WRAMC Us TOO, Inc.
A PROSTATE CANCER SUPPORT GROUP
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NEWSLETTER

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♦ YOU CAN HELP DIRECT RESEARCH F0R PROSTATE CANCER! ♦

The Prostate Cancer Research Program (PCRP) funded by the Department of Defense has $80 million to distribute among worthy research proposals during 2009. The PCRP is part of a larger medical research effort termed the Congressionally Directed Medical Research Programs (CDMRP) managed by the U.S. Army Medical Research and Materiel Command at Fort Detrick, MD. During 1997-2007, the PCRP received 8,401 research proposals and funded 1,837 proposals with a total of $710 million.

The PCRP relies on panels composed of scientists and consumer reviewers to recommend the most promising prostate cancer research proposals for funding. Consumer reviewers are prostate cancer survivors who represent the collective views of their communities. This unique partnership between scientists and consumer reviewers provides the participants with useful insights into the funding decisions; the scientists benefit by understanding the consumers perspectives on innovative research, and the consumer reviewers are enriched by participating in the discussion of the merits of the research proposals.

Us TOO International chapters and individual members have traditionally supported this unique research effort by volunteering to serve as consumer reviewers. You need not be a rocket scientist to participate! Past consumer reviewers agree that a well-read person who is concerned about prostate cancer issues will be comfortable in addressing the various research proposals.

So how do you get involved? Let the leader of your local prostate cancer support group know of your interest. He should be aware of the PCRP and be able to assist you with the application and nomination process. To get more information and obtain a nomination packet, contact:

Congressionally Directed Medical Research Programs
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♦ *INSIDE THIS ISSUE* ♦

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Was this newsletter forwarded to you at your new address? If so, it may be the last issue of the WRAMC Us TOO newsletter you receive! The newsletter is mailed First Class, so the USPS forwards it to you at your new address for six months after your move, and then it is returned to us as "Undeliverable." This is bad news on two counts: we just wasted $1.62 in printing and postal expense, you no longer get the newsletter! The best way to provide timely change-of-address notification is to contact the editor directly. Contact information is on the left.

♦ AUGUST SPEAKER'S REMARKS ♦

Dr. Ravi A. Madan, Center for Cancer Research, National Cancer Institute, was our speaker on Wednesday, November 5, 2008. His topic was "Dealing with Osteoporosis after Prostate Cancer." A summary of Dr. Madan's presentation is at page 8.

♦ MEETING SCHEDULE FOR FEBRUARY 4, 2009

Our program for February 4, 2009, offers a change of pace from our usual program. In the past we have presented a panel of prostate cancer survivors who frankly described their individual experiences with various prostrate cancer treatments, then answered questions. This approach was well-received and we have had requests about having a similar program. So here it is! Join us on Wednesday, February 4, 2009, at 7 PM in Joel Auditorium. Your guests are always welcome.

♦ FROM THE EDITOR'S DESK ♦

Vitamin E , Selenium and Prostate Cancer. A large government study of whether vitamin E and selenium protect men against prostate cancer has been suspended after an independent analysis determined that the nutrients did not reduce the risk for the common malignancy. The $119 million study, involving more than 35,000 men, also found hints that the nutrients might increase the risk for prostate cancer and diabetes, although officials stressed that those findings may be a coincidence. The stark conclusion is that selenium and vitamin C, taken alone or together for an average of five years, did not prevent prostate cancer. The study participants will be followed for another three years.

The announcement marks the latest in a series of disappointing findings about the potential health benefits of vitamins and other nutritional supplements, which earlier studies had indicated could have advantages. One theory was that antioxidants could affect the damaging free radicals, which are a natural byproduct of cellular processes in the body. But subsequent studies testing antioxidants and nutritional supplements have not confirmed the benefits, and several have even been alarming. For example, beta carotene increased, rather than decreased, the risk of lung cancer among smokers, and vitamin E -- also touted as helping to prevent heart disease -- appeared to boost the overall risk.

The so-called SELECT study was funded by the National Institutes of Health after earlier studies indicated the nutrients may protect against prostate cancer. An independent panel of experts monitoring the study discovered, after men had been taking the supplements for about five years, that there was no benefit and there were suggestions of possible harm, prompting officials to stop the project. A study coordinator said the important message for consumers is that taking supplements, whether antioxidants or others, is not necessarily beneficial and could be harmful.

A spokesman for the Council for Responsible Nutrition, an industry group, said in a statement that the findings did not discount the value of taking vitamin E and selenium for other general benefits. (*The Washington Post*, November 28, 2008)

Artificial Sphincter and Incontinence. Men who have undergone radical prostatectomy, prostate cancer radiation therapy, or other treatment resulting in significant urine leakage, experience a high level of "social continence." McAninch, et al., University of California, San Francisco, implanted artificial urinary sphincters in 30 men with urinary incontinence, 26 of whom had been treated for prostate cancer. Of those 26 patients, 18 had the sphincter placed via a standard approach and 8 artificial sphincters were placed with a transcorporeal approach. The devices have been in use since 1972; the newer transcorporeal approach was developed to allow placement in patients with urethral atrophy and previous urethral cuff erosion.

After two years, 69% of the patients were “socially continent" with standard placement of the sphincter, while 81% of patients who had the sphincter placed transcorporeally achieved “social continence.” Pad use declined from 8 to 9 pads a day beforehand to only 1 or 2 pads a day. So, the patients were considered to be “socially continent.” The researchers concluded that the transcorporeal placement is an effective salvage or primary incontinence treatment for high-risk patients after prostate adenocarcinoma therapy. (Source: *Urology* 2008;72:825-827, via Reuters Health Information, November 21, 2008)

New Technique Improves Post-Surgery Continence. In recent years there have been many improvements in aspects of radical retropubic prostatectomy. These include reduced complications and greater potency rates. However, incontinence may still affect as many as 83% of patients in the first three months after surgery. Japanese researchers at Kurume University School of Medicine report that following radical retropubic prostatectomy, placing sutures to anchor the vesico-urethral anastomosis to the puboprostatic ligaments leads to significantly enhanced early urinary continence.

The puboprostatic ligaments normally support the urethra in maintaining its position in the pelvic floor, a likely aid to continence after prostatectomy. The new technique uses just two sutures to preserve the anterior attachments of the urethra to the pubic bone.

The researchers randomized 60 patients with localized prostate cancer to radical retropubic prostatectomy with or without the suspension procedure. At one month, the continence rate was 53% in the suspension group and 20% in control patients. At three months, the corresponding proportions were 73% and 47%, and at 6 months, they were 100% and 83%. In addition, the median continence recovery interval was 31 days in the suspension group compared to 90 days in controls.

The researchers note that the new technique could be used in laparoscopic and robotic radical prostatectomy, and could result in earlier continence after surgery. (*BJU Int* 2008;102:958-963 via Reuters Health Information, October 31, 2008)

Aspirin and Lower PSA Levels. The use of aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) is significantly associated with lower PSA levels, especially among men with prostate cancer, according to Fowke, et al., Vanderbilt University.

The study involved 1,277 participants who underwent biopsy of their prostate. Approximately 46 percent of the men reported taking an NSAID, mostly aspirin. After adjusting for age, race, family prostate cancer history, obesity, and other variables, the researchers found that aspirin use was significantly associated with lower PSA levels. PSA levels were 9 percent lower in men taking aspirin compared with men who did not use aspirin.

Earlier studies reported anti-inflammatory drugs like NSAIDs were associated with lower prostate cancer risk. This new study also suggests that NSAID use has a beneficial effect on prostate cancer. On the other hand, the data also indicate that NSAID use could affect the ability to detect prostate cancer because aspirin and other NSAIDs may lower PSA levels below the level of clinical suspicion without having any effect on prostate cancer development. If that is the case, use of these agents could be hampering the ability to detect early-stage prostate cancer through PSA screening. The researchers conclude that future studies will need to find a way to determine if NSAID use is affecting prostate cancer risk or simply our ability to detect prostate cancer. (Source: *ScienceDaily*, November 17, 2008)

Controversy about CyperKnife. It's a high-tech, computerized, robotic device introduced in 2001 to treat patients with radiation for brain and spinal tumors. Now it is being aggressively used in the treatment of prostate cancer. Does it represent an important advancement or another example of an expensive and potentially profitable new technology proliferating too soon. The debate illustrates the issues that can arise when a costly new medical technology arrives before researchers have had time to evaluate their risks and benefits.

Some critics suggest that the push to expand the use of the CyberKnife may be motivated in part by financial incentives. The manufacturer wants to sell more machines, hospitals and private practices want to recover the cost of the systems, and urologists can receive a Medicare payment of about $1,200 for each patient who opts for the therapy.

Conventional external beam radiation subjects the tumor to relatively low doses spread over about 40 fifteen-minute sessions. The CyberKnife enables men to complete treatment in just four or five sessions by much more accurately delivering about quadruple the usual dose of radiation each time. Doctors inject four tiny gold cylinders into the prostate to create a precise target. The patient lies on his back for each one-hour session as a robotic arm swivels around to shoot dozens of beams from multiple angles.

The CyberKnife is quickly becoming the most popular option. In some locales, radio ads, bus signage, newspaper ads, mass mailings and even billboards, prominently tout the treatment. This aggressive marketing is cited by critics who see a seamier aspect.

To what extent can the CyberKnife reduce the complications, including incontinence, bleeding, problems urinating and impotence compared to other therapies? Skeptics say the studies done so far have been too small and followed patients for too short a time. Proponents suggest that the criticism of the CyberKnife is driven by doctors who are wedded to existing treatment, resistant to change and fearful they will lose patients to a superior alternative.

Despite the reservations, Medicare and private insurers in many parts of the country are paying for the treatment, which costs about the same as more traditional radiation therapy -- about $20,000 to $30,000. Other insurers, however, have decided against covering the treatment until more evidence is available, and Medicare, concerned that it was inadvertently creating a financial incentive to use the CyberKnife, next year will make doctors justify being reimbursed for referrals. (Source: *The Washington Post*, November 28, 2008)

Treating Benign Prostatic Dysplasia. Benign prostatic hyperplasia is a disease that affects between half and two thirds of men in their seventh decade of life. A recent study confirmed that the disease is progressive and likely to become more serious over time. Qizilbash, et al., Oxon Epidemiology Ltd., London, conducted a literature review and examined data from 16 studies involving more than 12,000 patients. While there was not a single summary conclusion from the studies, most studies showed progression among patients in the placebo groups, based on a worsening in clinical outcomes and the change from baseline in prostate volume and maximum urinary flow. The rates of surgery ranged from 1% to 10%, and the rates of acute urinary retention ranged from 0.4% to 6.6%. These rates tended to be worse with a longer follow-up. The researchers said that follow-up should be for life, and effective early interventions that favorably modify the natural history of the disease should be considered. (Source: *BJU Int* 2008; 102:981-986 via Reuters Health Information, October 29, 2008)

Testosterone Said Unrelated to Prostate Cancer Risk. Testosterone is the primary male hormone that helps maintain muscle mass and strength, fat distribution, bone mass, sperm production, sex drive and potency. The hormone's role in men's health is controversial, with the relationship between men's natural testosterone levels and overall health not well understood, researchers say.

Natural levels of a man's testosterone do not affect prostate cancer risk as some had thought. The reason scientists had believed it played a role in raising prostate cancer risk was because testosterone feeds tumor growth, which is why some treatments seek to block the hormone.

Roddham, et.al., University of Oxford, London, noted that 23 studies have examined a potential link between testosterone level and prostate cancer risk, but so far results have been inconclusive. For this study the researchers collected worldwide data on hormone levels of 3,886 men who eventually developed prostate cancer and 6,438 men who did not. A comparison of the two groups found no substantial relationship between their testosterone levels and their risk of developing the disease. According to a commentator, these latest findings should prod researchers to shift the focus of their research beyond testosterone into new risk factors for the disease. (Source: Reuters Health Information, April 15, 2008)

Battle of the Sexes: Prostate Cancer Research Funding Gets Left Out. Prostate cancer has been left out again when it comes to increases in disease research funding. The Prostate Cancer Research Program (PCRP) at the Department of Defense (DOD) maintained funding of $80 million for the fourth year in a row for fiscal year 2009. Meanwhile, Congress allocated an additional $11.5 million for breast cancer research ($150 million in total) and doubled research for ovarian cancer ($20 million in total).

Advocates say the prostate cancer community needs to be more vocal when it comes to pushing for government funding increases for prostate cancer research, insisting on nothing less than parity for men's health care issues. Since fiscal year 2001, prostate cancer research funding at the DOD has fallen from $100 million to the current level of $80 million while breast cancer research has continued to see increases.

In addition to increases in breast and ovarian cancer research funding, Congress expanded the peer-reviewed program at the DOD to include several other research programs such as vision, orthopedic and spinal cord research, among others. These additional research programs will likely affect funding for prostate cancer research in the future. (Source: ZERO, formerly the National Prostate Cancer Coalition)

Bone Drug Helps Some Men with Prostate Cancer. Men experience significant bone loss when they are given androgen-deprivation therapy (ADT) to eliminate the testosterone that is driving their prostate cancer. A recent study found that alendronate, usually given to women for osteoporosis, is also helpful for men undergoing hormone therapy to fight prostate cancer. Greenspan, et al., the University of Pittsburgh, examined the effect of alendronate, better known by the brand name Fosamax, on changes in bone density in 112 men on ADT for prostate cancer. After two years, continuous alendronate treatment produced the greatest increases in bone density. Men who had been receiving ADT for more than 36 months before beginning alendronate treatment had significantly less gain in bone density than did men who had been on ADT a shorter time.

The researchers concluded that improvements in bone mineral density in men with prostate cancer on androgen deprivation are greatest in men who continue to receive alendronate therapy. Furthermore, delay in treatment is detrimental to skeletal integrity. They advise that once-weekly oral therapy with alendronate should be considered early and continued for at least two years in men with prostate cancer who are receiving ADT. (Source: Reuters Health Information, October 22, 2008)

Long-Term Cancer Survivors Likely to Have Severe Psychological Distress. Long-term survivors of adult-onset cancers have nearly twice the rate of severe psychological distress (SPD) as people without a cancer diagnosis, according to a new national study. SPD is defined as distress that causes moderate to serious problems functioning in social, work, or school situations. The prevalence of SPD was significantly higher among long-term cancer survivors than among people never diagnosed with cancer. Long-term cancer survival was defined as having lived 5 years or more after an initial cancer diagnosis. The majority were survivors of breast (20%), gynecologic (19%), male genitourinary (12%), and colorectal (8%) cancer. Approximately 1 in 18 long-term cancer survivors report SPD.

The researchers identified several clinical and sociodemographic factors associated with SPD in long-term cancer survivors. The most pronounced factor is a younger age at diagnosis. Long-term cancer survivors younger than 45 years of age at diagnosis are 5.6 times more likely to experience SPD than survivors 65 years and older at diagnosis. People 45 to 65 years old at diagnosis are 2.7 times more likely to have SPD than those 65 years and older.

Survivors who had the following characteristics are more likely to experience SPD than those without the characteristics: (a) Not married or living with a partner; (b) Current or former smokers; (c) Less than a high school education; (d) Uninsured; (e) Difficulty with the activities of daily living. (Source: American Society for Therapeutic Radiology and Oncology (ASTRO) 50th Annual Meeting: Abstract 225, via Medscape Medical News, September 24, 2008)

Hormonal Therapy Sooner than Later. Results of a recent study indicate a significant benefit to initiating hormonal therapy sooner rather than later in men with early prostate cancer who experience a rapid doubling of their PSA level within 6 months of radiation therapy. The research also supports delaying hormonal therapy in men whose PSA increases more slowly during a longer period of time. This study helps to further refine the role of PSA doubling time in predicting which patients may benefit from androgen deprivation therapy (ADT) for biochemical failure, and which may be "expectantly observed" and spared the toxicity of hormonal therapy.

Earlier studies have indicated that if the PSA doubling time occurs within 12 months, there is an increased likelihood that the prostate cancer will spread and that hormone therapy will provide a potential benefit if started at that point. Horwitz, et al., Fox Chase Cancer Center, Philadelphia, say that the immediate use of ADT in patients with PSA doubling time less than 6

months was associated with significant improvements in cause-specific survival, although the benefit was less apparent in patients with longer PSA doubling times. (Source: Reuters Health Information, September 24, 2008)

Hormone Therapy before Brachytherapy for Older Men. Hormone therapy is often used before brachytherapy to shrink the size of the prostate and make the process of implanting radiation seeds technically easier. Men older than 70 years of age with early-stage prostate cancer have 20% higher mortality when treated with hormone therapy before brachytherapy than when treated with radiation seed implants alone, according to a new study.

This new study by Dosoretz, et al., Harvard Radiation Oncology Program, Boston, involved 1,709 men with localized prostate cancer who were at least 70 years of age (median age, 75 years). After a median follow-up of 4.8 years and adjustment for known prostate cancer prognostic factors and age, treatment with hormone therapy was found to be significantly associated with an increased risk for all-cause mortality. Increasing age and a Gleason score of 7 or higher were also significantly associated with an increased risk for mortality. (Source: American Society for Therapeutic Radiology and Oncology (ASTRO) 50th Annual Meeting: Abstracts 84 and 1050, via Medscape Medical News, September 24, 2008)

Erectile Dysfunction Varies With Androgen Deprivation Therapy. A substantial minority of men receiving androgen deprivation therapy for prostate cancer experience erectile dysfunction (ED). However, many respond well to ED therapy, according to a recent study.

Derweesh, et al, University of Tennessee Health Science Center, say ED is grossly underreported by men undergoing androgen deprivation therapy (ADT); studies that have been reported in the literature have tended to focus on decreased libido and have not examined the issue of erectile dysfunction per se. The researchers note that there is a lack of information on the prevalence of ED and the response to its treatment in patients undergoing ADT.

The researchers prospectively reviewed the data for 395 patients receiving androgen deprivation therapy for prostate cancer at their institution over a period of about 15 years. The mean age was 71.7 years and the men were followed for more than 7 years. During follow-up, 14.4% of patients reported ED. Seventy percent of these cases were new-onset. Being younger than 70 years and not having diabetes were significantly associated with reports of ED.

Seventy-two percent men with ED received phosphodiesterase type-5 inhibition (PDE5i) monotherapy, 11% received prostaglandin E1 analogues alone, 7% were treated with vacuum erection devices alone, 2% received an inflatable penile prosthesis, and 9% received a combination of therapy.

A successful response to ED treatment was reported by 47% of the patients. This included 44% of the PDE5i monotherapy group. The researchers say the study demonstrates for the first time in a large series, the significant efficacy of PDE5i therapy in ED caused by androgen deprivation therapy. They conclude that the data support serial monitoring of sexual and erectile dysfunction, and physician-directed attempts at restoring erectile function in patients undergoing ADT. (Source: *BJU Int* 2008;102:39-43 via Reuters Health Information, July 11, 2008)

DEALING WITH OSTEOPOROSIS AFTER PROSTATE CANCER

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(A summary of a presentation to the WRAMC Us TOO Chapter on November 5, 2008)

Introduction

Tonight I will be talking about osteoporosis, a condition that is often overlooked by men who are dealing with prostate cancer. They are more likely concerned about such matters as PSA, Gleason score, the selection of their primary therapy, and possible side effects. But there are other aspects of prostate cancer that cannot be ignored. Ten years ago or so men who faced hormonal therapy often were told that hormonal therapy was necessary in their case, and yes, there were side effects like hot flashes, breast enlargement and the like, but they just had to buck up and deal with them. More recently it has come to light that beyond these common side effects, there are other complications that need to be monitored. And one of those serious complications is osteoporosis. So my purpose tonight is to provide basic information about osteoporosis, how it is diagnosed, and how it can be treated. Then we can also talk about the inevitable risk of osteoporosis and prostate cancer and what we can do to deal with it as time goes on.

Dimensions of the Problem

Osteoporosis is a skeletal disorder characterized by low bone mass and microarchitectural disruption. This is just a technical way of saying that your bones are getting weaker. It is not an uncommon condition, and the public usually reads about it as primarily a female condition because it affects more than ten million people in the United States, eighty percent of them women. The truth is that osteoporosis in men is seriously under-reported, so the estimate that two million men are affected is likely inaccurate. In addition to those ten million people, another 18-20 million or so will have a bone mass condition called osteopenia that is not as serious as osteoporosis, but still a cause for concern. Again, most of the research to date addresses post-menopausal women; only now is attention being given to men, especially men being treated for prostate cancer with hormonal therapy. The good news is that there are excellent tests to detect osteoporosis and good treatments to deal with it when diagnosed. Also, there are relatively new treatments for osteoporosis that may help prevent bone complications associated with metastatic prostate cancer**.**

Bone Development

These next few slides illustrate the progression of bone development throughout the course of your life. The bones you have now are not the same bones you were born with. If they were you would have a big problem because they would be very weak and brittle. The body's natural process allows for old bones to be dissolved and new cells emerge to build up new bone. And this new bone will be stronger than the old bone was. This is a constant process that occurs throughout your life.

It is important that there be a balance between the cells that build up your bone (osteoblasts) and the cells that tear down your bone (osteoclasts) to allow for the bone infrastructure to be remodeled. As we get older, a cellular imbalance shifts to the osteoclasts. This is true for all of us, irrespective of whether a man has prostate cancer.

Here is a microscopic view of what your bone looks like. It is actually a series of honeycomb-appearing areas. This is a fairly strong, relatively dense, normal bone. Patients who are osteoporatic have less of what is termed trebecular bone. Instead, their bones appear to be more hollow in appearance; these are the bones that would be weaker and at higher risk for fracture.

If we examine bone loss over time, we note that both women and men experience a decline in bone mass at approximately age 50. The decline is steeper in women due to the onset of menopause at that age. This decline in bone mass for both sexes simply reinforces the ob-

servation that osteoporosis is just not a female problem. So we should be more aggressive in diagnosing and treating men for osteoporosis.

General Risk Factors

What are the general risk factors for osteoporosis in men? Smoking, high caffeine intake, high alcohol intake--these can really weaken your bones. They help shift that balance of bone-building osteoblasts in favor of the bone-destructive osteoclasts. A sedentary lifestyle can also lead to weaker bone structure. Some other risk factors may be beyond your control, but they should be mentioned. For example, men with certain lung ailments may require steroids that can also contribute to weaker bones. Family history is another factor. If your grandparents or parents were afflicted with serious osteoporosis, it is a good bet that you are at an increased risk. Finally, hypogonadism (low testosterone levels) also contributes to bone weakness—more about that and its relation to prostate cancer next.

Prostate Cancer-Related Risk Factors

The risk factors I just mentioned refer to men in general. Now let me mention two that are more related to prostate cancer. No doubt you are aware that testosterone, the male sex hormone, can fuel prostate cancer growth. If a patient has a recurrence after primary therapy, whether surgery or radiation, the physician might recommend an orchiectomy (surgical removal of the testicles) or chemical castration using testosterone-reducing agents. Unfortunately, both alternatives contribute to weak bones.

How does low testosterone lead to weak bones? Just as your bone mass declines with age, your testosterone level declines with age as well. Testosterone is generated by the testicles, and to a lesser degree by the adrenal glands. Testosterone is secreted into the bloodstream where it is converted to estrogen. (Yes, men have estrogen, too.) This conversion is important because it actually is the estrogen that plays a significant role in the essential balance of osteoblasts and osteoclasts I described earlier. Female estrogen levels drop sharply at menopause increasing the risk of significant osteoporosis. Similarly, men produce less testosterone as they age, so they convert less estrogen. Therefore decreased estrogen is the common cause of osteoporosis in both women and men. And as noted earlier, testosterone-lowering therapy is an important aspect of treatment if your prostate cancer recurs after initial therapy. So this is a real issue for men with prostate cancer.

Now let's look specifically at the effects of hormonal therapy on bone mineral density. This is one of many studies showing a decrease in bone density. If orchiectomy were the chosen treatment for prostate cancer recurrence, patients had almost a three to ten percent drop in the strength of their bones in the first year. If a GnRH agonist (like Lupron or Zolodex) were employed, it could lower bone strength by four percent. Perhaps you may be thinking, "four percent, that's not such big a deal." Remember, this is after only one year. The objective of the treatment is to keep you alive for many years beyond one year. So this risk builds on itself and becomes more of an osteoporatic issue if you are treated with these agents over a long period of time. For men on combined androgen blockade, that is, they receive Lupron or Zolodex supplemented by a drug like Casodex to control PSA elevation, their bone strength decreases by as much as six percent in the first year.

In short, there are several alternatives to coping with prostate cancer recurrence after primary therapy. Obviously they provide a benefit in controlling prostate cancer, but their likely effect on bone health cannot be ignored.

Hormonal Therapy and Bone Mineral Density

We are concerned about decreases in bone mineral density (BMD) because that increases your risk of fracture. Men without prostate cancer over the age of 65 who are not on hormonal therapy will have a fracture risk of only 0.5% per year. But if you are on hormonal therapy, your fracture risk is significantly higher. For example, there was a 5% incidence of osteoporotic fractures seen in a median of 22 months in men on hormonal therapy. Another study showed that within 7 years, 28% of prostate cancer patients treated with orchiectomy had a fracture compared to 1% of patients who did not undergo orchiectomy. The point I want to make is that

lower testosterone means lower estrogen which means weaker bones.

Significance of Fractures

I'm sure many of you here have fractured a bone in younger days and you bounced right back. But when you are older fractures present a bigger problem, and more so in men than women. The most serious type of fracture is a hip fracture. Studies have shown that only 41% of men who have a hip fracture regain their previous level of activity; after 1 year, 79% of men with hip fracture require some form of regular nursing care; and at one month the mortality of men who have a hip fracture is 16% (four times higher than women). A hip fracture affects not just your mobility; the surgery involved may lead to other complications, such as blood clots. These studies involved men with osteoporosis and not necessarily prostate cancer.

Getting the Diagnosis

The DEXA scan is the most common technique to diagnose osteoporosis because of its ease of use, low radiation exposure, and its ability to measure BMD at both the hip and spine. DEXA can also be used to measure peripheral sites, such as the wrist or finger. DEXA uses two x-ray beams of different energy levels to scan the region of interest and measure the attenuation as the beam passes through the bone.

The DEXA scan results in a "T-score," i.e., a statistical expression that compares the patient's bone mass to the peak bone mass in a young adult reference population of the same sex. The extent to which the patient's bone mass differs from the reference population is expressed as a "standard deviation." As this slide shows, one standard deviation from the reference population is considered to be normal. If you are beyond that, say 2.5 standard deviations from the reference population, you have osteopenia or weak bones. Any T-score more than 2.5 standard deviations from the reference population results in a diagnosis of osteoporosis. Osteoporosis is termed severe when it is accompanied by fragility fractures.

If you receive a DEXA report, it will look like the one on this slide. You should focus on the T-score. Looking at this report, we note a standard deviation of -3.1 in the lumbar spine which is consistent with a diagnosis of osteoporosis of the spine. The T-score for the leg reveals a standard deviation of -1.7, consistent with osteopenia of the leg. So which areas do you treat? The answer depends on what bones are being evaluated. For example, osteopenia in the wrist is of less concern because it is not a weight bearing. On the other hand, if the leg bones are involved, especially those near the hip, then a more aggressive response is required. In men over 55, there is a 3% increase in relative risk for hip fracture for every standard deviation from the reference population. Put another way, a man with a T-score of -2 is six times more likely to have a fracture than someone who has a completely normal, healthy bone.

Guidelines for BMD Measurement

What are the guidelines for the measurement of bone mineral density? When you start hormonal therapy for prostate cancer, you should have a baseline evaluation done within six months or so. We pay special attention to the hips and the spine. Compression fractures to the spine are most evident in men who are slightly hunched over. We don't want to overlook the wrist either, because it can serve as a barometer for osteoporatic development in other areas. There should be follow-up evaluations at 6 and 12 months thereafter until the bone mass stabilizes. Also, there may be secondary causes of low BMD, such as thyroid function, that will require a work-up as part of your evaluation.

Treatment Options – Non-Pharmalogical

No surprises here, just commonsensical adjustments to social habits and diet change: decreased caffeine consumption; smoking cessation; alcohol consumption in moderation; and a reasonable exercise program consistent with your age and overall physical condition.

There are other precautions you can take that you are more likely to read about in Readers Digest than to hear from your doctor! Fall-proof your home. What about rugs? Do the grandkids trip over them as they run around the house? Then eventually you will too! Turn on the lights if you must visit the bathroom at night, and rear-

range the furniture to reduce the obstacle courses we create in our homes. And don't forget, it eventually may become necessary to swallow one's macho image and accept the necessity of using a cane or walker when required. After all, a preventable fall could lead to fracture with all the attendant complications.

Pharmalogical Treatments

Calcium. If you have been watching TV, you undoubtedly have been seeing the emphasis in marketing the virtues of calcium as a product ingredient. Every time you see a Tropicana or Minute Maid commercial you have to decide between the calcium enriched or not! Calcium is very important to prevent the bone loss that we are discussing. Most studies show that calcium supplementation decreases bone loss and reduces fracture risk for persons who require it. The goal of supplementation is to provide the calcium you need, but don't think because you are taking calcium supplementation that you should stop drinking milk and similar products. Calcium is still essential in the dietary form. How much is enough? The recommended daily allowance for men between ages 25-65 is a minimum daily supplement of 1,000 mg; men over 65 should get 1,500 mg in supplement.

Your calcium supplementation could have adverse interactions with certain other medications you may be taking. So your doctor should review your medications before initiating your calcium supplementation.

Vitamin D. It is not just calcium that is important; vitamin D is equally important. It increases the absorption of the calcium that you take in from your intestines. When you eat foods with calcium and you don't have an adequate vitamin D level, then you will not absorb enough of it, and the effort is for naught. Vitamin D is also valuable because it stimulates both the osteoblasts and osteoclasts in the bone growth and resorption process that we described earlier. In times past rickets was a common disease caused by a vitamin D deficiency. It is less common now, especially in more developed countries.

The recommended daily dosage for vitamin D supplementation is usually 200-800 International Units. This may cause some increase in calcium beyond the need, but your doctor will be checking your lab work periodically to monitor the situation. As with calcium, there could be certain drug interactions, especially with hypertension medications such as hydrochlorothiazide. So it is always a good policy to have a review of your medications before you begin your vitamin D supplementation.

Calcium needs to be taken in tandem with vitamin D. Taken individually, neither is going to do much good for you. So if you are starting hormonal therapy, you should also start to take both calcium and vitamin D.

Bisphosphonates. The next treatment for osteoporosis is a class of drug called bisphosphonates. These work differently than calcium and vitamin D. Bisphosphonates bind around the architecture of the bone and actually become a permanent part of the bone structure. And that part becomes more resistant of being broken down. Think of it this way. If you have an old house and you reinforce it by applying cement, the foundation is stronger. This is one way to visualize what bisphosphonates do. Bisphosphonates also affect osteoclasts, those cells whose job it is to dissolve the bone; bisphosphonates alter their structure and function by preventing adherence and decreasing their ability to absorb bone. The end result is that your bones are stronger.

The effectiveness of bisphosphonates has improved dramatically over the past decade. If we assign an effectiveness value of one to an early bisphosphonate called Etidronate and compare it with an advanced bisphosphonate such as Zoledronate, we see that Zoledronate is 20,000 times more effective. With the evolution of these powerful drugs, as with all medications, we learn that with the power come side effects that we need to be aware of.

Several studies have clearly demonstrated the benefits of bisphosphonates. Two benefits are worth noting here. First, bisphosphonates increase total body BMD and help prevent the weakening of bones in these areas that could lead to fractures, i.e., the spine and hips. Second, if you take a bisphosophonate you also

need calcium and vitamin D to maximize its effectiveness.

One study directly addressed men with prostate cancer who eventually received hormonal therapy. During hormonal therapy there was a decrease in BMD in the spine (4%) and hip (2.5%). But one year after treatment with the bisphosphonate Pamidronate, the BMD decrease was not only reversed, BMD actually increased. Even more dramatic improvement occurred in a study involving Zoledronate, the more powerful bisphosphonate. Remember, bisphosphonates are more appropriate for persons who have a diagnosis of osteoporosis. Treatment with calcium and vitamin D would be sufficient for persons diagnosed with osteopenia.

A Phase III Zoledronate Trial involved patients with bone-metastatic prostate cancer; a rising PSA despite hormonal therapy; and no pain requiring narcotics. It was a randomized, placebo-controlled study. The key here was the incidence of skeletal-related events (e.g., fractures, spinal cord compression, radiation for bone pain, elevations in calcium). The patients receiving Zoledronate had an eleven percent reduction in the skeletal-related events. In addition to a reduction in the absolute number of events, there was an improvement in the time to occurrence. So there was a two-fold improvement in benefits. These significant differences are the basis for using the drug Zoledronic acid or Zometa in patients who have advanced prostate cancer and are on hormonal therapy or are on hormonal therapy and have osteoporosis.

Side Effects

Now let me discuss the side effects associated with bisphosphonates. Someone inquired earlier about a downside. Unfortunately, whenever there is an effective medication there is usually a downside, and bisphosphonates are no exception. Some patients experience fatigue, joint pain, bone pain, and fever at the outset. These can be managed with Tylenol and the like. In the Phase III Zoledronate Trial I just described, these side effects were not that different from those experienced by the placebo group. Having said that, there is a small group of patients who are very sensitive to this drug, but this is rare.

The most serious side effect, and the most unusual, is ostonecrosis, an erosion of the jawbone with attendant pain and tooth loss. It was first reported in 2004, and no one knew what to make of it. I wish I could tell you that four years later we have it all figured out, but I can't. It affects from 3-10% of patients and is associated with treatment in excess of one year. A more conservative approach for prostate cancer patients with osteoporosis and just starting hormonal therapy might be lifestyle modification, treatment with calcium and vitamin D, and then another DEXA scan before starting with bisphosphonates. The intravenous form of bisphosophonate, Zoledronic acid, the one that was 20,000 times more effective, is also the most frequent culprit in ostonecrosis. Many persons take Fosomax, an oral pill that is another type of bisphosphonate. Certainly it has a risk for ostonecrosis, but it is substantially less.

There are studies underway to cope with the ostonecrosis phenomenon. Possible causes could be related to trauma, local infection, drug concentration, and blood supply. At NIH we are studying how chemotherapy drugs may affect the blood supply to the tumor, but also may be affecting blood supply elsewhere, such as the jaw. Until we sort this out, we have become more judicious on how and when we use bisphosphonates.

If it makes sense to start a patient on bisphosphonates, there should be a thorough dental evaluation at the outset and any dental problems taken care then. Regular dental exams and conservative dental care are important throughout treatment for osteoporosis. If ostonecrosis of the jaw should occur, the bisphosophonate therapy should stop. Of course, your dentist must be made aware of your treatment for osteoporosis.

Conclusion

In conclusion, hormonal therapy after PSA recurrence accelerates your bone loss and increases your risk of bone fracture. Certainly not every prostate cancer patient is going to develop osteoporosis as a result of hormonal therapy. Nevertheless, there needs to be greater awareness of the risk. Let me make clear that if you are receiving hormonal therapy for your prostate

cancer, you should be receiving calcium and vitamin D supplementation unless your doctor determines there is a contraindication. Patients just beginning or already on hormonal should be evaluated to determine any clinical risk factors (e.g., family history of osteoporosis, smoking, caffeine and alcohol consumption). The evaluation helps to establish the patient's risk category, and is the basis for lifestyle changes. Next, a DEXA scan would establish a baseline BMD. If the resultant T-score is in the normal range, an appropriate follow-up plan can be established; if the T-score reveals osteopenia, a follow-up schedule is set and the lifestyle adjustments I have mentioned are appropriate; if the T-score reveals osteoporosis, then bisphosphonate therapy is indicated to prevent fractures and further bone loss.

Finally, you must be aware of the side effects associated with the treatment options for dealing with osteoporosis. The benefit versus risk issue must be weighed carefully.

Questions and Answers

Question: Will calcium supplementation affect the aggressiveness of prostate cancer?

Answer: There is no real concern that calcium intake is going to increase prostate cancer aggressiveness. Nevertheless, there are always concerns when you begin new medications that they may affect other medications you may be taking. Always consult your doctor before you do. Taking calcium may be a concern if you are taking iron for a blood condition; it could decrease the absorption of the iron. Again, consult your doctor.

Question: I had a radical prostatectomy and now have osteopenia. Is there any correlation between the type of primary therapy for prostate cancer and bone loss?

Answer: If you had your prostate removed, but your testicles are intact, and you are not on testosterone-lowering medication, there is no correlation between your having a radical prostatectomy (or radiation, for that matter) and subsequent osteoporosis or osteopenia. As I mentioned earlier, as men get older their bone density is going to decrease naturally. If I examined a group of 80 year-old men without prostate cancer, I would find many with osteopenia or osteoporosis. In your case, osteopenia is likely related to the aging process, or perhaps some decreased level of testosterone. Talk to your doctor about calcium and vitamin D supplementation if you are not already taking them.

Question: I noticed that your remarks focused almost exclusively on the relationship between osteoporosis and hormonal therapy. Is there a cause and effect relationship between osteoporosis and other types of prostate cancer therapy such as radical prostatectomy, brachytherapy, and external beam radiation?

Answer: This discussion of osteoporosis is related to hormonal therapy. It is specifically related to hormonal therapy for disease recurrence after **any** primary therapy for prostate cancer. There is no relationship between BMD and the individual primary therapies for prostate cancer (surgery or radiation). Hormonal therapy decreases your testosterone and leads to decreased estrogen. The evidence shows that even if you don't have prostate cancer, your bone density is going to decline as you age. So there is that general risk. It's when you start the hormonal therapy after primary therapy failure that the BMD risk increases significantly. Should you begin calcium and vitamin D supplementation now as a preventive measure against bone loss after primary therapy? Discuss that with your doctor. The decision should be based on your DEXA scan and risk factors.

Question: How often should I have a follow-up on calcium and vitamin D levels and the side effects of bisphosphonate therapy?

Answer: Remember, the benefits of the calcium and vitamin D supplementation for bone mineral density are not the serum levels of calcium and vitamin D. The serum levels really do not tell us very much. The effect on the strength of the bones is the most important thing, and we get this from the DEXA scan or the Qualitative CT. How often should you get that evaluated after your baseline scan? If you are on hormonal therapy and the baseline scan was normal, you probably can wait eighteen months to two

years. If outcome was not so good, you may need another scan in six to twelve months.

Regarding bisphosphonate therapy, you should have your blood drawn at least once a month, particularly if it is the intravenous bisphosphonate. There are concerns about its effect on such things as kidney function. If this is the case, then the dosage can be adjusted. If you are taking an oral bisphosophonate, a blood test once every three or four months probably would be sufficient.

Question: I am taking 100 units of vitamin D over-the-counter. I am not sure that I have enough vitamin D. During one check-up my vitamin D was low and I ended up having to take almost 8000 units for a month or so. I still take 5000 units of calcium.

Answer: There are always exceptions to the rule. Rather than individual levels of calcium and vitamin D, the bigger issue is the effect on BMD as revealed by your DEXA scan. If there is notable deterioration in your DEXA scan, there might be a reason to increase supplementation. In general, I would strongly recommend avoiding super-high doses of any medication. Often they can do more harm than good. Even vitamins in high doses have been shown to be harmful. I recommend you review your calcium and vitamin D supplementation with your doctor.

♦ OUR MEETING SCHEDULE ♦

The WRAMC Prostate Cancer Support Group has two types of meetings: **Monthly Meetings**: These are informal discussion groups where current topics of interest are considered. Newly diagnosed men and men whose prostate cancer condition has changed will find these meetings useful because they will meet men who "have been there – done that." These meetings are held on the **second Wednesday of every month** in two sessions. The day session is from 1:30-3:00 PM and the evening session is from 6:30 8:00 PM. Both sessions meet in the conference room of the Center for Prostate Disease Research (Ward 56), WRAMC.

Quarterly Meetings: A guest speaker makes a formal presentation and answers question on a topic of special interest to our prostate cancer community. These meetings are held on the first Wednesday of February, May, August, and November, and meet in Joel Auditorium on the second floor of the main hospital building at WRAMC. These meetings and their topics are always shown on page 2 and the mailing page of the newsletter.

COME JOIN US AND BRING A FRIEND!

THE CURRENT ISSUE OF THE WRAMC US TOO NEWSLETTER AND BACK ISSUES ARE AVAILABLE ON LINE AT THE WEB SITE OF THE CENTER FOR PROSTATE DISEASE RESEARCH AT WWW.CPDR.ORG/PATIENT/USTOO/NEWSLETTER.HTML.

♦ WRAMC US TOO COUNSELORS ♦ (As of December 31, 2008)

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

SURGERY			
Tom Assenmacher	Kinsvale, VA	(804) 472-3853	
Jack Beaver	Falls Church, VA	(703) 533-0274	
Gil Cohen	Baltimore, MD	(410) 367-9141	
Richard Dorwaldt	San Antonio, TX	(210) 310-3250	(Robotic Surgery)
Michael Gelb	Hyattsville, MD	(240) 475-2825	(Robotic Surgery)
Robert Gerard	Carlisle, PA	(717) 243-3331	
Ray Glass	Rockville, MD	(301) 460-4208	
Monroe Hatch	Clifton, VA	(703) 323-1038	
Tom Hansen	Bellevue, WA	(425) 883-4808	(Robotic Surgery)
Bill Johnston	Berryville, VA	(540) 955-4169	
Dennis Kern	San Francisco, CA	(415) 876-0524	
Steve Laabs	Fayetteville, PA	(717) 352-8028	(Laparoscopic Surgery)
Don McFadyen	Pinehurst, NC	(910) 235-4633	
George Savitske	Alexandria, VA	(703) 671-5469	
Artie Shelton, MD	Olney, MD	(301) 523-4312	
Jay Tisserand	Carlisle, PA	(717) 243-3950	
Don Williford	Laurel, MD	(301) 317-6212	
PROSTATE CANCER AND SEXUAL FUNCTION			
James Padgett	Silver Spring, MD	(301) 622-0869	
RADIATION			
John Barnes	Springfield, VA	(703) 354-0134	(Intensity-Modulated Radiation Therapy)
Leroy Beimel	Glen Burnie, MD	(410) 761-4476	(External Beam Radiation)
Ron Gabriel	Bethesda, MD	(301) 654-7155	(Brachytherapy)
Irv Hylton	Woodstock, VA	(540) 459-5561	(Brachytherapy)
Harvey Kramer	Silver Spring, MD	(301) 585-8080	(Brachytherapy)
Bill Melton	Rockville, MD	(301) 460-4677	(External Beam Radiation)
Oliver E. Vroom	Crofton, MD	(410) 721-2728	(Proton Radiation)
John Waller	Yorktown, VA	(757) 865-8732	(Brachytherapy)
Barry Walrath	McLean, VA	(703) 442-9577	(Brachytherapy)
INCONTINENCE			
Ray Walsh	Annandale, VA	(703) 425-1474	
HORMONAL			
"Mac" Showers	Arlington, VA	(703) 524-4857	
WATCHFUL WAITING			
Tom Baxter	Haymarket, VA	(703) 753-8583	
CLINICAL TRIALS			
Philip Brach	Washington, DC	(202) 966-8924	
SPOUSE SUPPORT			
Kay Gottesman	North Bethesda, MD	(301) 530-5504	
OTHER THERAPIES/MULTIPLE THERAPIES			
Howard Bubel	Fairfax, VA	(703) 280-5765	(Cryosurgery, Hormonal, Sexual Function)
Arthur E. Clough	Kerryville, TX	(210) 896-8826	(Surgery and Radiation)
Pete Collins	Mechanicsburg, PA	(717) 766-6464	(Surgery, Radiation, Hormonal)
S.L. Guille	Sumerduck, VA	(540) 439-8066	(Surgery, Radiation, Hormonal)
Richard Leber	Chapel Hill, NC	(919) 942-3181	(Surgery, Radiation, Hormonal)
Charles Preble	Annandale, VA	(703) 560-8852	(Cryosurgery, Hormonal, Intermittent Hormonal)
Emerson Price	Absecon, NJ	(609) 652-7315	(Hormonal, Radiation, Cryosurgery)
S.L. Ross	Alexandria, VA	(703) 360-3310	(Brachytherapy, Radiation, Hormonal)
Ken Simmons	Alexandria, VA	(703) 823-9378	(Radiation and Hormonal)
Bill Stierman	Vienna, VA	(703) 573-0705	(Surgery and Second Line Hormonal-Ketoconazole)
Ray Walsh	Annandale, VA	(703) 425-1474	(Surgery and Hormonal)

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♦ MEETING ANNOUNCEMENT ♦

WEDNESDAY, FEBRUARY 4, 2009
7 PM

JOEL AUDITORIUM (SECOND FLOOR)
MAIN HOSPITAL BUILDING, WRAMC

♦ SPEAKERS ♦

A PANEL OF FIVE PROSTATE CANCER SURVIVORS

DISCUSS THEIR PERSONAL EXPERIENCES

♦ TOPIC ♦

"DEALING WITH PROSTATE CANCER-
OUR STORIES"