins on page 6.

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◆ DIRECTING PROSTATE CANCER RESEARCH ◆

Would you like to participate in helping to direct prostate cancer research? Well, you can! In this issue, Mike Sterling, our Secretary, describes his recent personal experience in evaluating scientific research proposals aimed at the defeat of prostate cancer. If you are interested, go to the web site of the Congressionally Directed Medical Research Program at <http://cdmrp.army.mil/CWG>, or contact Mike directly for more information about his experience. He is at mjs.at.home@gmail.com.

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◆ MEETING SCHEDULE FOR NOVEMBER 2, 2011 ◆

"Everything You Always Wanted to Know about Radiation Therapy and Prostate Cancer, and Maybe More!" This is the topic of our November 2 evening meeting, presented by Dr. Patricia Lillis-Hearne, Radiation and Oncology Service, Walter Reed National Military Medical Center, Bethesda, MD. Learn more about recent developments in radiation therapy affecting the newly diagnosed and men dealing with other aspects of prostate cancer. Join us at 7:00 pm, Wednesday, November 2, 2011, at Clark Auditorium. Your family members and friends are always welcome. Come join us. **See the back page for important information about this meeting.**

DISCLAIMER: The materials contained in this newsletter are solely the individual opinions of the authors. They do not represent the views of any Department of Defense agencies. This newsletter is for informational purposes only, and should not be construed as providing health care recommendations for the individual reader. Consult with your physician before adopting any information contained herein for your personal health plan.

The association of diabetes and positive prostate biopsy in a US veteran population. Several studies have shown a protective effect of diabetes mellitus (DM) on incidence of prostate cancer; however, the data are not consistent. Moreover, whether or not DM is associated with a positive result among patients referred for prostate biopsy due to abnormal PSA and/or abnormal digital rectal examination is not clear.

Researchers at the Atlanta Veterans Affairs Medical Center reviewed the cases of 3,162 consecutive men who underwent prostate biopsy there between January 2000 and July 2009. The men with positive and negative biopsies were compared for various demographic and clinical factors. Race had no significant impact on these results.

The researchers reported that In this large series of prostate biopsies, diabetes is associated with higher odds of positive biopsy and higher Gleason grade. They recommended more studies investigating the role of DM and its associated comorbidities in prostate carcinogenesis. (Reference: Prostate Cancer Prostatic Dis. 2011 Sep 6. Epub ahead of print via *Euro Today*, September 30, 2011)

Surgical intervention for stress urinary incontinence (UI) on post-prostatectomy UI during sexual activity. It is well recognized that radical prostatectomy is associated with short- and long-term urinary incontinence (UI) and erectile dysfunction. Researchers at the Department of Urology, New York University, sought to evaluate the incidence, clinical significance and treatment of UI during sexual activity, and the impact of anti-incontinence surgical procedures (artificial urinary sphincter [AUS] or male sling). Twenty-seven men underwent anti-incontinence surgery with an AUS or male sling. Sixteen of them completed a questionnaire evaluating "bother" attributable to UI during arousal and orgasm and the impact of the AUS/male sling on UI and sexual quality of life (QoL).

In all, 15 men were evaluable. Of these, 11 were sexually active; four and seven men un-

derwent AUS and sling placement, respectively. All 11 men had a marked improvement in stress UI symptoms, which was the primary indication for surgery. All men undergoing AUS had an improvement in their sexual QoL, and most (three of four men) indicated marked improvement. Slightly more than half of men undergoing the sling procedure reported marked improvement in sexual QoL. The researchers say the study shows a beneficial effect of anti-incontinence surgery on UI during sexual activity. Whether these surgical approaches would benefit men with significant bother due to UI limited to sexual activity warrants further investigation. (Reference: BJU Int. 2011 Sep 2. Epub ahead of print via *Euro Today*, September 2, 2010)

Men's perspectives on selecting their prostate cancer treatment. In the context of scientific uncertainty, treatment choices for localized prostate cancer vary, but reasons for this variation are unclear. Researchers at the Department of Family Medicine, Karmanos Cancer Institute, Wayne State University, Detroit, explored how black and white American men made their treatment decisions. They conducted interviews of 21 American (14 black and 7 white) men with recently diagnosed localized prostate cancer.

Physician recommendation was very important in the treatment decision, but patient self-perception/values and attitudes/beliefs about prostate cancer were also influential. Patients who chose surgery believed it offered the best chance of cure and were more concerned that the cancer might spread if not surgically removed. Patients who chose radiation therapy believed it offered equal efficacy of cure but fewer side effects than surgery. Fear of future consequences was the most common reason to reject watchful waiting. Anecdotal experiences of family and friends were also important, especially in deciding "what not to do." The new technology of robotic-assisted prostatectomy provided optimism for men who wanted surgery but feared morbidity associated with traditional open surgery. Few men seemed aware that

treatment did not guarantee improved survival.

Most men reported making "the best choice for me" by taking into account medical information and personal factors. Perceptions of treatment efficacy and side effects, which derived mainly from physicians' descriptions and/or anecdotal experiences of family and friends, were the most influential factors in men's treatment decision. The researchers concluded that by understanding factors that influence patients' treatment decisions, clinicians may be more sensitive to individual patients' preferences/concerns and provide more patient-centered care. (Reference: J Natl Med Assoc. 2011 Jun;103(6):468-78 via *UroToday*, September 6, 2011)

Patient reported incontinence after radical prostatectomy is more common than expected and not associated with the nerve sparing technique. The reported incidence of urinary incontinence (UI) after radical prostatectomy (RP) ranges from 2.5 to 87%. Researchers at Duke University Medical Center, Durham, NC, reviewed data from the Center for Prostate Disease Research (CPDR) to determine the incidence of patient reported UI after RP (postRPUI) and establish risk factors for postRPUI.

We queried the CPDR database on all patients undergoing RP between 1990 and 2007. We assessed patient age, nerve sparing status, blood loss, margin status, stage, and patient self-reported incontinence status as entered into the database. Patients were counted as having UI only if the database showed patient reported UI in every follow-up encounter. Patients were counted as permanently dry if at any time in the follow-up they answered that they had no UI.

Four thousand three hundred seventy four patients underwent RP without radiation therapy or hormonal ablation between 1990 and 2007. Complete data were available for 1,616 (37%) and 1,459 (90.3%) reported UI more than 1 year after RP with a median follow-up of 50.7 months. Older age is an independent risk factor for UI. Nerve sparing, blood loss, stage of cancer, and margin status were not predictive for UI.

The researchers found that patient-reported post-RPUI is higher than expected but is not related to the nerve sparing technique, stage of cancer nor blood loss at the time of surgery. (Reference: *Neurourol Urodyn*. 2011 Aug 8, Epub ahead of print via *UroToday*, September, Sept 5, 2011)

Patient expectations on sexual function following prostate cancer treatment. There have been three recent research publications addressing sexual and erectile function in men following prostate cancer treatments.

The first, by Alemozaffar and colleagues (2011), reported on results of men in the Prostate Cancer Outcomes and Satisfaction With Treatment Quality Assessment. These men had untreated clinical stage T1 to T2 prostate cancer who went on to have prostatectomy (n=524), external beam radiotherapy (n=241), or brachytherapy (n=262). The authors defined functional erections as an answer of "firm enough for intercourse." The outcomes for erectile function were somewhat dismal as only 33% of men who underwent a prostatectomy had functional erections at 2 years. Men who were younger and had nerve-sparing technique had an increased chance of having functional erections after the surgery. The ability to attain functional erections at 2 years following external radiotherapy was 37%, and with brachytherapy it was 43%. The authors provide information about pre-treatment erectile function. Of men who were potent prior to treatment, most were using oral drug therapy (60%), and 74% of the men had tried all treatments (PDE5 inhibitors, vacuum erection devices, penile injections) reporting that penile injections were the most effective. But the authors note that the men who had undergone prostatectomy surgery were most likely to use these ED treatments. This study shows the importance of the need for clinicians to assist men prior to surgery in setting realistic sexual function expectations.

The second article by Wittmann, Foley and Balon (2011) addressed the biopsychosocial aspect of sexual recovery following prostatectomy. As seen in clinical practice, men report the loss of spontaneity of sexual intimacy and the disappointment they experience. But

most are not willing to discuss their problems with a wife or partner. The authors note that a lack of actual penetrative intercourse may not have as much of an impact on wives, who may not value that part of sexual activity as much as the man. Female partners may not be as accepting of erectile aids, which may also negatively impact sexual activity. The authors feel that men who have lost erectile function following prostatectomy may actually experience grief and mourning psychologically and physiologically.

The third article in this review also has clinical implications. It is by Wittman and colleagues (2011) and it discusses the fact that pre-operative expectations of urinary, bowel, hormonal, and sexual function by men undergoing radical prostatectomy do not match outcomes at one year post-procedure. This was a study at one site, University of Michigan, and involved preoperative counselling about expected outcomes after radical prostatectomy. Counselling was provided by a trained urological oncologist, a nurse practitioner, and in some cases, a social worker. Participants completed a questionnaire pre-operatively and at one year post-surgery that assessed urinary incontinence, urinary irritative symptoms, bowel function, hormonal function and sexual function.

The results indicated that a significant portion of the men (61% had same or better function) had overly optimistic expectations regarding UI and sexual function, despite counselling. A disturbing finding was that 17% expected improved erections following surgery and 70% expected the same bladder control, with 17% expecting better control. The authors concluded that men who undergo prostatectomy have unrealistic expectations, despite intensive counselling. As a clinician who routinely sees men with urinary incontinence following surgery, these findings were not surprising. (Reference: UroToday Exclusives, UroToday.com, September 27, 2011)

Agent Orange Expanded. The Veterans Administration announced an expansion of its list of Navy and Coast Guard ships whose crews may be eligible for disability compensation as a result of exposure to the toxic de-

foliant Agent Orange during the Vietnam War. The ships, mainly landing vessels and destroyers, operated along the Vietnam coast or in its inland waterways during 1962-1975. The ship list is flexible, so additional ships may be added from time to time as evidence discloses their eligibility. The VA pays compensation to veterans or survivors for fourteen medical conditions associated with Agent Orange, including prostate cancer. The VA said it paid \$2.2 billion in the past year to 89,000 veterans or survivors affected by Agent Orange. There is still a substantial backlog of related claims from the Vietnam War. (Reference: *Military Times*, September 2, 2011, via the *UsTOO Hot Sheet*, October 2011)

Brachytherapy versus external beam radiotherapy for low-risk prostate cancer.

Zelevsky, et al., Memorial Sloan-Kettering Cancer Center, studied 281 men treated by intensity-modulated radiotherapy (IMRT) and 448 men treated with brachytherapy during 1992-2003. The men were considered to have "favorable risk" prostate cancer. The researchers concluded that for 7-year biochemical tumor control, brachytherapy was superior to high-dose IMRT. They felt that the better outcomes were attributable to brachytherapy's ability to deliver higher dosage with fewer associated morbidities. They conceded that such factors as existing urinary obstructions, larger prostate size and the like, might favor IMRT. Regarding erectile dysfunction in men who had pre-therapy potency, 35% (brachytherapy) and 44% (IMRT) developed post-treatment impotence. The researchers cautioned against selecting a therapy based on a lower incidence of sexual dysfunction because of the many factors affecting potency. The bottom line is that brachytherapy is the preferred treatment for patients with low-risk prostate cancer because of improved tumor control outcomes. (Reference: *Urology*, April 2011, via *PCa Commentary*, Seattle Prostate Institute, Volume 71, September-October 2011)

WE ARE GRATEFUL TO FERRING PHARMACEUTICALS FOR ITS SUPPORT OF OUR PROGRAM.

NUTRITION AND PROSTATE CANCER: CAN DIET AND LIFESTYLE IMPROVE CANCER OUTCOMES?

by
DR. STACEY L. KOFF

(A summary of a presentation to the WRNMMC Prostate Cancer Support Group on August 3, 2011)

INTRODUCTION

Thank you so much for that kind introduction. You may have noticed among the nice things said about me is that I am not a nutritionist or dietician. I don't have formal training in those areas, but I do have a personal interest in them, and I have done much self-study. That is why I wanted to talk to you about what I have learned over time regarding diet, nutrition, lifestyle and prostate cancer. My motivation for studying diet, nutrition, and lifestyle stems from a question I often receive - "Doctor, is there anything else I should be doing to deal with prostate cancer?" My answer was often less than convincing, so I decided to do something about it. No doubt there are some here tonight who are well-versed in the areas of nutrition and diet. If you are, I welcome your comments and participation as appropriate.

IS IT WORTH THE EFFORT?

My first concern was whether there was any real evidence that exercising, eating right, and other healthy practices, would be of any benefit to my patients who wanted to prevent cancer or have better cancer-related outcomes. Here is one example from a study published in the Archives of Internal Medicine. It was a substantial effort sponsored by the National Institutes of Health and the American Association of Retired People. It found that persons in the top quartile of red meat consumption were more likely to develop cancer and die (for a multitude of reasons) than those in the lower quartiles. So daily red meat intake was found to be especially risky to health.

A 2002 study reported in the New England Journal of Medicine had some interesting findings for urology patients related to diet and the formation of kidney stones. Prior to this study, most persons prone to kidney stones were counseled to eat low-calcium diets. There were two groups in the study; one

one group was told to restrict its calcium intake, and the other group told to restrict protein (meat) and salt intake. It turned out that the second group, with normal calcium intake, but low protein (meat) and salt intake, was more successful in preventing kidney stone formation. It had half the rate of kidney stone relapses than the calcium-restricted group. A more recent study learned that persons prone to kidney stone formation were very willing to take prescribed medications, adjust their fluids, change their diet, etc., in order to avoid another stone event. This straightforward conclusion was remarkable in that urologists did not realize how much patients were willing to cooperate in lifestyle changes in order to avoid kidney stone formation.

There was an large, older study of bladder cancer (1999) involving 48,000 men who were followed for ten years; 252 were diagnosed with bladder cancer during that time. Participants who had greater daily fluid intake (about 2.5 liters of fluid), had half the cancer risk than those with the lowest intake (about 1.3 liters of fluid). Put another way, participants who drank at least six cups of water had half the risk of developing bladder cancer compared to the risk of the participants who drank about one cup of water. These findings regarding water intake have not been consistent in every trial, but these findings make a lot of sense to me. One theory about the formation of bladder cancer is that there are carcinogens in the urine itself. So if you drink more fluids, or perhaps more importantly if you empty your bladder more frequently, you dilute those carcinogens and there is less contact time with the bladder lining, so there is a decreased risk of developing cancer. More is better!

PROSTATE CANCER ISSUES

There is much to read about diet, nutrition, and lifestyle and the prostate. I want to discuss what we know about these relationships across the spectrum of prostate issues such as benign changes,

prevention, prostate cancer diagnosis, active surveillance, prostate cancer treatments, and androgen deprivation.

Benign changes. In the older urology textbooks, benign prostatic hyperplasia (BPH) problems meant urinary symptoms such as getting up during the night, having a weak stream, frequent urination, and the like. These older texts found that there was an association between beef intake, milk intake and the urinary symptoms. We have more current data about BPH as a result of the classic Prostate Cancer Prevention Trial. During the seven years of assessment 876 men were diagnosed with BPH. (i.e., they received medications or had surgery for BPH). An analysis of food questionnaires showed a lower risk for intake of protein, alcohol, and vegetables, but an increased risk for fat intake and red meat. To clarify, it was not protein intake per se, but specifically red meat that constituted the risk. For those of you who enjoy frequent red meat intake, you may not be happy to hear this!

There is also some data on the effects of exercise and BPH symptoms. A 2008 study found that among runners, those who ran longer and who could run faster had a decrease in urinary symptoms. I must say that this study, especially, the speed portion, doesn't make intuitive sense to me. But it does reflect the overall interest in these sorts of issues, an interest in finding out if these disease processes are inevitable, or whether they can be modified with good diet habits and an active lifestyle.

PROSTATE CANCER PRINCIPLES

Let's transition from BPH to prostate cancer. Based on autopsy studies, many men have had latent prostate cancer. The rates of latent prostate cancer are uniform across populations worldwide and are about 30% for men under age 50 and 60-70% for men over 80 years of age. But, clinically-evident prostate cancer affects only roughly 1 in 6 men in the United States. This clinically-evident rate varies widely between and even within countries.

Genetic aspects. Most prostate cancer cases (85%) are felt to be sporadic, but evidence does exist for a genetic or hereditary component (15%) in prostate cancer incidence. This conclusion is based on observations that relatives of patients younger than 55 years are at higher risk for prostate cancer than are those with older affected rela-

tives. The number of affected family members and their ages at onset are the important determinants of risk among relatives.

Environmental aspects. Evidence of environmental risk for prostate cancer is found in the fact that Japanese and Chinese men who reside in the United States are diagnosed and die from prostate cancer more than Japanese and Chinese men who remain in their native lands and presumably consume their traditional native diets. The "westernization" experience of these men, especially of their diet, results in increased diagnoses and death rates from prostate cancer. Furthermore, as the Japanese diet in general becomes "westernized," we observe that more Japanese men are being diagnosed and dying from prostate cancer than historically has been the case.

Androgens. It is well known that androgens such as testosterone "feed" prostate cancer. It is not entirely clear what role estrogen plays in the development of prostate cancer. Estrogen is thought to protect against prostate cancer by inhibiting prostate epithelial cell growth. Alternatively, it may increase cancer risk by encouraging inflammation in concert with androgens. Also, increases in age-related prostatic disease parallel increases in serum estrogen levels; and on the other hand, there is a lower incidence of prostate cancer in those cultures with diets rich in phytoestrogens (phytoestrogens are plant sources of estrogen). The bottom line is that outcomes are mixed regarding the impact of estrogen on prostate cancer.

Other factors. Let me mention some other cancer-inducing phenomena. Insulin-like growth factor (IGF-1) slows desirable, normal cell death (apoptosis). When the normal cell death process slows, cancer formation may occur. IGF-1 also promotes cell proliferation, and there has been some association of high levels of IGF-1 and prostate cancer. IGF also has been found in modified foods and supplements. Leptin is produced by fat cells and it appears in vitro to have growth factors that induce cancer.

Vitamin D. You read a lot about vitamin D and its relationship to prostate cancer and other cancers as well. Indications are that low levels of Vitamin D are associated with prostate cancer. We get some of our vitamin D from diet, but much of it comes from exposure to sunlight converted in the skin. Men in northern climes with less exposure to sunlight, and African American men with darker skin, get less benefit from the normal absorption of sun-

light, and have higher rates of prostate cancer. Whereas Japanese men who tend to consume more fish with high vitamin D content have less prostate cancer incidence. Studies also indicate that calcium tends to depress vitamin D, so men getting excessive calcium from diet and supplements may be at increased risk for prostate cancer. Other studies indicate that vitamin D has anti-proliferative growth affect on cancer cells.

Prostate cancer prevention. Many of the steps proposed to prevent prostate cancer (and other cancers for that matter) are directed at decreasing levels of oxidative stress and DNA damage at the cellular level. That is why foods which are considered "antioxidants" are said to be "anti cancer." There are several oft-studied dietary factors that may affect prostate cancer risk. They are lycopene, selenium, Vitamin E, cruciferous vegetables, fish, and meat/dairy/fat, and soy. They act as antioxidants against the formation of free radicals. Free radicals can be mutagenic and damage the DNA of cells causing them to lose their ability to regulate their normal replication and death.

Lycopene often has been in the news. It is a red-colored chemical which is thought to be a strong antioxidant. Most studies are about tomatoes, probably because the tomato industry has better marketing skills! Actually there are other products such as watermelon that have more lycopene in them. One study in favor of lycopene as a cancer preventive was the Health Professions Follow-up study that showed a 35 percent decreased risk of prostate cancer in men who ate ten versus a man who ate one and a half weekly servings of a tomato-based food. Other studies have not been as conclusive, but one metanalysis found that there was probably a ten to twenty percent decreased risk of prostate cancer with lycopene intake.

Selenium at one point held a lot of promise for cancer prevention. One published study found that selenium is only helpful if an individual's selenium level is low at a base line. Americans tend to be a well-nourished group so low selenium levels is not the problem. Selenium is an antioxidant has been shown to inhibit tumor growth in the laboratory. Some of you may have been in the so-called Select Trial. It was a well-conceived randomized trial, but it had negative aspects, and it was stopped early for that reason.

Vitamin E has also been shown to inhibit prostate cancer cells in the laboratory and the Health Professions Follow-up Study. There was some evi-

dence of a decrease in advanced disease with Vitamin E supplementation. But there has been nothing conclusive. Evaluating supplements is difficult because establishing the dosage is always tricky.

Cruciferous vegetables have antioxidant proteins which in laboratory models have decreased tumor growth. Some controlled studies have demonstrated a mild association between reduced prostate cancer and vegetable intake. The common cruciferous vegetables are broccoli, cauliflower, cabbage and kale. About half of the case-control studies have demonstrated a mild association of vegetables with reduced prostate cancer risk. In the Health Professions Study there did not seem to be a decreased risk with vegetable intake until the researchers considered the years prior to entry of the study. Then men who consumed a high amount (more than 5 servings/wk) of cruciferous vegetables in the years before entrance into the study did have lower risk of developing prostate cancer, suggesting that more long-term intake may in fact reduce prostate cancer risk

Fish contain omega-3 fatty acids, a group of essential unsaturated fats that are believed to reduce cardiovascular risk as well as carcinogenesis Two prospective studies have demonstrated an inverse association between fish consumption and prostate cancer risk. Fish is also a natural source of vitamin D.

Meat, dairy, and fat consumption can affect the levels of such hormones as testosterone and estrogen, as well as IGF, the insulin-like growth factor I mentioned earlier. In addition, red meat and dairy products contain complex fatty acids which, when metabolized, can act as a preferential energy source in cancer cells and increase hydrogen peroxide production, an oxidative stressor for cells. Charring of meats during the cooking process produces heterocyclic amines, which are carcinogenic and increase prostate cancer risk in animal models. Again, bad news for people who like to grill steaks! Moderation in meat, dairy and fat intake should be considered by anyone trying to prevent prostate cancer and other cancers.

Soy and Omega Acids has a multitude of agents called isoflavones which act like estrogen. These isoflavones have been shown to inhibit benign and cancerous prostate cell growth in animal models. Soy intake may be one of the reasons that those men who eat a traditional Asian diet, with an emphasis on soybeans and foods made from soy, have lower incident of prostate cancer. The tradi-

tional western diet has very little soy intake. There is considerable interest in soy, so you will see frequent trials and studies involving soy or isoflavones. Here is an example of a small, randomized, controlled study. Eighteen men diagnosed with prostate cancer were randomized to either a low-fat, high-fiber soy-supplemented diet or to a typical Western diet that had about 40% of daily calories from fat. Next their blood serum was used to grow prostate cancer cells. The cancer grew less successfully on the serum from those patients following the low fat, high fiber diet with soy. Those patients had a desirable decrease in omega 6 and an increase in omega 3. A very similar study involved 40 men who had undergone prostatectomy and were felt to be at high risk of recurrence. They were followed for six months and the serum of those on the "healthy" diet had lower levels of IGF and their serum seemed to inhibit growth of LnCap cells in vitro. Let me add something about omega acids. What are they? They are fatty acids that come from our diet. The body takes the fatty acid compounds and makes hormones from them. The hormones derived from omega 6 tend to be detrimental because they can lead to inflammation and an increase in cell proliferation. The byproducts of omega 3 fatty acids tend to be beneficial, working against inflammation and cell proliferation. Even though it would seem that you only want the omega 3 in your body, ideally the omega 6 and 3 fatty acid levels should be balanced.

Active surveillance. I want to call the Prostate Cancer Lifestyle trial to your attention because it is apropos to our discussion tonight. It was a randomized intervention trial with a control arm. The patients had been diagnosed with what was felt to be low-risk prostate cancer, so they had selected active surveillance for their therapy. The treated group was counseled to change towards a low-fat, plant-based diet combined with exercise and stress reduction. The control group got "the usual care." The patients were followed for two years and the treated group had much lower rates of switching from active surveillance to more aggressive treatment for their cancer. Only 5% of the treated group had done so by the trial's end compared to 27% of the patients under usual care. The researchers concluded that patients with early-stage prostate cancer on active surveillance might be able to avoid or delay the necessity for conventional treatment for at least two years by making changes in diet and lifestyle.

Another small but interesting study addressed the role of diet and stress after radical prostatectomy. In this study ten patients had a rising PSA following surgery for prostate cancer. They all were placed on a low-fat, high-fiber, plant-based diet combined with a stress reduction program. The researchers noticed that the rate of rise in PSA decreased in eight of the ten men after they started following this regimen. The calculated PSA doubling time of their PSA increased dramatically from six and half months to eighteen months.

Flaxseed. Interest in the influence of flax seed remains high. So what is flaxseed? It is a tiny seed packed with healthy fatty acids. Its value as a health food has been recognized for centuries, often as a laxative. King Charlemagne reportedly required his subjects to consume it for their health. It is the seed portion, not the oil, that contains lignans. Lignans are plant compounds that mimic the action of estrogen and act like antioxidants. It is best to grind the flaxseeds and consume them with cereal or a like product rather consume them as flaxseed oil. There was a study of 163 men who had elected radical prostatectomy. They were randomized to different diets, with and without flaxseed, prior to surgery. After surgery their actual tumors were examined for proliferation (proliferation the abundant generation of abnormal cells). The tumors of the patients who included flaxseed in their diets showed decreased proliferation compared to patients without flaxseed in their diets.

Androgen deprivation therapy. I don't want to finish tonight without talking about androgen deprivation therapy (ADT). Most of you are familiar with it, and perhaps had received this therapy. Sometimes it is used in combination with radiation therapy, sometimes it is used alone for metastatic prostate cancer. ADT has a clear association with bone loss and it has recently been recognized for increased risk for cardiac events. Several trials have focused on the cardiac issue with mixed results. Some are finding that even men on short term ADT as an adjuvant therapy with radiation may experience increased cardiac events. Hormone therapy is thought to contribute to decreased glucose tolerance, cholesterol issues and obesity, especially central obesity. It is recommended that men initiating ADT see their primary care doctors to get a check of their blood pressure, lipids and glucose levels. Quite frankly, these are things that need to be done anyway for general health screening. The current guidelines are to keep lipids in check, maintain blood pressure in the normal range, and control

glucose levels. A baby aspirin a day is a good idea for those who don't have any contraindications to it. And don't smoke!

Regarding bone health, bone loss is one of the unseen complications of ADT. It can be ongoing and unnoticed until a fracture occurs. The risk of fracture is related to how long you have been receiving ADT. If you have preexisting osteoporosis and then get metastases from your prostate cancer, the risk of bone-related events increases. Osteoporosis is not just a disease affecting men on ADT. It is related to age and about five percent of men are osteoporotic before they even start hormone therapy. So careful monitoring is required.

Proper prevention of bone events starts with monitoring, typically with a DEXA scan. About 30% of men have osteopenia and 5 % have osteoporosis before even starting ADT. Patients should be aware of the recommended intake of calcium and try to achieve it through diet or calcium supplements with vitamin D (1,000 to 1200 depending on age). Weight bearing exercises are very important and bisphosphonates should be considered. And, of course, don't smoke, and limit the use of caffeine and alcohol. Bisphosphonates may affect jaw bone disease, so a dentist needs to be involved to avoid complications.

CONCLUSION

At the outset, our question was "Can diet and lifestyle improve cancer outcomes?" Certainly the available evidence is often inconclusive. Nevertheless, there are sufficient reasonable indications that you can be proactive in prostate cancer prevention and control by the commonsense application of certain diet and lifestyle principles. Moreover, these principles also have a positive impact on overall health beyond prostate cancer. I highly recommend the American Cancer Society's evidence-based guidelines for cancer prevention as your primary source for advice. They are:

Maintain a healthy weight throughout life; Adopt a physically active lifestyle; Consume a healthy diet emphasizing plants; and Limit alcohol consumption. In addition, I believe the evidence supports these related conclusions and recommendations: red meat and dairy consumption increase the risk of cancer; high calcium intake, especially with supplements, increases the risk of more aggressive cancer; consider having one or two meals a week of a soy-based protein; consider adding flaxseed to

your diet; be aware of what your vitamin D level and restore it as necessary by spending more time outside and adding a supplement as required; consider increasing lycopene intake; balance your fatty acids; and don't overlook about your bone health; All of these things are good for your heart, too, and even though we all struggle with your prostate cancer, the real killer in the US is heart disease.

My purpose tonight was to generate some interest in the topic of diet and lifestyle as it relates to prostate cancer, and I am happy to answer any questions you might have.

QUESTIONS AND ANSWERS

Question: Does there come a time when a man no longer needs an annual regular PSA testing and digital rectal examination.

Answer: An influential article several years ago argued that after age 75 it is probably unproductive to have an annual PSA test because at that age and beyond treating prostate cancer was really not very valuable because it didn't seem to extend longevity. The argument has merit, but I do think the annual digital rectal exam after age 75 is useful. After all, if your doctor can detect a hard and lumpy prostate no matter what your age, you may want to know it. I want to find advanced prostate cancer that may cause you bone pain, and if left untreated, could shorten your life. So I would say the PSA testing needs to stop at some point such as age 75, but the rectal exams should continue. That is my opinion. Having said that, there is unlikely to be a consensus among urologists on the matter.

Question: I have read that if you want to enhance the lycopene found in tomatoes it is best to have the tomato processed like sauce or tomato paste instead of the fresh vegetable.

Answer: Yes, there are higher levels of lycopene in processed tomatoes.

Question: What I can do about my low testosterone. Is there any diet regimen I can do to raise my testosterone level?

Answer: First and foremost, you must have a frank discussion with your physician about your low testosterone concerns. It is may be that he is trying to suppress your testosterone level to combat your disease. Tell him about any fatigue, muscle loss, low libido, and the like. You can certainly work on those kind of symptoms with diet, exercise, stress reduction, etc.

Question: I have read of late that a complete vegan diet is effective in preventing cancer or its metastasis.

Answer: I have reservations about the health claims for the vegan lifestyle. Of course, any sensible, balanced diet undertaken with medical supervision is likely to be heart-healthy and promote one's general health. I myself am not a big booster for the vegan style. I don't think the data is there to justify the claims heard from boosters, especially the claims regarding cancers of any type.

Question: Earlier you mentioned the issue of annual PSA testing after age 75. I am 68 with very early stage prostate cancer. I have selected active surveillance as my therapy. Other than scheduled PSA testing, the digital rectal examinations (DRE) and an annual biopsy, are there any other indicators of accelerating cancer growth?

Answer: I have not seen anything that is clinically used. There is the prostate antigen 3 gene (PCA3), a urine test for cancer aggressiveness, but it is in the investigational stage. As far as being a standard of care, your scheduled PSA testing, DRE, and biopsy seems appropriate. Some medical centers use the MRI as a resource to evaluate whether a patient is a candidate for active surveillance.

Question: I have prostate cancer. Is there any downside to continuing PSA testing after 75?

Answer: No, because you are in a different situation in that you already have a diagnosis of prostate cancer, so the annual PSA test is part of your continuing therapy. On the other hand, I believe that the use of the PSA test as a screening device for early prostate cancer is unnecessary in men in their mid-70s.



(Directing Prostate Cancer Research-continued from page 1)

In the second phase of the review process, an Integration Panel reviews the scoring and summary statements from the peer reviews and evaluates the applications across multiple disciplines for programmatic relevance and merit. This evaluation phase results in a list funding recommendations submitted to the Commanding General of the U.S. Army Medical Research and Materiel Command.

The remainder of this article focuses on my experience as a Consumer Reviewer, how I decided to become involved, the application requirements, and what I experienced as a first-year participant in the peer review process. I first learned about the program at an UsTOO monthly support group meeting at Walter Reed Army Medical Center. As a PC survivor, I felt this would be a unique opportunity to learn more about the developments in PC research and to participate in a process that supports that research. I obtained an application package by visiting the U.S. Army Medical Research and Materiel Command web site (<http://cdmrp.army.mil/CWG>). The application form asked for the usual biographic information and requested a short essay describing my advocacy experience, my current advocacy/support group role, how I would represent the survivor/patient community, how I kept up-to-date on issues and developments related to prostate cancer, and how I would balance my own views with the views of patients, survivors, family mem-

bers. About two months prior to the Peer Review Panel meetings, I was informed that I was selected as a Consumer Reviewer. As a first-year novice, I was paired with a mentor - a reviewer who had participated in prior peer reviews and who would help familiarize me with the process by sharing his knowledge and experience.

For the 2011 review cycle, 218 applications were evaluated. To facilitate the process, the applications were divided into functional categories. I was assigned to a panel that reviewed applications focusing on the training of postdoctoral and physician researchers to become principal investigators in the area of PC detection and experimental therapeutics. I, along with a second Consumer Reviewer and three Scientific Reviewers, made up a panel assigned to review 16 applications. Our applications were competing for grants that would fund research and training projects that focused on PC identification and treatment. These grants would be awarded to investigators in the early stages of their careers. Key features to be considered in the evaluation were the active involvement of established prostate cancer researchers and mentors, the presence of an individualized training program for the researcher, and the responsiveness of the proposed research to the Prostate Cancer Research Program's overarching challenges of developing effective treatments for advanced prostate

cancer and distinguishing between the aggressive and indolent forms of the disease.

About a month and a half prior to the Peer Review Meetings, we were provided access to our assigned applications via a web-based tool called the Program and Peer Review Management Information System (P2RMIS). In addition to the applications, the tool provided a structured format for the reviewers to enter critiques and scores for each evaluation criteria associated with a proposed research project. As a Customer Review, I was to focus on the Impact Criterion. Under this criterion, evaluations were to stress the potential relevance of the proposed research to patients and survivors, the impact the proposed work might have on the research field, and the impact of the proposed training program on the development of a principal researcher who would be focused on PC.

The Consumer Reviewers were provided with training materials and on-line "webinars" to prepare for their work. After drafting critiques for our first two or three applications, we shared our drafts with our mentor and the Scientific Review Officer to ensure we were on the right track. For each application, the reviewer wrote a summary paragraph critiquing the strengths and weaknesses of the application relative to a specific criterion. The reviewer was also asked to assign a numerical score (1 to 10, ranging from 1-2 being Deficient and 9-10 being Outstanding). In addition, we were asked to give a second score for our evaluation of the overall application. After the first few reviews, I found that it took me around two hours to critique and score each of my assigned applications and enter the data into the P2RMIS tool. I had a month to complete my critiques prior to the plenary peer review meetings that were scheduled for early August. I set the goal of cranking out one or two applications per day, and I was able to finalize and submit them well before the July 28 deadline.

The plenary peer review meeting brought together multiple panels into a single forum. The meeting lasted three days. During these sessions, each panel member briefed their assigned critiques and scores to the assembled peer reviewers. A question and answer session followed. Then each panel member was given an opportunity to modify his or her scores if they chose to do so. Next, the Chairman of the peer review meeting summarized the discussion and instructed the entire body of peer reviewers to score the application. As you

might expect, some of the applications were evaluated quickly; but others took somewhat longer.

In years past, the plenary peer review meetings took place over a three day period in a hotel conference facility in Washington D.C.; however, this year, due to the current budgetary environment and the need to economize, the entire meeting process was accomplished using telephone conferencing and the on-line P2RMIS tool. All the scoring was done on-line. Although this was the first time the reviews were conducted as a teleconference, the process worked surprisingly well. All the assigned applications were reviewed and scored by the end of the third day.

To summarize, my experience as a Consumer Peer Reviewer was rewarding, and I was honored to participate. If asked, I will volunteer again. The Prostate Cancer Research Program supports cutting edge research leading the way to improved diagnostic and therapeutic tools to fight PC. In addition, the program helps fund the training of the next generation of independent PC researchers.

The work of a Consumer Peer Reviewer requires a commitment of time and energy, especially for a first year novice who is learning the process and the language of scientific community. There is about a 60 to 70 hour time commitment, extended over about a month and a half, but there is also an honorarium provided at the end of the process in appreciation for work done. If this activity sounds appealing to you, I urge you to look into the program. You do not need a technical background. What you do need is the ability to advocate for the survivor and patient communities and describe the potential impact of the proposed research projects on those communities. If you have questions, contact me at mjs.at.home@gmail.com.

Finally, despite the good work being done by this program, in the climate of DoD budget woes, some voices in Congress question whether this program should be funded in the future. My conviction after participating in the program is that it should continue. The proposed research projects are innovative and cover multiple focus areas ranging from tumor biology and immunology to biomarkers and genetics. The evaluation process appears to be efficient and objective. The current funding level of 80 million dollars is modest but important. In short, I believe it is a good investment that well deserves our continued support and advocacy.

◆ **WRNMMC US TOO COUNSELORS** ◆ (As of October 1, 2011)

(THESE PERSONS ARE WILLING TO SHARE THEIR EXPERIENCES WITH YOU. FEEL FREE TO CALL THEM.)

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Gil Cohen	Baltimore, MD	(410) 367-9141	
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PROSTATE CANCER AND SEXUAL FUNCTION

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INCONTINENCE

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Ken Simmons	Alexandria, VA	(703) 823-9378	(Radiation and Hormonal)
Bill Stierman	Vienna, VA	(703) 573-0705	(Surgery and 2nd Line Hormonal-Ketoconazole)
Ray Walsh	Annandale, VA	(703) 425-1474	(Surgery and Hormonal)

◆ **MEETING ANNOUNCEMENT** ◆

WEDNESDAY, NOVEMBER 2, 2011

7 PM

CLARK AUDITORIUM (SECOND FLOOR)

BUILDING 10

WALTER REED NATIONAL MILITARY MEDICAL CENTER

◆ **SPEAKER** ◆

PATRICIA LILLIS-HEARNE, MD

Radiation/Oncology Service

Walter Reed National Military Medical Center

◆ **TOPIC** ◆

**"Everything You Always Wanted to Know about Radiation Therapy
and Prostate Cancer, and Maybe More!"**

We meet at Clark Auditorium (Bldg 10, 2nd Floor) at the Walter Reed National Military Medical Center located at 8901 Wisconsin Avenue, Bethesda, MD 20889. Building 10 is at the official entrance to the hospital and on a circular drive with a flagpole.

Gate/Parking: If you enter the base through South Gate (Gate 2) off Rockville Pike/Wisconsin Ave, take the first right (Palmer Road South). On your left you will see the Emergency Room (Bldg 10). The entrance to Building 10 is just past the Emergency Room on your left. Take the first left after Building 10 (Brown Drive) and the parking garage (Bldg 55) will be directly on your right.

Security: A military ID is required to get on base. Persons without a military-related ID card who are attending the meeting are required to register in advance in order to gain entry. To register, contact Jane Hudak at 301-319-2918 or jane.hudak@med.navy.mil no later than Monday, October 31 so she can arrange for entry. Have a photo ID card ready.