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

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♦ RAYMOND M. WALSH ♦

Raymond M. Walsh, a loving husband, father and grandfather, U.S. Army veteran, and resident of Fairfax, VA, died the evening of Saturday June 13, 2015, following a prolonged battle with prostate cancer. He was 80 years old.

Born in Fall River, MA, Ray was a graduate of Northeastern University and made his career in telecommunications engineering. During his 22 years of active duty officer in the Army Signal Corps, Ray served in Korea, Italy, Vietnam, and Bolivia, as well as various domestic stations. His military honors include The Legion of Merit and Bronze Star Medal. After retiring from active duty, he continued telecommunications work for a succession of companies that included Northern Telecom and Sprint.

In May 1999, Ray was diagnosed with prostate cancer. Throughout his years fighting this disease, Ray displayed a generous spirit, often volunteering in research, education, and support efforts for the greater good of the prostate cancer community. Over the span of 15 years, Ray participated in our Walter Reed Prostate Cancer Support Group where he held leadership positions for many years. He also was active in the Virginia Prostate Cancer Coalition (VPCC); and he served as a Red Cross Volunteer in the Center for Prostate Disease Research (CPDR) at the Walter Reed Army Medical Center. His greatest contribution likely was the one-on-one peer counseling to newly diagnosed individuals and their families as they dealt with their diagnoses. He was a recognized expert in the relationship of Agent Orange and prostate cancer. In that capacity, he helped uncounted Vietnam veterans negotiate the process leading to their service-connected disability status.

Interment with honors at Arlington National Cemetery will be October 27, 2015.

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WRNMMC Us TOO NEWSLETTER EDITOR

Write or Call
Vincent P. McDonald
8661 Chase Glen Circle
Fairfax Station, VA 22039
Telephone: (703) 643-2658
E-Mail: vpmjam@aol.com

♦ FROM THE EDITOR ♦

Do you know persons who would benefit from receiving this newsletter? Put them in contact with the editor as shown at the top, left, of this page. Also, we solicit your recommendations for topics for our quarterly meetings. Contact the editor with your suggestions.

♦ SPEAKER'S REMARKS - MAY 7, 2015 ♦

Our May program featured a presentation by Dr. Timothy Donahue, Urologic Oncologist, Department of Urology, WRNMMC. His topic was "Rise in PSA after Treatment for Prostate Cancer." A summary of his presentation begins on page 11.

♦ MEETING SCHEDULE FOR AUGUST 6, 2015 ♦

Our speaker for Thursday, August 6, 2015, is Dr. Stephen Lewis, a radiation oncologist at WRNMMC. His topic is "Emerging Therapies in Radiation and Immunology." Your family members and friends are also welcome. Come join us.

(The presentation also may be viewed via video teleconference at the Fort Belvoir Community Hospital. Go to the Oaks Pavilion, 1st floor, Room 332, to participate.)

SEE THE BACK PAGE OF THIS NEWSLETTER FOR IMPORTANT INFORMATION ABOUT THIS MEETING.

♦ PROSTATE-SPECIFIC ISSUES ♦

Increased Resort to Active Surveillance. More physicians are sparing their low-risk prostate cancer patients from prostatectomy, radiation, and androgen deprivation monotherapy in favor of active surveillance/watchful waiting, according to a research letter published in the July 7 issue of the *Journal of the American Medical Association*.

Last week, a study published in *JAMA Internal Medicine* suggested that the wide majority of men with low-risk prostate cancer between 2010 and 2011 had treatment. But, that study defined low-risk in various ways that included between 11 and 40 percent of prostate cancer patients. The new study examines the medical records of 10,472 men from 45 urology practices. And, it uses a single definition of low-risk. The current study also looks at information through 2013.

The researchers found the use of surveillance for low-risk disease to be 7 to 14 percent from 1990 through 2009, but increased to 40 percent in 2010 through 2013. This is "excellent news," study author Matthew Cooperberg, M.D., M.P.H., the Helen Diller Family Chair in Urology at the University of California, San Francisco, told *HealthDay*. "We expected to see a rise in surveillance rates, but were surprised by the steepness of the trajectory," he said. "This really does represent a paradigm change, and it's faster than the typical pace of medical evolution."

In addition to finding a higher rate of surveillance in all men, the researchers also found that those aged 75 and older were much less likely to get potentially unnecessary treatment. Among low-risk men aged 75 and older, the rate of surveillance rose from 21.9 percent in 2000-2004 to 76.2 percent in 2010-2013, the researchers found. As for patients at greater danger, "we're seeing more aggressive management of higher-risk disease with surgery, radiation, or both, which is also a trend toward better management." (Source: HealthDay News, July 8, 2015)

Developments in Penile Prostheses Use. Penile prosthesis surgeries in Medicare beneficiaries dropped by half over the course of 8 years, possibly due to improvements in chemical therapies, researchers reported. From 2002 to 2010, the use of penile prostheses to treat erectile dysfunction went from 4.6% to 2.3%, with the greatest declines seen in the American Midwest and in men ages 70 to 74, according to Richard K. Lee, MD, MBA, et al., Weill Cornell Medical College, New York, who published their study in *The Journal of Sexual Medicine*.

Based on a sample from the Medicare Public Use Files from 2002 to 2010, the researchers found that 1,763,260 men were diagnosed with erectile dysfunction from 2001 to 2010, and 3% of that group, or 53,180 men, had a penile prosthesis surgically placed. Over the same 8-year period, despite the drop in the number of penile prosthesis surgeries, the rate of erectile dysfunction increased 165%, from 100,840 to 266,908.

In 92% of the surgeries, multi-component inflatable penile prostheses were used. Semi-rigid inserts were used for the remaining surgeries. The use of multi-component inflatable penile prostheses increased over time, which peaked after 2007. Within prosthesis type and surgical outcome variations, African-American men and other minorities were more likely to receive

semi-rigid penile prostheses, and more likely to have a revision or removal compared with white men, who were more likely to receive a multi-component inflatable prosthetic insert .

The reduction in penile prostheses was largest among white men (-2.4%), and men ages 70 to 74 (-2.6%). Throughout the study period, the greatest increase in penile prostheses was seen among men with Charlson scores of 2 or more, a group who experienced a 91% increase, from 12% of patients in 2002 to 23% of patients in 2010. However, men who underwent radical prostatectomy maintained a rate of penile prostheses surgery of 2% throughout the study period. Revision or removal surgeries were associated with increasing age, and African-American men were more likely than white men to undergo a second surgery.

Ranjith Ramasamy, MD, the Baylor College of Medicine, Houston, told *MedPage Today* that he was not surprised by the finding, ascribing the decline in prosthetic implantations to a combination of factors, including cost, better oral therapies, and more successful bilateral nerve-sparing prostatectomy. “African-American men had a higher rate of malleable prosthesis probably because of cost and insurance coverage,” said Ramasamy, who was not involved with the study. “Infection and revision rates in these men could have been higher due to a higher incidence of diabetes mellitus and more comorbidities.”

The study's limitations include retrospective, nonrandomized design, and the use of Medicare claims data, which did not provide specific clinical information. (Source: MedPageToday, June 22, 2015)

Repeat Biopsies and Significant Cancers. Abraham, M.D., et al., New York University School of Medicine, collected data on 1,837 men who underwent prostate biopsy during January 1, 1995, to January 1, 2010). The authors sought to determine characteristics of repeat biopsy (indication for biopsy, the number of repeat biopsies performed, the number of cores obtained, and total prostate-specific antigen before biopsy), as well as features of prostate cancer diagnosed on repeat biopsy (including Gleason score, number of positive cores, percent of tumor and treatment choice).

Among a group of men with an initial negative prostate biopsy, clinically significant cancer is still found in subsequent repeat sampling rounds, according to a study published in the April issue of *The Journal of Urology*. Researchers found an increased likelihood of prostate cancer with fourth repeat biopsy and in patients older than 70.

The researchers found that 1,213 men had negative initial biopsies, but that 798 repeat biopsies were performed in 255 men. Gleason score was ≤6 in 33 of 63 men diagnosed with prostate cancer, 7 in 22, and 8 to 9 in 8 men. The rate of clinically insignificant cancer diagnosis decreased substantially by the third and fourth repeat biopsies. An increased likelihood of prostate cancer diagnosis was seen in men ≥70 years with repeat biopsies, biopsies including more than 20 cores, and the fourth repeat biopsy.

The study concluded that given the continued likelihood of cancer detection even by the fifth biopsy, early consideration of saturation or image guided biopsy may be warranted in the repeat biopsy population. (Source: HealthDay News, April 14, 2015)

Surgery and Survival for PCa Patients under 50. Results from the study done on the National SEER database show that the surgical procedure improves the 5-, 10-, 15- and 20-year survival for younger patients, when compared with other standard treatments such as radiotherapy or watchful waiting.

"When given the choice between surgery, watchful waiting or external beam radiotherapy, patients younger than 50 with moderately and poorly differentiated prostate cancers have better long-term overall and cancer-specific survival when they opt for surgery," according to Pokala, M.D., et al. Henry Ford Hospital.

Based on findings from the study, the researchers strongly recommend retropubic radical prostatectomy – a surgical procedure that removes the entire prostate gland plus some of the tissue around it – as the treatment of choice for prostate cancer patients under the age of 50.

Although the majority of all prostate cancer are diagnosed in men older than 65, its prevalence is growing among men younger than 50. In fact, about one in 10,000 men under the age of 40 will be diagnosed this year with prostate cancer. To determine which treatment option offers the best chance for long-term survival for younger prostate cancer patients, the researchers studied more than 8,200 men under age 50 with prostate cancer.

Among the study group, 73 percent were white and about 22 percent were black. The mean age was 46, and over 70 percent had moderately and 22 percent had poorly differentiated cancers. Of the patients, 1,065 were managed with no definitive treatment (watchful waiting); 6,614 (79.9 percent) with radical retropubic prostatectomy; and 600 with external beam radiotherapy.

The cancer-specific survival in the watchful waiting group was 78 percent at 16 years, in the radiation group cancer-specific survival was 63 percent at 17 years; and 94 percent in the radical prostatectomy at 21 years. On a subset analysis, the outcome was significantly better after radical prostatectomy in patients with moderately and poorly differentiated prostate cancer.

Overall, the study shows the 5-year, 10-year, 15-year and 20-year overall survival and cancer specific survival is significantly increased in patients who were less than 50 years of age with moderately and poorly differentiated cancers in the surgery group.

Medicare and Hospice. The federal government announcing recently the expansion of a pilot project that paves the way for Medicare beneficiaries to use hospice services while still getting treatments that aim for a cure. A successful test could lead to a fundamental shift in the delivery of health-care at the end of patients' lives. Under current Medicare payment rules, beneficiaries can't get both curative treatment and hospice care at the same time.

That choice may be one reason overall hospice participation at the end of life remains relatively low—less than 45% of Medicare beneficiaries use hospice at the end of life, according to the federal government. Many enter hospice in the final days of their lives, with a median of about 14 days in hospice.

Patients typically obtain hospice services when they are expected to have about six months or less to live. The pilot will expand hospice care to beneficiaries with advanced cancer, congestive heart failure, chronic obstructive pulmonary disease, and HIV and AIDS, according to officials. The Obama administration has lined up more than 140 hospices to participate in the pilot, enabling as many as 150,000 Medicare beneficiaries to participate, according to federal officials. The administration had announced plans for a smaller pilot program with 30 hospices more than a year ago but hadn't yet started it. The administration expanded the project and extended its duration from three to five years.

Some private insurers already cover concurrent treatments for a cure along with hospice care, which focuses on relieving symptoms and providing other support. Dr. Bruce Smith, executive medical director of Seattle-based Regence BlueShield, said many insurers agree it is the right thing to do.

Hospices provide care management, home health aides, social workers, spiritual counselors, and bereavement assistance for families, typically in patients' homes. In 2013, an estimated 1.5 million to 1.6 million patients received hospice services, according to the National Hospice and Palliative Care Organization.

The pilot project is part of a broader effort by the Obama administration to overhaul the delivery of health care in the U.S. That has included recent initiatives to improve the care and safety in nursing homes and changing Medicare to make half of its payments to doctors and hospitals based on quality of care rather than quantity by the end of 2018.

The Centers for Medicare and Medicaid Services will pay a monthly fee for each beneficiary getting the care—ranging from $200 to $400 to participating hospices. About 70 hospices in the program will provide services from Jan. 1, 2016 through Dec. 31, 2020. The remaining will provide services from Jan. 1, 2018 through Dec. 31, 2020.

Patients and families can struggle with the decision, which is one reason some patients may enter hospice late, said Dr. Jeffrey Berger, chief of the division of palliative medicine and bioethics Winthrop University Hospital in Mineola, N.Y. For example, patients with pulmonary hypertension, a progressive lung dysfunction, may find hospices won't take them if they are getting infusions of an expensive medication that helps them to breathe, he said. Without the infusions, patients die quickly. (Source: The Wall Street Journal, June 21, 2015)

Pomegranate and Prostate Cancer. Not long ago, pomegranate juice was being touted as a "prostate cancer fighter" in the popular media. The primary objective of this study was to compare the effects of pomegranate juice on PSA doubling times (PSADT) in subjects with rising PSA levels after primary therapy for prostate cancer.

Double-blind, placebo-controlled multi-institutional study, evaluated the effects of pomegranate liquid extract on serum PSA levels. The primary end point of this study was change in serum PSADT. Additional secondary and exploratory objectives were to evaluate the safety of pomegranate juice and to determine the interaction of manganese superoxide dismutase (MnSOD) AA genotype and pomegranate treatment on PSADT.

One-hundred eighty-three eligible subjects were randomly assigned to the active and placebo groups with a ratio of 2:1. The majority of adverse events were of moderate or mild grade. Median PSADT increased from 11.1 months at baseline to 15.6 months in the placebo group compared with an increase from 12.9 months at baseline to 14.5 months in the extract group, and an increase from 12.7 at baseline to 20.3 in the juice group. However, none of these changes were statistically significant between the three groups. Placebo AA patients experienced a 1.8 month change in median PSADT from 10.9 months at baseline to 12.7 months , while extract patients experienced a 12 month change in median PSADT from 13.6 at baseline to 25.6 months..

Compared with placebo, pomegranate extract did not significantly prolong PSADT in prostate cancer patients with rising PSA after primary therapy. A significant prolongation in PSADT was observed in both the treatment and placebo arms. Men with the MnSOD AA genotype may represent a group that is more sensitive to the antiproliferative effects of pomegranate on PSADT; however, this finding requires prospective hypothesis testing and validation. (Source: Urology News, July 15, 2015)

Managing High Risk Prostate Cancer. The management of high-risk prostate cancer (HRPC) is becoming a top priority for improving prostate cancer (PCa) outcomes. There is still no consensus on a definition of high-risk prostate cancer at the moment. In 1998 d'Amico classified PCa patients according to PSA, Gleason grade, and clinical stage. However, the classification in only 3 risk groups and considering only 3 factors is probably insufficient. In this article we discuss the different classifications and updates in view of giving a more precise prediction of outcomes, especially the need for sub-stratification.

There has been a historical trend to treat HRPC with radiotherapy (RT) and/or androgen deprivation therapy (ADT), even in the absence of level 1-evidence to support it. On the other hand, many studies that we present here have proven the feasibility of radical prostatectomy (RP) in HRPC, and analysis of the SEER database concluded that the greatest benefit of RP over RT in CSS was in otherwise fit patients with HRPC.

The biggest issue in HRPC is the selection of patients for surgery, given the heterogeneity of their prognosis. Briganti has produced a nomogram to address this patient selection issue and predictably found that the presence of more than one high-risk factor was associated with a significantly lower rate of specimen confinement.

We discuss the controversial role of clinical staging in risk stratification. Most HRPC cases have extraprostatic disease, but the disease is organ-confined in 26-31% of the cases and those with specimen-confined pT3 disease have good biochemical and clinical PFS. It also seems that multiparametric MRI, and especially T2-weighted imaging, may be useful in staging selected patients with intermediate- to high-risk PCa.

This article also shows that RP is a reasonable option in Gleason 8-10 patients, even more taking into account that up to 45% are downgraded on prostatectomy specimen. Multiparametric MRI with DWI may have a role in detecting high-grade cancer as there seems to be a correlation of ADC with biopsy Gleason score.

It is well known that radical prostatectomy for clinical T3 disease requires some surgical expertise to keep the morbidity acceptable. We show evidence that minimally invasive surgery is gaining its space in HRPC, bringing reduced intra-operative blood loss and faster convalescence. Furthermore the decision to perform a nerve-sparing surgery (NSS) should be adapted to each patient and to each side of the prostate. Our LRP series has shown that overall PSM rate correlates with pathological T stage but is not influenced by NSS . Multiparametric MRI with DWI seems to have a role in reducing PSM caused by inadequate NSS by predicting extraprostatic extension.

In HRPC it is essential to perform an extended pelvic lymph node dissection (ePLND). Besides the known importance of high lymph node yield, we discuss the results from Briganti and Studer's groups concluding that patients with 1-2 positive nodes on ePLND have significantly better long-term CSS than the ones with 3 or more. It is our belief that there will soon be enough evidence to change the TNM staging classification for prostate cancer in order to divide node-positive patients into N1 and N2 depending on the number of positive nodes, as they carry different prognosis.

When discussing surgery with a patient with HRPC, it should be made clear that a multimodality treatment may be required. In cases where the need for radiotherapy is extremely predictable, one might think that the patient should have primary RT. However a surgery-first approach to multimodal treatment may have advantages, as salvage radiotherapy following surgery is better tolerated than salvage surgery following radiotherapy.

In conclusion, HRPC comprises a very significant number of patients who seem to be the most likely to benefit from treatment in the long term. However this is a very heterogeneous group, given the multiple classifications and the high rates of downstaging and downgrading by the time of surgery. Outcomes are therefore not uniform and are difficult to interpret. RT is a treatment with proven value in high-risk localized and locally advanced PCa, but we now have strong evidence that surgery has also an important role in the management of HRPC. The biggest issue is to have the right criteria to select the patients most likely to benefit from a "surgery first" approach, always keeping in mind that a multimodal treatment may be needed. (Source: UroToday, June 5, 2015)

The Partner's Role in Dealing with Prostate Cancer. Partners of cancer patients are often the first to respond to the demands related to their husband's illness and thus are likely to be the most supportive individuals available to the patients. It is therefore important to examine how spouses react and handle their husband's prostate cancer diagnosis.

The aim of this study was to explore how the prostate cancer diagnosis and the participation in their partners' behavioral lifestyle intervention program influenced the spouses' life, their relationship with their partner, and how they handle the situation. Interviews were recorded with 8 spouses of potential low-risk prostate cancer patients on active surveillance as part of a clinical self-management lifestyle trial.

We identified 3 phases that the spouses went through: feeling insecure about their situation, coping strategies to deal with these insecurities, and feeling reassured. The framework of a clinical trial should include mobilizing spousal empowerment so that they

can take on an active and meaningful role in relation to their husband's disease. The observations here substantiate that the framework of active surveillance in combination with a lifestyle intervention in a specific prostate cancer clinical trial can mobilize spousal empowerment.

Creating well-designed clinical patient programs that actively involve the spouse appears to promote empowerment (meaningfulness, self-efficacy, positive impact, and self-determination) in spouses. Spousal participation in clinical patient programs can give spouses relief from anxieties while recognizing them as a vital support for their husband. (Source: UroNews, June 1, 2015)

Excess Weight and Prostate Cancer Prognosis. Radiation therapy for prostate cancer may be less effective for overweight and obese men than for men of normal weight, a new study suggests. Higher rates of prostate cancer relapse, prostate cancer death, and death from other causes were seen for overweight and obese men in this study of more than 1,400 prostate cancer patients.

"It isn't the weight per se, but there must be some association with increased weight that's making the treatment less effective," said lead researcher Dr. Eric Horwitz, chairman of radiation oncology at Fox Chase Cancer Center in Philadelphia. It's not that radiation doesn't work, but it doesn't seem to work as well," he said. "It's still better than not having any treatment."

Being overweight or obese was associated with a small -- 3 percent -- higher rate of prostate cancer relapse and a 7 percent higher rate of cancer spreading. Heavier patients also had a 15 percent increased rate of dying from their cancer and a 5 percent greater rate of dying from other causes, the researchers found.

Obesity among U.S. adults has more than doubled in the past four decades, according to the U.S. Centers for Disease Control and Prevention. While obesity has been linked to certain other cancers, its association with prostate cancer isn't clear, the researchers explained in background notes. Unlike thinner patients who might be candidates for surgical treatment, overweight and obese men with prostate cancer often have just one option: radiation.

The study was published May 29 in the journal *Cancer*. It involved 1,442 men, average age 68, treated with radiation therapy for localized prostate cancer between 2001 and 2010. They were followed for an average of four years. One expert said that numerous theories have been floated to explain the poorer outcomes of obese men with prostate cancer.

"One biological mechanism for the worse survival outcomes among obese men is due to more rapid progression [of the tumor] to distant metastasis" after treatments begin to fail, said Dr. David Samadi, chairman of urology and chief of robotic surgery at Lenox Hill Hospital in New York City. But while this and other factors might explain the added risk to obese men, "additional research is needed to confirm this relationship," he said.

The researchers showed that even with state-of-the-art radiation therapy, which includes better imaging and higher doses, obesity was associated with worse outcomes. This study adds to the existing evidence that obesity appears to be associated with increased risk of prostate cancer and more aggressive prostate cancer. Perhaps additional research will uncover the exact

ways obesity leads to more aggressive prostate cancer. Based on these and other results, it seems that the next step is to investigate whether enrolling patients in a weight-loss program during and after their prostate cancer treatment could improve patients' chances of being cured of prostate cancer, according to an observer..

Horwitz said the lesson from this study could be that patients who are overweight and obese need different treatment. (Source: HealthDay News, May 29, 2015)

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♦ RISING PSA AFTER TREATMENT FOR PROSTATE CANCER ♦

by

TIMOTHY DONAHUE, MD
Department of Urology, WRNMMC

(A summary of a presentation to the WRNMMC Prostate Cancer Support Group, May 7, 2015)

INTRODUCTION

Prostate cancer is the most common cancer in US men with an estimated 240,890 new cases annually. It is also the second leading cause of death in US men with an estimated 33,720 deaths in 2011. One in nine men will be diagnosed with prostate cancer, but only one in thirty-five will succumb to the disease. At the time of diagnosis about one-third of new cases are locally advanced or metastatic.

PREDICTIVE FACTORS AT TIME OF DIAGNOSIS

The three predictive factors affecting the possibility for disease progression are: Gleason score, the PSA at the time of diagnosis, and clinical stage. A man with a Gleason score of ≤ 6, a PSA of ≤10, and a cTI clinical stage is considered to be at "low risk" for progression; a man with a Gleason score of 7, a PSA of 10-20, and a clinical stage of cT2 is considered to be at "intermediate risk" of progression; and a man with a Gleason score of ≥ 8, a PSA of ≥ 20, and a clinical stage of ≥cT3, is considered to be "high risk."

There also are several pre-treatment nomograms that are used to estimate the likely outcomes of treatment. No doubt many of you are aware of the so-called Partin Tables developed at Johns Hopkins Hospital.

PSA RECURRENCE AFTER PROSTATECTOMY

There are several predictive factors for PSA recurrence after radical prostatectomy: a Gleason score of 7 or more; surgical margin status (positive or negative); evidence of extra-capsular extension; seminal vesicle invasion; and lymph node involvement. Detectable PSA after surgery may be due to benign prostate tissue left behind, local spread of prostate cancer cells beyond the margin of the prostate, spread to lymph nodes not removed during surgery, and spread to distant bone or organs outside the pelvis. Ideally, the PSA should drop to zero after the prostate is removed, defined as a PSA of less than 0.05 ng/dl. PSA "failure" is defined as a PSA greater than 0.20 - 0.40 ng/dl after surgery. This indicates that the PSA elevation is not due to residual benign prostate glands, and the likelihood that the PSA will continue to rise if left untreated. Recurrence after RP may be seen as local or systemic. It is likely a local recurrence if it occurs 36 months after surgery. The recurrence may be systemic if: (1) the PSA does not drop to zero after surgery; (2) the recurrence is detected early after surgery; and (3) there is a rapid doubling time of the PSA.

TREATMENT OPTIONS FOR RECURRENCE AFTER RADICAL PROSTATECTOMY

A patient with recurrent prostate cancer after RP has several options:

Observation. Of late, there has been an increased willingness to consider observation (aka watchful waiting) rather than immediate resort to definitive therapy. Instead, the patient is closely monitored for changes to levels that would warrant more aggressive therapy.

In one example, the so-called Pound Paper reported on 1997 men who underwent radical prostatectomy as primary therapy for prostate cancer. The group eventually experienced a 15 % PSA recurrence rate (315 men). These men were then "observed" until radiographic evidence of metastatic disease became evident in 34% of them (103 men). Their average time to metastases was eight years. Androgen deprivation therapy (ADT) was begun when their metastases were detected. Their average time from ADT until death by prostate cancer was five years. In the analysis, time to progression, Gleason score, and PSA doubling time were predictive of the time to metastatic progression.

Salvage Radiation Therapy. The goal of salvage radiation therapy is to eliminate prostate cancer cells in the pelvis and prostate surgery bed. The first task is to locate the residual cancer cells. The principal tools are the CT scan, bone scan, and MRI, all three of which are unreliable when the PSA is less than 10 ng/ml. The Prostascint scan also has limitations because it is less reliable when the PSA is less than 5 ng/ml. And the PMSA scan is still considered experimental.

Salvage radiation therapy is more likely to be successful when given when (1) the PSA is low (e.g., less than 0.5 ng/ml); (2) the PSA doubling time is greater than six months; (3) The PSA recurrence occurred more than three years after the RP; (4) low risk at initial diagnosis (e.g., Gleason score of 6 and a PSA less than 10 ng/ml). Nevertheless, more than half of the men who undergo salvage radiation therapy eventually will have a PSA recurrence, probably due to unrecognized systemic spread of microscopic disease or the radiation-resistance of the residual prostate cancer cells.

PSA RECURRENCE AFTER RADIATION THERAPY

The issue here is how to interpret recurring PSA values after failed radiation therapy. The several definitions of PSA failure/recurrence after radiation therapy are: a PSA greater than 0.2 ng/ml; three consecutive rises in the PSA; and the so-called Phoenix Criteria - the rise in PSA by more than 2.0 ng/ml above the lowest level achieved after treatment. The sources of PSA after radiation therapy are normal prostate cells and prostate cancer cells. The latter may be in the prostate, in the local area around the prostate, in the lymph, or in a distant site.

There are two prognostic factors for a rising PSA after RT:

(1) **PSA doubling time** - PSA cut points at 3, 6, 8, 12 months can be predictive of dying of prostate cancer over ten years.

(2) **Time from treatment to PSA failure** - If the PSA is less than 1.5 ng/ml at two years after therapy, there is only an 8% risk of developing metastases over ten years without treatment. Survivability is better if the PSA rises after 18 months than if it rises sooner.

There is an interesting phenomenon after RT called "PSA bounce." It is a temporary elevation of the PSA by as much as 40%. It often falls again within 6-12 months. The "PSA bounce" has no long-term clinical significance for cancer recurrence or survival.

Salvage Treatment Options for Rising PSA after Radiation Therapy

These treatment options are designed to address local recurrence. A prostate biopsy is required to determine if viable prostate cancer cells are still present in the prostate gland, and there must be no evidence of distant disease as determined by imaging such as CT, bone scan and MRI.

Salvage Radical Prostatectomy. Salvage RP is an option when a biopsy shows prostate cancer cells; there is no evidence of distant metastasis; the PSA is less than 4.0 ng/ml; the PSA doubling time is greater than 6-8 months; and there is a life expectancy of more than ten years. The salvage RP is a technically challenging procedure with high risk for such complications as erectile dysfunction, incontinence, and bowel injury.

Salvage Cryotherapy. Salvage cryotherapy has similar preconditions as the salvage RP, except that the PSA must be less than 10 ng/ml, and PSA doubling time should be greater than 16 months. Long-term survival rates are unknown, and post-treatment biopsy reveal residual prostate cancer in up to 37% of patients. PSA failure rates for salvage cryotherapy at five years after treatment range from 27% for low risk cancer to 89% for high risk cancer. Either cryotherapy did not kill residual prostate cancer cells in the prostate or the prostate cancer had spread distantly before the salvage cryotherapy.

Androgen Deprivation Therapy (ADT). ADT is the standard first-line therapy when systemic involvement is known or suspected. It suppresses testicular production of testosterone, blockades the effect of testosterone on the prostate gland, suppresses adrenal androgens, blocks androgen production by the cancer itself, and results in programmed cell death.

The traditional methods of ADT are orchiectomy, the surgical removal of the testicles; LHRH therapy which acts on the pituitary gland/brain to decrease LH levels and testosterone synthesis; and Combined Androgen Deprivation which adds an anti-androgen to block androgens from binding to the androgen receptor. ADT has notable side effects, the most common being hot flashes, osteoporosis, anemia, impotence, weakness, and muscle loss.

There is no consensus about when to begin ADT. The issue is whether early initiation will provide a significant survival advantage. Should it be at the time of PSA failure, the time of radiographic evidence of disease, or in the case of rapid PSA doubling time? The use of ADT as a salvage option must weigh the potential benefits against the side effects and risks of treatment.

Another issue is whether once begun, should ADT be continuous or intermittent. Continuous ADT is the full-time suppression of testosterone with medications. Intermittent ADT suppress-

es testosterone for a given period, e.g., 6-9 months and then stopped. to be restarted once the PSA rises again to a specified level. This cycle is repeated until the PSA stops responding.

In one randomized trial, men who had a PSA greater the 3.0 ng/ml after radiation therapy were divided into two groups, one got continuous ADT, and the second group got intermittent ADT. The intermittent group was treated for eight months and stopped. ADT was resumed once PSA was greater than 10 ng/ml and continued for eight months. After seven years the overall survival rate was equal for both groups. However, the intermittent group reported fewer hot flashes, better libido, and fewer urinary symptoms.

OPTIONS AFTER ANDROGEN THERAPY

(Dr. Donovan displayed a series of slides showing and comparing the effectiveness of recent FDA approvals of multiple new treatments include: Docetaxel, Cabazitaxel, Abiraterone, Cabozantinib, Sipuleucel-T, and Alpharadin)

TAKE HOME MESSAGE

- **KNOW YOUR GLEASON SCORE**
- **KNOW YOUR PSA AND HOW TO ESTMATE THE DOUBLING TIME IF IT IS RISING**
- **STAY ENGAGED WITH YOUR ONCOLOGY TEAM**

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♦ WRNMMC US TOO COUNSELORS ♦ (As of August 1, 2015)

(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	1998 (Open RP)
Rob Calhoun	Annapolis, MD	(410) 293-6635	2011 (Robotic Surgery)
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	
Tony Giancola	Washington, DC	(202) 723-1859	2008 (Radical Prostatectomy)
Ray Glass	Rockville, MD	(301) 460-4208	
Monroe Hatch	Clifton, VA	(703) 323-1038	
Tom Hansen	Bellevue, WA	(425) 883-4808	1998 (Robotic Surgery)
Bill Johnston	Berryville, VA	(540) 955-4169	
Dennis Kern	San Francisco, CA	(415) 876-0524	
Sergio Nino	Dale City, VA	(703) 590-7452	
Ed Postell	Collegeville, PA	(610) 420-6765	(Robotic Surgery)
George Savitske	Hellertown, PA	(703) 304-3081	2000 (Open RP)
Artie Shelton, MD	Olney, MD	(301) 523-4312	
Jay Tisserand	Carlisle, PA	(717) 243-3950	

PROSTATE CANCER AND SEXUAL FUNCTION

James Padgett	Silver Spring, MD	(301) 622-0869	
George Savitske	Hellertown, PA	(703) 304-3081	

RADIATION

Leroy Beimel	Glen Burnie, MD	(410) 761-4476	1987 (External Beam Radiation)
Bob Bubel	Grand Junction, CO	(970) 263-4974	2010 (Proton Beam Radiation)
Harvey Kramer	Silver Spring, MD	(301) 585-8080	1998 ((Brachytherapy)
Joseph Rosenberg	Kensington, MD	(301) 495-9821	2009 (Brachytherapy)
Barry Walrath	McLean, VA	(571) 969-8269	2001 (Brachytherapy)

WATCHFUL WAITING

Tom Baxter	Haymarket, VA	(703) 753-8583	Active Surveillance

SPOUSE SUPPORT

Renate Bubel	Fairfax, VA	(703) 280-5765
Karen Collins	Mechanicsburg, PA	(717-766-6464
Betty Kramer	Silver Spring, MD	(301) 585-8080
Ellen Rosenberg	Kensington, MD	(301) 495-9821
Nancy Wallrath	McLean, VA	(703) 915-8108

OTHER THERAPIES/MULTIPLE THERAPIES

Howard Bubel	Fairfax, VA	(703) 280-5765	1995,1996 (Hormonal, Cryosurgery, Sexual Function
Arthur E. Clough	Kerryville, TX	(830) 896-8826	1993 (Surgery and Radiation)
Pete Collins	Mechanicsburg, PA	(717) 766-6464	2007, 2009 (Surgery, Radiation, Hormonal)

♦ MEETING ANNOUNCEMENT ♦

THURSDAY, AUGUST 6, 2015

7:00 - 8:30 PM

AMERICA BUILDING (2D FLOOR)
ROOM 2525
(DIRECTLY ABOVE THE LAB/PHARMACY)

WALTER REED NATIONAL MILITARY MEDICAL CENTER

♦ SPEAKER ♦

STEPHEN LEWIS, MD

RADIATION ONCOLOGIST, WRNMMC

TOPIC

"EMERGING THERAPIES IN RADIATION AND IMMUNOLOGY"

Gate/Parking: If you enter the base through South Gate (Gate 2) off Rockville Pike/Wisconsin Avenue, take the first right (Palmer Road South). On your left will be the Emergency Room. Continue to follow signs to the America Building and the America parking garage.

Security: A military ID card 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 the CPDR front desk at 301-319-2900 at least four business days prior to Thursday, May 7, 2015, to arrange entry. Have a photo ID card ready when arriving at the gate.